

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

HiperScan GmbH

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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.

Validity scope of this document

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 database is exclusively established from spectra which have been recorded by *HiperScan GmbH* for 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.
 - In three separately evaluated validation runs, calibration spectra, spectra from independent samples and spectra from independent field samples (described further below as *Type A*, *B* or *C*) are presented to the *IdentModule* for evaluation.
 - 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*).
- For each individual substance, the unambiguous identifiability with *Apo-Ident* and the demarkation against all other database substances is proven.

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) Checking the distances between the limits of the separable substances: the distance matrix incorporates the *Mahalanobis distances* from each substance to all the others. If a distance is less than 10, both two substances must be declared as inseparable or *both two* must be removed from the database. (The spectra of removed substances remain as independent *Type B* spectra in the validation.)
- e) Testing the model based on the reference spectra. If *false positive* results arise, you must proceed as in the case of *Mahalanobis distances* which are too small.
- f) If chemometric models are available for all substance classes which meet both criteria (distance matrix and no *false positives*), they are joined together with the evaluation algorithms as an *IdentModule* and encrypted. This unit can no longer be changed. Its overall function is tested by validation.

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 established. 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 from independent samples not included in the generation of the respective model received but were measured by *HiperScan GmbH*. These also include reference spectra from other substance classes and spectra which are not declared as reference spectra.
- c) *Type C*: Spectra from independent field samples. These measurements were recorded under normal everyday conditions by pharmacy staff. The spectra belong both to substances of the substance class to be examined and to substances from different classes.

All manufacturers' batches from which spectra flow into 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 spectrum error 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.

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 14000 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.

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, *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

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

[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). $\vec{\mathbf{X}}$ 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 $\mathbf{X}$.

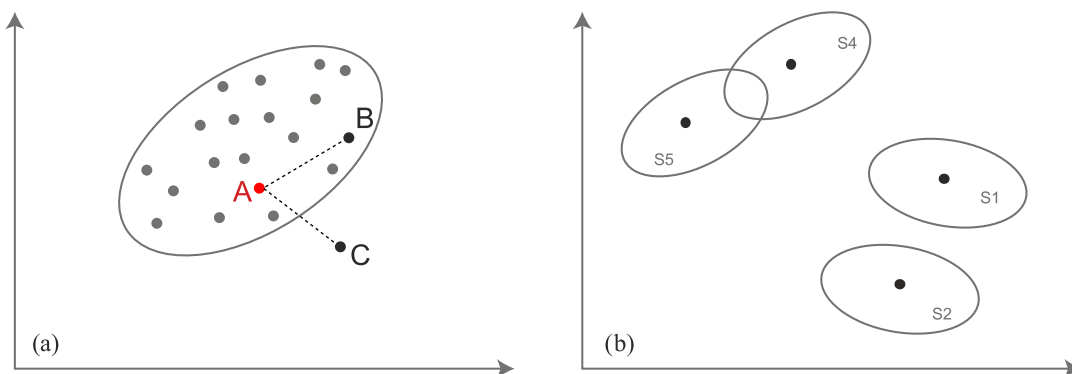


Figure 1: (a) The *Mahalanobis distance* from *A* to *B* is less than from *A* to *C*. However, the *Euclidean distances* are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the *Euclidean distances* are identical.

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].

As sample applies the substance from a package. Multiple extractions of substance from the same package for spectrum recordings will be ascribed to the same sample. This also applies if multiple of such samples originate from the same batch.

Does a supplier conversely take 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 35 362 spectra from 2048 different batches for a total of 177 substances were used to validate the substance class *APIs & excipients, liquid/semi-solid (other)*.

Validation samples

The validation samples can be categorised as follows:

Type 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)	144	377	16 259

From category *A* a total of 16 259 spectra from 377 batches for a total of 144 substances were taken into account for validation.

Type 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)	177	438	16 304

From category *B* a total of 16 304 spectra from 438 batches for a total of 177 substances were taken into account for validation.

Type 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)	117	1508	2799

From category *C* a total of 2799 spectra from 1508 batches for a total of 117 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	16 259	0	1 495 828
Type B	0	13 157	1116	1 501 159
Type C	0	2405	240	257 618

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
Type A	100.000 00 % (> 99.999 43 %)	100.000 00 % (> 99.946 60 %)
Type B	100.000 00 % (> 99.999 36 %)	90.844 18 % (> 90.811 56 %)
Type C	100.000 00 % (> 99.981 10 %)	83.203 25 % (> 82.395 77 %)

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

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

IdentModul 1.3-2017-05

Validated substance/substance group **Alfason Basis Cresa[®]**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30723-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Alfason Basis Cresa[®]

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	50	not required
Astellas Pharma	Alfason Basis Cr...	13D06/75	31071	40	not required
Astellas Pharma	Alfason Basis Cr...	15I46/79	32064	40	not required
Astellas Pharma	Alfason Basis Cr...	16D35/77	32815	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 170 spectra of 4 reference samples from the substance/substance group *Alfason Basis Cresa*[®]. These samples are listed above in the [calibration samples](#) section.
- 16 089 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 64 spectra of 3 reference samples from the substance/substance group *Alfason Basis Cresa*[®].

Supplier	Substance	Batch	Sample ID	Spectra
Astellas Pharma	Alfason Basis Cresa [®]	12B11/77	30723 [†]	4
Astellas Pharma	Alfason Basis Cresa [®]	15I46/79	32064 [†]	20
Astellas Pharma	Alfason Basis Cresa [®]	16D35/77	32840	40

- 16 240 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 27 spectra from 6 *Apo-Ident* customers from 14 batches from the substance/substance group *Alfason Basis Cresa*[®].

[†]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*.

Supplier	Substance	Batch	Spectra
Astellas	Alfason Basis Cresa [®]	13A16/76	1
Astellas Pharma	Alfason Basis Cresa [®]	13K15/75	2
Astellas Pharma	Alfason Basis Cresa [®]	14C32/78	1
Astellas	Alfason Basis Cresa [®]	14c32-78	1
Astellas Pharma	Alfason Basis Cresa [®]	14J02/77	2
Astellas	Alfason Basis Cresa [®]	14J02/77	1
Astellas / Noweda	Alfason Basis Cresa [®]	14J02/77	1
Astellas Pharma	Alfason Basis Cresa [®]	15D11/79	3
Astellas / Noweda	Alfason Basis Cresa [®]	15D11/79	2
Astellas / Noweda	Alfason Basis Cresa [®]	15D1179	1
Caeo/Noweda	Alfason Basis Cresa [®]	15H06/80	1
Astellas Pharma	Alfason Basis Cresa [®]	15H06/80	1
Astellas / Noweda	Alfason Basis Cresa [®]	15J35/76	1
Astellas Pharma	Alfason Basis Cresa [®]	16A06/76	1
Lamotte/ Noweda	Alfason Basis Cresa [®]	16A06/76	2
A.H.D.	Alfason Basis Cresa [®]	12/05/75	1
Sanacorp	Alfason Basis Cresa [®]	12F23/76	1
Sanacorp	Alfason Basis Cresa [®]	13A16/76	1
AHD	Alfason Basis Cresa [®]	13A18/76	1
Ichtyol/Phönix	Alfason Basis Cresa [®]	13E08/75	1
Sanacorp	Alfason Basis Cresa [®]	13E08/75	1

- 2772 spectra from 264 *Apo-Ident* customers from a total of 1460 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	170	0	16 089
Type B	0	64	0	16 240
Type C	0	27	0	2772

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9464 %)	100.0000 % (> 96.4706 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.6250 %)
Type C	100.0000 % (> 98.2290 %)	100.0000 % (> 77.7778 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30723	30723	0.00	25.33
31071	31071	0.00	23.87
32064	32064	0.00	29.16
32815	32815	0.00	27.83

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Allergika evening primrose oil cream 20% / Dermi...**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30970-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

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

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	Dermifant [®] kids ...	1210082	30970	80	not required
Allergika	Dermifant [®] kids ...	1303033	31062	40	not required
Allergika	Allergika evenin...	1504021	31725	40	not required
Allergika	Allergika evenin...	1511051	31871	40	not required

Validation samples

A total of 35 362 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 *Allergika evening primrose oil cream 20% / Dermifant® kids cream*. These samples are listed above in the [calibration samples](#) section.
- 16 059 spectra from a total of 371 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 160 spectra of 5 reference samples from the substance/substance group *Allergika evening primrose oil cream 20% / Dermifant® kids cream*.

Supplier	Substance	Batch	Sample ID	Spectra
Allergika	Allergika evening primrose o...	1504021	31725 [†]	20
Allergika	Allergika evening primrose o...	1511051	31871 [†]	20
Allergika	Dermifant® kids cream	1607032	32754	40
Allergika	Allergika evening primrose o...	1607031	32756	40
Allergika	Allergika evening primrose o...	1410062	32909	40

- 16 144 spectra from a total of 421 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

Supplier	Substance	Batch	Spectra
Gehe	Dermifant [®] kids cream	1312102	2
Allergika Pharma GmbH	Dermifant [®] kids cream	1410072	1
Gehe	Dermifant [®] kids cream	1407053	1

- 2795 spectra from 265 *Apo-Ident* customers from a total of 1471 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	200	0	16 059
Type B	0	160	0	16 144
Type C	0	4	0	2795

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9464 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9400 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 98.2469 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	23.95
31062	31062	0.00	28.77
31725	31725	0.00	26.57
31871	31871	0.00	23.16

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **alpha-bisabolol (racemic) at least 85%**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31464-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Caelo	alpha-bisabolol ...	13360114	31465	40	not required

Validation samples

A total of 35 362 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 *alpha-bisabolol (racemic)* at least 85%. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 374 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 120 spectra of 4 reference samples from the substance/substance group *alpha-bisabolol (racemic)* at least 85%.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	alpha-bisabolol (racemic) at...	13360114	31464 [†]	20
Caelo	alpha-bisabolol (racemic) at...	13360114	31465 [†]	20
Caelo	alpha-bisabolol (racemic) at...	16271902	32782	40
Caelo	alpha-bisabolol (racemic) at...	17065801	33417	40

- 16 184 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *alpha-bisabolol (racemic)* at least 85%.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

[†]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*.

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

Validation results

The validation runs checked whether the substance/substance group *alpha-bisabolol (racemic)* at least 85% can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *alpha-bisabolol (racemic)* at least 85% and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	119	1	16 184
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	99.1667 % (> 96.6667 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31464	31464	0.00	46.62
31465	31465	0.00	54.85

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Angelica root oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30535-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Angelica root oil; Angelica archangelica oleum; Oleum angelicae (e radice)

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Angelica root oil	2829199-122587	31780	40	not required
Taoasis	Angelica root oil	3029209-123992	32068	40	not required

Validation samples

A total of 35 362 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 *Angelica root oil*. These samples are listed above in the [calibration samples](#) section.
- 16 099 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 140 spectra of 5 reference samples from the substance/substance group *Angelica root oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Angelica root oil	pending	30535	40
Taoasis	Angelica root oil	4053-116078	31682 [†]	20
Taoasis	Angelica root oil	2829199-122587	31780 [†]	20
Taoasis	Angelica root oil	3029209-123992	32068 [†]	20
Taoasis	Angelica root oil	3029209-125059	32477	40

- 16 164 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Angelica root oil	4053-117762	1
Caelo	Angelica root oil	11352706	1
Caelo	Angelica root oil	11352704	1
Taoasis	Angelica root oil	33019-110236BAG904	1

- 2795 spectra from 265 *Apo-Ident* customers from a total of 1470 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	160	0	16 099
Type B	0	100	40	16 164
Type C	0	2	2	2795

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9401 %)	71.4286 % (> 69.2857 %)
Type C	100.0000 % (> 98.2469 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30964	30964	0.00	36.82

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31682	31682	0.00	41.25
31780	31780	0.00	38.06
32068	32068	0.00	40.25

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Anise oil, organic**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30670-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Anise oil, organic

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	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 35 362 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 *Anise oil, organic*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Anise oil, organic*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Anise oil, organic	B080009-99431BAG90451	30670	40
Taoasis	Anise oil, organic	2241027-120475	31681 [†]	20

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 23 spectra from 12 *Apo-Ident* customers from 17 batches from the substance/substance group *Anise oil, organic*.

Supplier	Substance	Batch	Spectra
Taoasis/Noweda	Anise oil, organic	1465-121083h08	1

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

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Supplier	Substance	Batch	Spectra
Taoasis	Anise oil, organic	1492-121627	1
Taoasis	Anise oil, organic	2241027-120196	1
Taoasis	Anise oil, organic	26569-115911	2
Caelo	Anise oil, organic	12322503	2
Schubert	Anise oil, organic	1236E0-1518	1
Taoasis	Anise oil, organic	130910-113040	1
Taoasis	Anise oil, organic	1492-123225	1
Taoasis	Anise oil, organic	1492-125315	1
Taoasis	Anise oil, organic	1492-125379	2
Taoasis	Anise oil, organic	26735-108555	1
Caelo	Anise oil, organic	15148901	1
Taoasis	Anise oil, organic	26735-110455	1
Taoasis	Anise oil, organic	26735-111137	2
Taoasis/Sanacorp	Anise oil, organic	26735-111137	2
Taoasis/Sanacorp	Anise oil, organic	26735-112250	1
Taoasis	Anise oil, organic	26735-113054	1
Apotheker S Bauer&Comp	Anise oil, organic		1

- 2776 spectra from 263 *Apo-Ident* customers from a total of 1457 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	120	0	16 139
Type B	0	60	0	16 244
Type C	0	20	3	2776

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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.2295 %)	86.9565 % (> 73.9130 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	38.38
32794	32794	0.00	40.84
32935	32935	0.00	44.01

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Aqueous ointments**
 Substance class APIs & excipients, liquid/semi-solid (other)
 Report date 08/09/2017
 Report number 30726-2017-09-08
 Executing company HiperScan GmbH
 Weißeritzstraße 3
 01067 Dresden
 Germany

Relevant substance names

Aqueous ointments; Dermatest base ointment; Excipial[®] lipo cream; Fabitop[®] base cream

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
 Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
 AA004 *Erstellung und Validierung eines IdentModul-Updates*
 Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Spirig Pharma	Excipial [®] lipo c...	I011	30726	40	not required
Fontapharm	Fabitop [®] base cr...	6RWW2	31082	40	not required
Spirig Pharma	Excipial [®] lipo c...	N017	31088	40	not required
Spirig Pharma	Excipial [®] lipo c...	R011	31520	40	not required
Fontapharm	Fabitop [®] base cr...	GWWL3	31576	40	not required

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
P&M Cosmetics	Dermatest base o...	251115	31627	40	not required
P&M Cosmetics	Dermatest base o...	180317	31950	40	not required
P&M Cosmetics	Dermatest base o...	121217	33039	40	not required
Spirig Pharma	Excipial [®] lipo c...	T081	33207	40	not required
Fontapharm	Fabitol [®] base cr...	GLWD5	33221	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 10 reference samples from the substance/substance group *Aqueous ointments*. These samples are listed above in the [calibration samples](#) section.
- 15 859 spectra from a total of 365 batches from further 141 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 300 spectra of 10 reference samples from the substance/substance group *Aqueous ointments*.

Supplier	Substance	Batch	Sample ID	Spectra
Fontapharm	Fabitol [®] base cream	GRWW1	30555	40
P&M Cosmetics	Dermatest base ointment	120911	30737	40
Fontapharm	Fabitol [®] base cream	GRWW1	30835	40
P&M Cosmetics	Dermatest base ointment	70615	31053	20
Spirig Pharma	Excipial [®] lipo cream	N017	31276	40
P&M Cosmetics	Dermatest base ointment	231115	31288	40
Spirig Pharma	Excipial [®] lipo cream	R011	31520 [†]	20
Fontapharm	Fabitol [®] base cream	GWWL3	31576 [†]	20
P&M Cosmetics	Dermatest base ointment	251115	31627 [†]	20
P&M Cosmetics	Dermatest base ointment	180317	31950 [†]	20

- 16 004 spectra from a total of 417 batches from further 174 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

[†]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*.

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

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

- 173 spectra from 27 *Apo-Ident* customers from 49 batches from the substance/substance group *Aqueous ointments*.

Supplier	Substance	Batch	Spectra
Sanacorp	Dermatest base ointment	70615	1
P&M Cosmetics/Anzag	Dermatest base ointment	122631	1
P&M	Dermatest base ointment	241115	1
Caelo	Excipial [®] lipo cream	9031	1
Caelo	Excipial [®] lipo cream	L0TS023	1
Spirig	Excipial [®] lipo cream	N061	2
Spirig/Anzag	Excipial [®] lipo cream	R011	1
Galderma	Excipial [®] lipo cream	R012	3
Galderma	Excipial [®] lipo cream	R026	2
Galderma/Phönix	Excipial [®] lipo cream	R026	2
Galderma	Excipial [®] lipo cream	R035	2
Galderma	Excipial [®] lipo cream	R042	1
Galderma/Galderma	Excipial [®] lipo cream	R042	9
Spirig/Phönix	Excipial [®] lipo cream	R042	1
Galderma/Gehe	Excipial [®] lipo cream	R042	2
spirig	Excipial [®] lipo cream	r042	1
Galderma	Excipial [®] lipo cream	R012	1
Galderma/Phönix	Excipial [®] lipo cream	R012	1
Galderma/Galderma	Excipial [®] lipo cream	R026	1
Galderma/Galderma	Excipial [®] lipo cream	ro26	1
Galderma/Phönix	Excipial [®] lipo cream	R042	1
Galderma/Anzag	Excipial [®] lipo cream	S011	1
Galderma/Galderma	Excipial [®] lipo cream	S023	8
Spirig/Anzag	Excipial [®] lipo cream	S023	1
Galderma/Noweda	Excipial [®] lipo cream	s023	6
Galderma/Phönix	Excipial [®] lipo cream	S023	1
Wolff	Excipial [®] lipo cream	S031	1
Galderma/Noweda	Excipial [®] lipo cream	S031	9
Spirig/Anzag	Excipial [®] lipo cream	S031	1
Galderma/Phönix	Excipial [®] lipo cream	S031	1
Phönix/Galderma	Excipial [®] lipo cream	S023	1
Galderma/Galderma	Excipial [®] lipo cream	T021	8
Galderma/Phönix	Excipial [®] lipo cream	T021	1
Galderma	Excipial [®] lipo cream	T021	1
Galderma/Noweda	Excipial [®] lipo cream	T021	5
Galderma/Noweda	Excipial [®] lipo cream	T021	1
Galderma/Noweda	Excipial [®] lipo cream	t022	5
Galderma/Noweda	Excipial [®] lipo cream	T022	4
Spirig (Galderma)	Excipial [®] lipo cream	T061	1
spirig	Excipial [®] lipo cream		1
Spirig/Gehe	Excipial [®] lipo cream	L0TN021	2
Spirig/Anzag	Excipial [®] lipo cream	L0TN021	2
Anzag/Chiesi	Excipial [®] lipo cream	L0TR012	2
Spirig/Gehe	Excipial [®] lipo cream	L0TR012	1
spirig	Excipial [®] lipo cream	N018	4
Spirig Pharma AG/Allian...	Excipial [®] lipo cream	N018	1
spirig	Excipial [®] lipo cream	N021	5

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Supplier	Substance	Batch	Spectra
Spirig	Excipial [®] lipo cream	N021	1
Gehe	Excipial [®] lipo cream	N061	1
Galderma	Excipial [®] lipo cream	N061	2
Spirig / Anzag	Excipial [®] lipo cream	N018	1
Spirig / Gehe	Excipial [®] lipo cream	R012	1
spirig	Excipial [®] lipo cream	R012	3
Spirig	Excipial [®] lipo cream	R012	1
Spirig/Gehe	Excipial [®] lipo cream	R012	1
Spirig Pharma Europe GmbH	Excipial [®] lipo cream	R026	1
Spirig/Phönix	Excipial [®] lipo cream	4622	1
Spirig / Anzag	Excipial [®] lipo cream	813994/09	1
Spirig Pharma	Excipial [®] lipo cream	813994/09	2
spirig	Excipial [®] lipo cream	813994/09	1
Spirig	Excipial [®] lipo cream	K021	1
Sanacorp	Excipial [®] lipo cream	LOTN016	1
Alliance Healthcare	Excipial [®] lipo cream		1
spirig	Excipial [®] lipo cream	M016	4
spirig	Excipial [®] lipo cream	M017	1
Spirig/AHD	Excipial [®] lipo cream	M017	1
Spirig / Anzag	Excipial [®] lipo cream	M017	1
spirig	Excipial [®] lipo cream	M041	5
Spirig/AHD	Excipial [®] lipo cream	M041	2
Spirig/Phoenix	Excipial [®] lipo cream	M042	2
Spirig / Anzag	Excipial [®] lipo cream	M042	3
spirig	Excipial [®] lipo cream	M042	2
Spirig Pharma AG	Excipial [®] lipo cream	M042	1
Alliance Healthcare	Excipial [®] lipo cream	M045	1
Sanacorp	Excipial [®] lipo cream	M027	1
Spirig / Anzag	Excipial [®] lipo cream	N018	3
Spirig/AHD	Excipial [®] lipo cream	N018	2
Spirig Pharma AG/GEHE	Excipial [®] lipo cream	R012	1
Fontapharm	Fabitop [®] base cream	GLWD2	1
Fontapharm/Gehe	Fabitop [®] base cream	GLWD4	1
Gehe	Fabitop [®] base cream	GRWW2	6
Fontapharm	Fabitop [®] base cream	GLWW4	1
Artesan	Fabitop [®] base cream	GLWW5	1
jenne artesan	Fabitop [®] base cream	GLWWW5	1
Phönix/Fontapharm	Fabitop [®] base cream	GRWW2	1
Jenne	Fabitop [®] base cream	GWWL1	1

- 2626 spectra from 264 *Apo-Ident* customers from a total of 1433 batches from a further 114 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Aqueous 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 *Aqueous ointments* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	15 859
Type B	0	243	57	15 914
Type C	0	145	28	2616

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9462 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9403 %)	81.0000 % (> 80.0000 %)
Type C	100.0000 % (> 98.2347 %)	83.8150 % (> 82.0809 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30726	30726	0.00	47.85
31082	31082	0.00	25.13
31088	31088	0.00	39.48
31520	31520	0.00	39.09
31576	31576	0.00	20.79
31627	31627	0.00	16.20
31950	31950	0.00	17.60
33039	33039	0.00	17.79
33207	33207	0.00	37.04
33221	33221	0.00	30.41

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Argan oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 32168-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	-*
Caelo	Argan oil	16035101	32571	40	not required

Validation samples

A total of 35 362 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 *Argan oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Argan oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Argan oil	161443	32168 [†]	20
Caelo	Argan oil	16035101	32306	40
Caelo	Argan oil	162759	32679	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Argan oil*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

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

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	100	0	16 204
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	24.08
32571	32571	0.00	20.66

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Balm Bio Nature**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31645-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Balm Bio Nature	150422-5106	31724	40	not required
Taoasis	Balm Bio Nature	151210-5337	32994	40	not required

Validation samples

A total of 35 362 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 *Balm Bio Nature*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 132 spectra of 5 reference samples from the substance/substance group *Balm Bio Nature*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Balm Bio Nature	150422-5106	31645 [†]	20
Taoasis	Balm Bio Nature	150422-5106	31724 [†]	20
Taoasis	Balm Bio Nature	160401-6083	32786	40
Taoasis	Balm Bio Nature	170403-7087	33436	40
Taoasis	Balm Bio Nature	151210-5337	not required	12

- 16 172 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Balm Bio Nature*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	127	5	16 172
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9401 %)	96.2121 % (> 93.9394 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31645	31645	0.00	18.74
31724	31724	0.00	23.10
32994	32994	0.00	10.42

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Basil oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30751-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Basil oil; Ocimum basilicum oleum; 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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	21022-108746BAG90451	30751	40	not required
Taoasis	Basil oil	121018-109872BAG90451	30963	40	not required
Taoasis	Basil oil	561-119057	31755	40	not required

Validation samples

A total of 35 362 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 *Basil oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Basil oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Basil oil	561-119057	31755 [†]	20
Taoasis	Basil oil	1500312-126393	32972	40
Taoasis	Basil oil	1500312-126393	32973	40

- 16 204 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	20	80	16 204
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9402 %)	20.0000 % (> 17.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30751	30751	0.00	91.68
30963	30963	0.00	23.72
31755	31755	0.00	95.54

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Benzoin siam oil 20%**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30456-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Benzoin siam oil...	63287-126233	32974	40	not required

Validation samples

A total of 35 362 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 *Benzoin siam oil 20%*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Benzoin siam oil 20%*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Benzoin siam oil 20%	474034-96350	30456	40
Taoasis	Benzoin siam oil 20%	51939-123084	31843 [†]	20
Taoasis	Benzoin siam oil 20%	63287-126233	33028	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 15 spectra from 6 *Apo-Ident* customers from 14 batches from the substance/substance group *Benzoin siam oil 20%*.

Supplier	Substance	Batch	Spectra
Taoasis	Benzoin siam oil 20%	17578-116819	1
Taoasis	Benzoin siam oil 20%	23478-116955	2

continued on the next page

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

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Supplier	Substance	Batch	Spectra
Taoasis	Benzoin siam oil 20%	41242-121512	1
Taoasis	Benzoin siam oil 20%	59023-125420	1
Taoasis	Benzoin siam oil 20%	62330-124547	1
Taoasis	Benzoin siam oil 20%	63287-126233	1
Taoasis	Benzoin siam oil 20%	31343-118365	1
Taoasis	Benzoin siam oil 20%	51939-123084	1
Taoasis	Benzoin siam oil 20%	541389-111081	1
Taoasis	Benzoin siam oil 20%	41242-120661	1
Taoasis	Benzoin siam oil 20%	548481-111780	1
Taoasis	Benzoin siam oil 20%	548442-113119	1
Taoasis	Benzoin siam oil 20%	474084-96350	1
Taoasis	Benzoin siam oil 20%	518434-108321	1

- 2784 spectra from 265 *Apo-Ident* customers from a total of 1460 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	120	0	16 139
Type B	0	100	0	16 204
Type C	0	14	1	2784

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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2314 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	287.10
31843	31843	0.00	281.46
32974	32974	0.00	298.91

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Bepanthen® Wund- und Heilsalbe**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31048-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bepanthen® Wund- und Heilsalbe

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Bayer	Bepanthen® Wund-...	GP00LB9	31048	40	not required
Bayer	Bepanthen® Wund-...	GP012SS	31758	40	not required

Validation samples

A total of 35 362 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 *Bepanthen® Wund- und Heilsalbe*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Bepanthen® Wund- und Heilsalbe*.

Supplier	Substance	Batch	Sample ID	Spectra
Bayer	Bepanthen® Wund- und Heilsalbe	GP012SS	31758 [†]	20
Bayer	Bepanthen® Wund- und Heilsalbe	GP018T5	32720	40
Bayer	Bepanthen® Wund- und Heilsalbe	GP019ZF	32948	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Bepanthen® Wund- und Heilsalbe*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	100	0	16 204
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31048	31048	0.00	38.43
31758	31758	0.00	38.99

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Bergamot oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30307-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bergamot oil; Oleum bergamottae; Oleum citrus bergamia

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Bombastus	Bergamot oil	290998	31760	40	not required
Taoasis	Bergamot oil	3221028-121642	31784	40	not required

Validation samples

A total of 35 362 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 *Bergamot oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 4 reference samples from the substance/substance group *Bergamot oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Bombastus	Bergamot oil	237459	30307	40
Bombastus	Bergamot oil	290998	31641 [†]	20
Bombastus	Bergamot oil	290998	31760 [†]	20
Taoasis	Bergamot oil	3221028-121642	31784 [†]	20

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 12 *Apo-Ident* customers from 14 batches from the substance/substance group *Bergamot oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Bombastus	Bergamot oil	53731-125890	1
Taoasis	Bergamot oil	d01be14m-121110bag90	1
Caelo	Bergamot oil	12020702	1
Kaders	Bergamot oil	130564	1
Caelo	Bergamot oil	13141501	2
Taoasis	Bergamot oil	32579-111866	1
Noweda	Bergamot oil	271858	1
Taoasis	Bergamot oil	32338-109135	1
Taoasis	Bergamot oil	33110-110701	1
Taoasis	Bergamot oil	33697-112408	1
Taoasis	Bergamot oil	B130301-110610	1
Taoasis	Bergamot oil	96243	1
Bombastus	Bergamot oil	280260	1
Bombastus	Bergamot oil	264008	1

- 2784 spectra from 264 *Apo-Ident* customers from a total of 1460 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	74	26	16 204
Type C	0	12	3	2784

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9402 %)	74.0000 % (> 71.0000 %)
Type C	100.0000 % (> 98.2314 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31641	31641	0.00	62.46
31760	31760	0.00	60.69
31784	31784	0.00	63.19

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Cajeput / Niaouli oil
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	31136-2017-09-08
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cajeput / Niaouli oil; Cajeput; Niaouli oil; Oleum Cajeputi artificiale; Oleum melaleuka viridiflora; Oleum niaouli

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Cajeput	130829-112094BAG90451	31136	40	not required
Caelo	Niaouli oil	13099606	31420	40	AR-14-FG-012561-01

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Niaouli oil	34167-116962	31548	40	not required
Taoasis	Cajeput	1662-124326	32173	40	not required
Taoasis	Niaouli oil	40428-124242	32174	40	not required
Taoasis	Niaouli oil	1500450-125771	32970	40	not required

Validation samples

A total of 35 362 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 *Cajeput / Niaouli oil*. These samples are listed above in the [calibration samples](#) section.
- 16 019 spectra from a total of 369 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 200 spectra of 6 reference samples from the substance/substance group *Cajeput / Niaouli oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Cajeput	T149I11	30382	40
Caelo	Niaouli oil	13099606	31420 [†]	20
Taoasis	Niaouli oil	34167-116962	31548 [†]	20
Taoasis	Niaouli oil	1500450-125771	32971	40
Taoasis	Cajeput	1724-127033	33022	40
Taoasis	Cajeput	1724-127033	33023	40

- 16 104 spectra from a total of 421 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

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

- 25 spectra from 5 *Apo-Ident* customers from 20 batches from the substance/substance group *Cajeput / Niaouli oil*.

Supplier	Substance	Batch	Spectra
PVL	Cajeput	150712	1
Aurica	Cajeput	11024710	1
Taoasis	Cajeput	1301-121889	1
Taoasis	Cajeput	1301-32758	1
Taoasis	Cajeput	130829-113045	2
Taoasis	Cajeput	131010-115487	2
Taoasis	Cajeput	131010-117241	2
Taoasis	Cajeput	131010-117257	1
Taoasis	Cajeput	1518-122691	1
Taoasis	Cajeput	1518-122790	1
Taoasis	Cajeput	1724-125910	1
Taoasis	Cajeput	24077-106468	1
Taoasis	Cajeput	661027-117257	2
Taoasis	Cajeput	661027-118368	1
Taoasis	Cajeput	L201323018-113057	1
Taoasis	Cajeput	6781012-119058	1
Taoasis/Sanacorp	Cajeput	L201323018-113057	1
Taoasis	Niaouli oil	22553-120413	1
Taoasis	Niaouli oil	22553-121510	1
Taoasis	Niaouli oil	22553-120482	1
Taoasis	Niaouli oil	40428-123092	1

- 2774 spectra from 265 *Apo-Ident* customers from a total of 1454 batches from a further 115 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 / Niaouli 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 / Niaouli oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	16 019
Type B	0	192	8	16 104
Type C	0	17	8	2774

The substance/substance group *Cajeput / Niaouli 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 % (> 99.9463 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9400 %)	96.0000 % (> 94.5000 %)
Type C	100.0000 % (> 98.2292 %)	68.0000 % (> 56.0000 %)

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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31136	31136	0.00	44.85
31420	31420	0.00	27.43
31548	31548	0.00	40.71
32173	32173	0.00	63.21
32174	32174	0.00	29.48
32970	32970	0.00	31.17

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Carrot seed oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31555-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Carrot seed oil	26058_119083BAG90451	31636	40	not required
Taoasis	Carrot seed oil	1775-125361BAG90451	32812	40	not required

Validation samples

A total of 35 362 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 *Carrot seed oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Carrot seed oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Carrot seed oil	937-117443	31555 [†]	20
Taoasis	Carrot seed oil	26058119083BAG90451	31636 [†]	20
Taoasis	Carrot seed oil	1775-125361BAG90451	33203	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	80	0	16 224
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31555	31555	0.00	29.86
31636	31636	0.00	29.85
32812	32812	0.00	86.96

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Cedar wood oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30654-2017-09-08
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:

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Cedar wood oil	7891018-121034	31777	40	not required
Apotheker Bau...	Cedar wood oil	2.880926.1507	31851	40	not required
Taoasis	Cedar wood oil	1627-125061	33199	40	not required

Validation samples

A total of 35 362 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 *Cedar wood oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 160 spectra of 5 reference samples from the substance/substance group *Cedar wood oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Cedar wood oil	pending	30654	40
Taoasis	Cedar wood oil	26473-83914BAG90451	30750	40
Taoasis	Cedar wood oil	7891018-121034	31777 [†]	20
Apotheker Bauer & Cie	Cedar wood oil	2.880926.1507	31851 [†]	20
Taoasis	Cedar wood oil	1627-124623	32268	40

- 16 144 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 4 *Apo-Ident* customers from 12 batches from the substance/substance group *Cedar wood oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis/Phönix	Cedar wood oil	3292687	1
Taoasis	Cedar wood oil	831018-122540	1
Taoasis	Cedar wood oil	831018-123089	2
Taoasis	Cedar wood oil	1627-125061	1
Taoasis GmbH	Cedar wood oil	32812	1
Biofrid / Noweda	Cedar wood oil	17066	1
Taoasis	Cedar wood oil	32812-113008	3
Taoasis	Cedar wood oil	7891018-120108	1
Taoasis	Cedar wood oil	381008-116967	1
Taoasis	Cedar wood oil	831018-124172	1
Taoasis	Cedar wood oil	7891019-121034	1
Taoasis	Cedar wood oil	7711023-120348	1

- 2784 spectra from 265 *Apo-Ident* customers from a total of 1462 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	120	0	16 139
Type B	0	120	40	16 144
Type C	0	15	0	2784

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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9400 %)	75.0000 % (> 73.1250 %)
Type C	100.0000 % (> 98.2314 %)	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.

Identity according to identity test using NIR spectroscopy

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

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	77.52
31851	31851	0.00	20.79
33199	33199	0.00	79.98

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Cinnamon bark oil, Ceylon**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30957-2017-09-08
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:

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Cinnamon bark oi...	121108-109782BAG90451	30957	40	not required
Taoasis	Cinnamon bark oi...	1311130547-119819	31648	40	not required

Validation samples

A total of 35 362 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 *Cinnamon bark oil, Ceylon*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Cinnamon bark oil, Ceylon*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Cinnamon bark oil, Ceylon	1311130547-119819	31648 [†]	20
Taoasis	Cinnamon bark oil, Ceylon	415-126411	32791	40
Taoasis	Cinnamon bark oil, Ceylon	415-126411	33202	40

- 16 204 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Cinnamon bark oil, Ceylon*.

[†]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*.

- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	100	0	16 204
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	297.66
31648	31648	0.00	309.50

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR

bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Citric oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31558-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Citric oil; Limonis aetheroleum; Oleum citri

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Citric oil	D04LI14M-117513	31558	40	not required
Taoasis	Citric oil	3681027-122724	31838	40	not required

Validation samples

A total of 35 362 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 *Citric oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 120 spectra of 4 reference samples from the substance/substance group *Citric oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Citric oil	D04LI14M-117513	31558 [†]	20
Taoasis	Citric oil	3681027-122724	31838 [†]	20
Taoasis	Citric oil	3LI16M-125453I09	32771	40
Taoasis	Citric oil	3LI16M-125453I09	32941	40

- 16 184 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 8 batches from the substance/substance group *Citric oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Sanacorp	Citric oil	15182703	1
Caelo	Citric oil	16028702	1
Fagron	Citric oil	13K14-B03-294704	1
Fagron	Citric oil	14H06-B02-299949	1
Caelo	Citric oil	15182703	1
Bombastus	Citric oil	15F29-B04-325354	1
Bombastus	Citric oil	301912	1
Taoasis	Citric oil	3681003-124333	1
Caelo	Citric oil	14365212	2

- 2789 spectra from 263 *Apo-Ident* customers from a total of 1466 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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* can clearly be 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* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	16 179
Type B	0	120	0	16 184
Type C	0	10	0	2789

The substance/substance group *Citric 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 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.2342 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31558	31558	0.00	31.77
31838	31838	0.00	37.24

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Citronella oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31550-2017-09-08
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:

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Citronella oil	140121-115623	31550	40	not required
Taoasis	Citronella oil	1291021-122850	31840	40	not required

Validation samples

A total of 35 362 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 *Citronella oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 120 spectra of 4 reference samples from the substance/substance group *Citronella oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Citronella oil	140121-115623	31550 [†]	20
Taoasis	Citronella oil	1291021-122850	31840 [†]	20
Taoasis	Citronella oil	108494-126305	32798	40
Taoasis	Citronella oil	108494-126776	33047	40

- 16 184 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Citronella oil	5211028-120284	1

- 2798 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	120	0	16 184
Type C	0	1	0	2798

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.3099 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	38.46
31840	31840	0.00	40.01

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Clary sage oil / Petitgrain oil
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	31669-2017-09-08
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Clary sage oil / Petitgrain oil; Clary sage oil; Oleum citrus aurantium; Oleum salviae sclarea; Petitgrain oil

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Clary sage oil	2098-115222	31669	40	not required
Taoasis	Petitgrain oil	26056-120864	31778	40	not required

continued on the next page

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Apotheker Bau. . .	Petitgrain oil	6.56267.16.02	31852	40	not required
Taoasis	Petitgrain oil	4031015-126048	33024	40	not required
Taoasis	Clary sage oil	1834-127059	33033	40	not required

Validation samples

A total of 35 362 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 *Clary sage oil* / *Petit-grain oil*. These samples are listed above in the [calibration samples](#) section.
- 16 059 spectra from a total of 370 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 260 spectra of 8 reference samples from the substance/substance group *Clary sage oil* / *Petit-grain oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Petitgrain oil	pending	30653	40
Taoasis	Clary sage oil	487962-107805BAG90451	30749	40
Taoasis	Petitgrain oil	29551-105402BAG90451	30752	40
Taoasis	Clary sage oil	2098-115222	31669 [†]	20
Taoasis	Petitgrain oil	26056-120864	31778 [†]	20
Apotheker Bauer & Cie	Petitgrain oil	6.56267.16.02	31852 [†]	20
Taoasis	Clary sage oil	2098-115222	32797	40
Taoasis	Petitgrain oil	4031015-126048	33025	40

- 16 044 spectra from a total of 420 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

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

- 3 spectra from 2 *Apo-Ident* customers from 3 batches from the substance/substance group *Clary sage oil / Petitgrain oil*.

Supplier	Substance	Batch	Spectra
Taoasis	Clary sage oil	2098-115222	1
Taoasis	Clary sage oil	2098-119159	1
Taoasis	Clary sage oil	487962-106655	1

- 2796 spectra from 265 *Apo-Ident* customers from a total of 1471 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Clary sage oil / Petitgrain 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 *Clary sage oil / Petitgrain oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	16 059
Type B	0	260	0	16 044
Type C	0	2	1	2796

The substance/substance group *Clary sage oil / Petitgrain 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 % (> 99.9464 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9399 %)	100.0000 % (> 97.6923 %)
Type C	100.0000 % (> 98.2539 %)	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.

Identity according to identity test using NIR spectroscopy

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

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31669	31669	0.00	28.85
31778	31778	0.00	17.10
31852	31852	0.00	57.66
33024	33024	0.00	18.53
33033	33033	0.00	32.13

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Clove oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31270-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Clove oil; Caryophylli floris aetheroleum; Oleum caryophylli

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	38	not required
Taoasis	Clove oil	2891012-116936	31557	40	not required
Taoasis	Clove oil	1426-120481	31683	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 158 spectra of 4 reference samples from the substance/substance group *Clove oil*. These samples are listed above in the [calibration samples](#) section.
- 16 101 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 122 spectra of 5 reference samples from the substance/substance group *Clove oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Clove oil	12380605	31270 [†]	2
Taoasis	Clove oil	2891012-116936	31557 [†]	20
Taoasis	Clove oil	1426-120481	31683 [†]	20
Taoasis	Clove oil	1598-124689	32938	40
Taoasis	Clove oil	1598-124689	32940	40

- 16 182 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

Supplier	Substance	Batch	Spectra
Caelo	Clove oil	15119304	1
Caelo	Clove oil	15316103	1

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	158	0	16 101
Type B	0	122	0	16 182
Type C	0	2	0	2797

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9465 %)	100.0000 % (> 96.2025 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.0820 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31035	31035	0.00	630.79
31270	31270	0.00	634.38
31557	31557	0.00	607.36
31683	31683	0.00	620.24

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Common wormwood oil
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	30842-2017-09-08
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

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Apotheker Bau...	Common wormwood ...	10815310556	33013	40	not required

Validation samples

A total of 35 362 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 *Common wormwood oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Common wormwood oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Common wormwood oil	7.9363	30842	40
ASAV Apotheken-Service	Common wormwood oil	10116310555	31637 [†]	20
ASAV Apotheken-Service	Common wormwood oil	10815310556	32770	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 batches from the substance/substance group *Common wormwood oil*.

Supplier	Substance	Batch	Spectra
Caelo	Common wormwood oil	79363	2

[†]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*.

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	60	40	16 204
Type C	0	0	2	2797

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	60.0000 % (> 57.0000 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31637	31637	0.00	88.91
33013	33013	0.00	96.92

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das

alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Coriander oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31552-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Coriander oil; Oleum coriandri

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Coriander oil	9324-114961	31552	40	not required
Taoasis	Coriander oil	25134-117444	31690	40	not required
Taoasis	Coriander oil	104709-126301	32792	40	not required

Validation samples

A total of 35 362 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 *Coriander oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Coriander oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Coriander oil	9324-114961	31552 [†]	20
Taoasis	Coriander oil	25134-117444	31690 [†]	20
Taoasis	Coriander oil	104709-127188	33053	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

Supplier	Substance	Batch	Spectra
Caelo	Coriander oil	16140401	1
Caelo	Coriander oil	15229607	1

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *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 *Coriander oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	80	0	16 224
Type C	0	2	0	2797

The substance/substance group *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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	24.97
31690	31690	0.00	32.89
32792	32792	0.00	26.26

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Cumin oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30449-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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 35 362 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.
- 16 139 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 2 reference samples from the substance/substance group *Cumin oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Cumin oil	348912-71369	30449	40
Taoasis	Cumin oil	51764-124375	32266	40

- 16 224 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Taoasis	Cumin oil	24081-106027	1
Taoasis	Cumin oil	121217-111221	1

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	40	40	16 224
Type C	0	1	1	2797

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	50.0000 % (> 46.2500 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31141	31141	0.00	162.70
32267	32267	0.00	164.98
32904	32904	0.00	179.50

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR

bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Cypress oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30457-2017-09-08
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:

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Cypress oil	732-119820	31656	40	not required
Taoasis	Cypress oil	107527-125443	32806	40	not required

Validation samples

A total of 35 362 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 *Cypress oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Cypress oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Cypress oil	457749-105281	30457	40
Taoasis	Cypress oil	732-119820	31656 [†]	20
Taoasis	Cypress oil	107527-125443	33045	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 13 spectra from 2 *Apo-Ident* customers from 10 batches from the substance/substance group *Cypress oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Cypress oil	487749-107790	1
Taoasis	Cypress oil	487749-108547	1
Taoasis	Cypress oil	514085-111139	1
Taoasis	Cypress oil	341012-123298	1
Taoasis	Cypress oil	1039-121894	3
Taoasis	Cypress oil	1039-122434	1
Taoasis	Cypress oil	33720-115882	1
Taoasis	Cypress oil	33720-118895	2
Taoasis	Cypress oil	33720-118623	1
Taoasis	Cypress oil	107527-125443	1

- 2786 spectra from 265 *Apo-Ident* customers from a total of 1464 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	80	0	16 179
Type B	0	100	0	16 204
Type C	0	13	0	2786

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 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2323 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	67.18
32806	32806	0.00	67.63

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Dermatop[®] base ointment**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31060-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dermatop[®] base ointment

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

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

Validation samples

A total of 35 362 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 *Dermatop[®] base ointment*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Dermatop[®] base ointment*.

Supplier	Substance	Batch	Sample ID	Spectra
Sanofi aventis	Dermatop [®] base ointment	5F080A	31717 [†]	20
Sanofi aventis	Dermatop [®] base ointment	5F089A	32718	40

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 12 batches from the substance/substance group *Dermatop[®] base ointment*.

Supplier	Substance	Batch	Spectra
Sanof/Noweda	Dermatop [®] base ointment	4F075A	2
Sanofi/Noweda	Dermatop [®] base ointment	5F075A	1

continued on the next page

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

continued from previous page

Supplier	Substance	Batch	Spectra
Sanofi/ Noweda	Dermatop [®] base ointment	5F076A	1
Sanofi/Gehe	Dermatop [®] base ointment	5F078A	1
Caelo	Dermatop [®] base ointment	5F080A	1
Sanofi/Noweda	Dermatop [®] base ointment	5F081A	1
Sanofi/Noweda	Dermatop [®] base ointment	5F083A	1
Sanofi/Noweda	Dermatop [®] base ointment	5F086A	1
Sanofi/Noweda	Dermatop [®] base ointment	6F091A	1
Sanofi/Noweda	Dermatop [®] base ointment	5F084A	1
Sanofi/Noweda	Dermatop [®] base ointment	3F059A	1
Sanofi/Noweda	Dermatop [®] base ointment	4F067A	2

- 2785 spectra from 265 *Apo-Ident* customers from a total of 1462 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	60	0	16 244
Type C	0	14	0	2785

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.2318 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	14.35
31717	31717	0.00	18.51

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Dexeryl®**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31512-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

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

Validation samples

A total of 35 362 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 *Dexeryl*[®]. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Dexeryl*[®].

Supplier	Substance	Batch	Sample ID	Spectra
Pierre Fabre	Dexeryl [®]	G99016	31512 [†]	20
Pierre Fabre	Dexeryl [®]	G00419	31630 [†]	20
Pierre Fabre	Dexeryl [®]	G00623	32762	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Dexeryl*[®].

Supplier	Substance	Batch	Spectra
Pierre Fabre /Noweda	Dexeryl [®]	G00606	1
PiereFabre/Now	Dexeryl [®]	G00577	1

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

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	74	6	16 222
Type C	0	2	0	2797

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9409 %)	92.5000 % (> 88.7500 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	13.99
31630	31630	0.00	15.48

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Labor-

prüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Dichloroacetic acid**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30417-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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 KGaA	Dichloroacetic a...	S6674841451	31642	40	not required
Merck KGaA	Dichloroacetic a...	S6674841614	32750	40	not required

Validation samples

A total of 35 362 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 *Dichloroacetic acid*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Dichloroacetic acid*.

Supplier	Substance	Batch	Sample ID	Spectra
Sigma-Aldrich	Dichloroacetic acid	STBC3539V	30417	40
Merck	Dichloroacetic acid	S6674841451	31642 [†]	20

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	20	40	16 244
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9404 %)	33.3333 % (> 28.3333 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31642	31642	0.00	178.76
32750	32750	0.00	177.37

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Dimeticone ointment 10% SR / Optiderm® lotion**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31243-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

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

Special notes

When selecting the *Dimeticone ointment 10% SR / Optiderm® lotion* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Dimeticone ointment 10% SR / Optiderm® lotion*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
apomix	Dimeticone ointm...	08B041213	31243	30	not required
Almirall	Optiderm® lotion	341431	31266	40	not required
apomix	Dimeticone ointm...	10A181214	31638	40	not required
Almirall	Optiderm® lotion	511951	31759	40	not required
apomix	Dimeticone ointm...	11A271216	33041	40	not required
Almirall	Optiderm® lotion	706961	33268	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 230 spectra of 6 reference samples from the substance/substance group *Dimeticone ointment 10% SR / Optiderm[®] lotion*. These samples are listed above in the [calibration samples](#) section.
- 16 029 spectra from a total of 369 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 170 spectra of 6 reference samples from the substance/substance group *Dimeticone ointment 10% SR / Optiderm[®] lotion*.

Supplier	Substance	Batch	Sample ID	Spectra
apomix	Dimeticone ointment 10% SR	7B140711	30356	30
apomix	Dimeticone ointment 10% SR	5B120412	30553	40
apomix	Dimeticone ointment 10% SR	10A181214	31638 [†]	20
Almirall	Optiderm [®] lotion	511951	31759 [†]	20
Almirall	Optiderm [®] lotion	633771	32757	20
Almirall	Optiderm [®] lotion	706961	33267	40

- 16 134 spectra from a total of 420 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 12 batches from the substance/substance group *Dimeticone ointment 10% SR / Optiderm[®] lotion*.

[†]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*.

Supplier	Substance	Batch	Spectra
apomix/Holdermann	Dimeticone ointment 10% SR	1A120116	1
apomix/Holdermann	Dimeticone ointment 10% SR	1A150115	1
Apomix	Dimeticone ointment 10% SR	3B180214	1
apomix/Phönix	Dimeticone ointment 10% SR	4A010415	1
apomix/Holdermann	Dimeticone ointment 10% SR	4A080414	1
apomix/Phönix	Dimeticone ointment 10% SR	5A020616	1
apomix/Gehe	Dimeticone ointment 10% SR	6A190614	1
apomix/Phönix	Dimeticone ointment 10% SR	7A170816	1
apomix/Holdermann	Dimeticone ointment 10% SR	6A300616	1
apomix/Holdermann	Dimeticone ointment 10% SR	8A090915	1
apomix/Gehe	Dimeticone ointment 10% SR	10A181214	1
Apomix/Phönix	Dimeticone ointment 10% SR	8A041213	1

- 2787 spectra from 264 *Apo-Ident* customers from a total of 1462 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	230	0	16 029
Type B	0	165	5	16 134
Type C	0	12	0	2787

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 % (> 99.9463 %)	100.0000 % (> 97.3913 %)
Type B	100.0000 % (> 99.9400 %)	97.0588 % (> 95.2941 %)
Type C	100.0000 % (> 98.2328 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31243	31243	0.00	21.28
31266	31266	0.00	18.94
31638	31638	0.00	22.26
31759	31759	0.00	16.70
33041	33041	0.00	29.23
33268	33268	0.00	14.70

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Ethanol 70% pure / denatured**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30779-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Hofmann's	Ethanol 70% pure...	271012	30779	80	1402563
apomix	Ethanol 70% pure...	54A170613	31055	40	not required

Validation samples

A total of 35 362 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 *Ethanol 70% pure / denatured*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 2 reference samples from the substance/substance group *Ethanol 70% pure / denatured*.

Supplier	Substance	Batch	Sample ID	Spectra
Hofmann's	Ethanol 70% pure / denatured	570916	32591	40
apomix	Ethanol 70% pure / denatured	1A020117	33217	40

- 16 224 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 241 spectra from 74 *Apo-Ident* customers from 200 batches from the substance/substance group *Ethanol 70% pure / denatured*.

Supplier	Substance	Batch	Spectra
eigen	Ethanol 70% pure / denatured		2
Apomix	Ethanol 70% pure / denatured	6A040213	1
Hirsch	Ethanol 70% pure / denatured	714E-02320	1
Kremer/Gehe	Ethanol 70% pure / denatured	130116	1
A.Pflüger/Noweda	Ethanol 70% pure / denatured	130116	2

continued on the next page

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Supplier	Substance	Batch	Spectra
Kremer	Ethanol 70% pure / denatured	130206	1
Gutenberg-Apotheke	Ethanol 70% pure / denatured	130502003	1
A. Pflüger/Phönix	Ethanol 70% pure / denatured	130607	1
Pflüger	Ethanol 70% pure / denatured	130607	1
Kremer GmbH Wuppertal/G...	Ethanol 70% pure / denatured	130729	1
Kemer Phönix	Ethanol 70% pure / denatured	130628	1
Stern-Defektur	Ethanol 70% pure / denatured	130705003	1
A. Pflüger/Phönix	Ethanol 70% pure / denatured	130729	1
Noweda/KremerGmbH	Ethanol 70% pure / denatured	130821	1
Pflüger	Ethanol 70% pure / denatured	131108	2
Doppeleiche Apotheke	Ethanol 70% pure / denatured	131227003	1
A. Pflüger/Jenne	Ethanol 70% pure / denatured	131108	1
Kremer/Gehe	Ethanol 70% pure / denatured	140121	1
Post-Apotheke 15.01.2014	Ethanol 70% pure / denatured	15012044	1
Berkel AHK/HWA	Ethanol 70% pure / denatured	1410T31040613/70	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	140303003	1
Caelo	Ethanol 70% pure / denatured	151008	2
Eigenherstellung	Ethanol 70% pure / denatured	1823	2
Defektur	Ethanol 70% pure / denatured	200114Et0H70	1
Berkel AHK	Ethanol 70% pure / denatured	20042012397	1
A.Pflüger	Ethanol 70% pure / denatured	21111301	1
Defektur	Ethanol 70% pure / denatured	270613Et0H	1
Hohe-Wart-Apotheke	Ethanol 70% pure / denatured	23072013/1	1
Eigenherstellung	Ethanol 70% pure / denatured	2753	2
frischhergestellt	Ethanol 70% pure / denatured		1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	3013A-02320	1
Hofmann	Ethanol 70% pure / denatured	320713	1
Mühlen-Apotheke	Ethanol 70% pure / denatured	3713A-02320	1
Phönix	Ethanol 70% pure / denatured	351213	1
Römer-Apotheke	Ethanol 70% pure / denatured	4314A-03043	1
Hirsch	Ethanol 70% pure / denatured	4413I-02320	1
Belous	Ethanol 70% pure / denatured	4613E-02320	1
Fischar / Sanacorp	Ethanol 70% pure / denatured	7023091	1
Fischar / Noweda	Ethanol 70% pure / denatured	7023111	1
Martinus-Apotheke	Ethanol 70% pure / denatured	A-061213-3D	4
Martinus-Apotheke	Ethanol 70% pure / denatured	A-311013-1D	2
Martinus-Apotheke	Ethanol 70% pure / denatured	E-020314-1D	2
Martinus-Apotheke	Ethanol 70% pure / denatured	E-100114-1D	2
Eigene Herstellung	Ethanol 70% pure / denatured	SPV7025	1
Fagron	Ethanol 70% pure / denatured	Probemessung	1
Noweda	Ethanol 70% pure / denatured	120420	1
phönix,29.12.2012	Ethanol 70% pure / denatured	121130	1
Post-Apotheke	Ethanol 70% pure / denatured	250612	1
Defektur	Ethanol 70% pure / denatured	4712M-02320	1
Hersteller: selbst	Ethanol 70% pure / denatured	12203	1
Plüger/Anzag	Ethanol 70% pure / denatured	32016	1
Eigenherstellung	Ethanol 70% pure / denatured		1
A.Pflüger GmbH & Co.KG/...	Ethanol 70% pure / denatured	130514	1
A.Pflüger GmbH & Co.KG/...	Ethanol 70% pure / denatured	131011	1
Kremer/Noweda	Ethanol 70% pure / denatured	131011	1
Heck/Wittich	Ethanol 70% pure / denatured	2113N-02320	1
Euro OTC	Ethanol 70% pure / denatured	220713	1
Hubertus Apotheke	Ethanol 70% pure / denatured	261113	1
Eigenherstellung	Ethanol 70% pure / denatured	4733	1
Fischar / Anzag	Ethanol 70% pure / denatured	7023091	1
Defektur	Ethanol 70% pure / denatured		2
Rondell Apotheke	Ethanol 70% pure / denatured	415M-03043	1
Rondell Apotheke	Ethanol 70% pure / denatured	416M-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	517Q-02320	1
Rondell Apotheke	Ethanol 70% pure / denatured	615E-02320	1

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Supplier	Substance	Batch	Spectra
Rondell Apotheke	Ethanol 70% pure / denatured	615E-07145	1
Eigenherstellung	Ethanol 70% pure / denatured	616Q-02320	1
eigene Herstellung	Ethanol 70% pure / denatured	6180115	1
HirschApotheke	Ethanol 70% pure / denatured	10151-02320	1
Eigen/Defektur	Ethanol 70% pure / denatured	1116E-03043	1
Kastner (eigen)	Ethanol 70% pure / denatured	1215E-02320	1
Gehe/Pflüger	Ethanol 70% pure / denatured	1204021712	1
Claudia Lange	Ethanol 70% pure / denatured	1234	1
Brinn- Holtz	Ethanol 70% pure / denatured	1234-04/18	1
Brinn- Holtz	Ethanol 70% pure / denatured	1257-06/17	1
apomix/Phoenix	Ethanol 70% pure / denatured	12A250116	1
Rosen Apotheke	Ethanol 70% pure / denatured	1317A-07095	1
Gehe 27.2.14	Ethanol 70% pure / denatured	140121	1
KremperGmbH & Co. KG	Ethanol 70% pure / denatured	140507	1
Kremer GmbH / Noweda	Ethanol 70% pure / denatured	140627	1
Pflüger/Phoenix	Ethanol 70% pure / denatured	140902	1
Kremer GmbH & Co.KG	Ethanol 70% pure / denatured	140902	2
Doppeleiche Apotheke	Ethanol 70% pure / denatured	140927002	1
Kremer	Ethanol 70% pure / denatured	141027	1
Pflüger	Ethanol 70% pure / denatured	141027	1
Kremer/Phönix	Ethanol 70% pure / denatured	141127	1
Kremer GmbH / Noweda	Ethanol 70% pure / denatured	141127	2
Doppeleiche Apotheke	Ethanol 70% pure / denatured	141029011	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	141208001	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	150114010	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	150219007	1
Stiftsapotheke	Ethanol 70% pure / denatured	150420005	1
Kremer/Phönix	Ethanol 70% pure / denatured	150327	1
Kremer GmbH & Co.KG	Ethanol 70% pure / denatured	150602	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	150504003	1
Klenk	Ethanol 70% pure / denatured	150730	1
Kremer/Phoenix	Ethanol 70% pure / denatured	150730	1
Caelo	Ethanol 70% pure / denatured	150730	1
Kremer/Phönix	Ethanol 70% pure / denatured	151123	1
Eigenherstellung	Ethanol 70% pure / denatured	1515I-02320	1
Libellen Apotheke	Ethanol 70% pure / denatured	1515Q-02320	1
Apomix/Alliance Healthc...	Ethanol 70% pure / denatured	15A170215	1
Caelo	Ethanol 70% pure / denatured	160330	1
Kremer/Gehe	Ethanol 70% pure / denatured	160414	2
Kremer	Ethanol 70% pure / denatured	160414	1
Kremer GmbH	Ethanol 70% pure / denatured	160512	1
Kremer	Ethanol 70% pure / denatured	161017	1
Kremer	Ethanol 70% pure / denatured	170208	1
Defektur	Ethanol 70% pure / denatured	1716M-03043	1
Rondell Apotheke	Ethanol 70% pure / denatured	1814Q-07145	1
Caelo	Ethanol 70% pure / denatured	20140403	1
Eigenherstellung	Ethanol 70% pure / denatured	2015E-02320	1
Apotärze	Ethanol 70% pure / denatured	2015I-02320	1
Defektur	Ethanol 70% pure / denatured	2015Q-03043	1
Rezeptur Apotheke	Ethanol 70% pure / denatured	2016Q-03043	1
Eigenherstellung	Ethanol 70% pure / denatured	2124	1
Eigenherstellung	Ethanol 70% pure / denatured	2216A-02320	1
Defektur	Ethanol 70% pure / denatured	23/14	1
kremer gmbh	Ethanol 70% pure / denatured	23081605	1
Eigenherstellung	Ethanol 70% pure / denatured	2314I-02320	1
Rosenapotheke	Ethanol 70% pure / denatured	2317E-07095	1
HirschApotheke	Ethanol 70% pure / denatured	2315I-02320	1
Eigen/Defektur	Ethanol 70% pure / denatured	2516M-03043	1
Defektur	Ethanol 70% pure / denatured	2517A-07097	1
Rondell Apotheke	Ethanol 70% pure / denatured	26151-07145	1

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Supplier	Substance	Batch	Spectra
Rondell Apotheke	Ethanol 70% pure / denatured	2616M-02320	1
Fischar	Ethanol 70% pure / denatured	27031501	1
Eigen/Defektur	Ethanol 70% pure / denatured	2716M-03043	1
Kastner (eigen)	Ethanol 70% pure / denatured	3114E-03043	1
Defektur	Ethanol 70% pure / denatured	2617I-07097	1
Rondell Apotheke	Ethanol 70% pure / denatured	3414M-02320	1
Rondell Apotheke	Ethanol 70% pure / denatured	3414M-07145	1
Eigenherstellung	Ethanol 70% pure / denatured	3416E-02320	1
Eigen/Defektur	Ethanol 70% pure / denatured	3416E-03043	1
Apomix / Alliance Healt...	Ethanol 70% pure / denatured	37A110416	1
Met/ Noweda	Ethanol 70% pure / denatured	3815M-03043	1
Fagron	Ethanol 70% pure / denatured	390414	1
Engel/Engel	Ethanol 70% pure / denatured	39-28715	1
Rondell Apotheke	Ethanol 70% pure / denatured	4015A-03043	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	40722/51Hk	1
Fagron	Ethanol 70% pure / denatured	40929/52La	1
Apomix / Phönix	Ethanol 70% pure / denatured	41A180515	1
Rezeptur	Ethanol 70% pure / denatured	4215Q-03043	1
Eigenherstellung	Ethanol 70% pure / denatured	4215I-02320	1
eigene Herstellung	Ethanol 70% pure / denatured	431140218	1
eigene Herstellung	Ethanol 70% pure / denatured	4315Q-07016	1
Eigenherstellung	Ethanol 70% pure / denatured	4414A-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	4615	1
HirschApotheke	Ethanol 70% pure / denatured	4614A-02320	1
Defektur	Ethanol 70% pure / denatured	4714E-03043	1
Eigenherstellung	Ethanol 70% pure / denatured	4715M	1
Apomix/Alliance Healthc...	Ethanol 70% pure / denatured	56a020715	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	51019/51Wlo	1
Defektur	Ethanol 70% pure / denatured	50427/52Wlo	1
Eigenherstellung	Ethanol 70% pure / denatured	5214A-02320	1
Hoffmann & Sommer GmbH ...	Ethanol 70% pure / denatured	580916	1
Apomix/Noweda	Ethanol 70% pure / denatured	58A020715	1
Caelo	Ethanol 70% pure / denatured	60307/50La	1
Berkel AHK	Ethanol 70% pure / denatured		1
Otto Fischar GmbH & Co...	Ethanol 70% pure / denatured	7024021	1
Caelo	Ethanol 70% pure / denatured	7023111	1
Claudia Lange	Ethanol 70% pure / denatured	61107/50La	1
Claudia Lange	Ethanol 70% pure / denatured	61010/51La	1
Apotheke	Ethanol 70% pure / denatured	70105/51Dre	1
Otto Fischar	Ethanol 70% pure / denatured	7023111	1
Fischar / Noweda	Ethanol 70% pure / denatured	7024021	1
Fischar	Ethanol 70% pure / denatured	7024051	1
Anzag/ Otto Fischar GmbH...	Ethanol 70% pure / denatured	7024051	1
Otto Fischar GmbH/ Amzag	Ethanol 70% pure / denatured	7024091	1
Otto Fischar GmbH & Co...	Ethanol 70% pure / denatured	7024071	1
otto Fischer/Noweda	Ethanol 70% pure / denatured	7024121	1
Otto Fischer / Noweda	Ethanol 70% pure / denatured	7025031	1
Otto Fischar GmbH & Co...	Ethanol 70% pure / denatured	7025031	2
Fischar/Phönix	Ethanol 70% pure / denatured	7026092	1
Fischar/Phönix	Ethanol 70% pure / denatured	7026111	1
Fischar / Alliance Hea...	Ethanol 70% pure / denatured	7026051	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	Bulk	1
Hustadt A	Ethanol 70% pure / denatured		1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-021116-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-050515-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-080514-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-110716-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-121214-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-180714-1D	1
	Ethanol 70% pure / denatured		1

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Supplier	Substance	Batch	Spectra
Eigene Herstellung	Ethanol 70% pure / denatured	SP70140	1
eigene herstellung	Ethanol 70% pure / denatured	SPV7026	1
Eigene Herstellung	Ethanol 70% pure / denatured	SPV7029	1
Eigenherstellung	Ethanol 70% pure / denatured	5131213	1
Eigenproduktion	Ethanol 70% pure / denatured	714Q-02320	2
Sanacorp	Ethanol 70% pure / denatured	130124	1
Eigenherstellung	Ethanol 70% pure / denatured	1313I-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	2613I-03043	1
Gutenberg-Apotheke	Ethanol 70% pure / denatured	1813M-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	4513I-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	3413I-02320	1
Caelo	Ethanol 70% pure / denatured		1
Caelo	Ethanol 70% pure / denatured	814E-02320	1
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	1234567	1
Stiftsapotheke	Ethanol 70% pure / denatured	13052016	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	140630003	1
Hustadt Apotheke	Ethanol 70% pure / denatured	141212	1
Post-Apotheke	Ethanol 70% pure / denatured	1414A-02320	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	150126002	1
Hustadt apotheke	Ethanol 70% pure / denatured	150618	1
Caelo	Ethanol 70% pure / denatured	1715E-02320	1
Rondell	Ethanol 70% pure / denatured	1715E-07145	1
Caelo	Ethanol 70% pure / denatured	1915I-02320	1
Caelo	Ethanol 70% pure / denatured	2614E-03043	1
sittig	Ethanol 70% pure / denatured	310316	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	41125/52Hk	1
Wolf-Apotheke	Ethanol 70% pure / denatured	40331/52La	1
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	41211/51Hk	1
Defektur	Ethanol 70% pure / denatured	50427/1La	1
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	50714/51Hk	1
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	50714/53Hk	1
Defektur	Ethanol 70% pure / denatured	60209/51Hk	1
Defektur / Wolf-Apotheke	Ethanol 70% pure / denatured	60902/50Hk	1
Claudia Lange	Ethanol 70% pure / denatured	60919/50La	1
Purren Apotheke	Ethanol 70% pure / denatured	17043	1
Hofmann Sommer	Ethanol 70% pure / denatured	320713	1
eigene Herstellung	Ethanol 70% pure / denatured	4411312106	1
Gutenberg-Apotheke	Ethanol 70% pure / denatured	3412I-03043	1

- 2558 spectra from 255 *Apo-Ident* customers from a total of 1275 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ethanol 70% pure / denatured* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ethanol 70% pure / denatured* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	80	0	16 224
Type C	0	204	37	2558

The substance/substance group *Ethanol 70% pure / denatured* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2262 %)	84.6473 % (> 83.4025 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	103.36
31055	31055	0.00	83.89

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Eucalyptus oil / Rosmary oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30966-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Eucalyptus oil / Rosmary oil; Eucalypti aetheroleum; Eucalyptus oil; Oleum eucalypti; Oleum rosmarini; Rosemary oil; Rosmarini aetheroleum

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Eucalyptus oil	527885-109705A	30966	40	not required
Taoasis	Rosemary oil	3231031-117639	31551	40	not required

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Rosemary oil	1921019-120666	31691	40	not required
Taoasis	Eucalyptus oil	7271001-121014	31694	40	not required
Taoasis	Eucalyptus oil	043127A-125381	32903	40	not required
Taoasis	Rosemary oil	1862-126630	32933	40	not required

Validation samples

A total of 35 362 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 *Eucalyptus oil* / *Rosemary oil*. These samples are listed above in the [calibration samples](#) section.
- 16 019 spectra from a total of 369 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 192 spectra of 7 reference samples from the substance/substance group *Eucalyptus oil* / *Rosemary oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Eucalyptus oil	T150I11	30384	40
Taoasis	Eucalyptus oil	T51I10	30387	40
Taoasis	Rosemary oil	3231031-117639	31551 [†]	20
Taoasis	Rosemary oil	1921019-120666	31691 [†]	20
Taoasis	Eucalyptus oil	7271001-121014	31694 [†]	20
Taoasis	Rosemary oil	1614-125089	32802	40
Taoasis	Rosemary oil	1614-125089	not required	12

- 16 112 spectra from a total of 420 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

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

- 21 spectra from 12 *Apo-Ident* customers from 20 batches from the substance/substance group *Eucalyptus oil* / *Rosemary oil*.

Supplier	Substance	Batch	Spectra
Euro OTC	Eucalyptus oil	1412030-01	1
Caelo	Eucalyptus oil	15063309	1
Caesar & Loretz GmbH Hi...	Eucalyptus oil	15063312	1
Caesar & Loretz GmbH Hi...	Eucalyptus oil	15400203	1
Caelo	Eucalyptus oil	15400217	1
Taoasis	Eucalyptus oil	43703-122178	1
Taoasis	Eucalyptus oil	43703-122404	1
Taoasis	Eucalyptus oil	52046-124692	1
Caelo	Eucalyptus oil	11324112	1
Caelo	Eucalyptus oil	13106407LOT	1
Anzag, 10.12.2012	Eucalyptus oil	273979	1
Taoasis	Eucalyptus oil	33364-110871	1
Taoasis	Eucalyptus oil	543495-112704	1
Taoasis	Eucalyptus oil	130205-111868	1
Taoasis	Rosemary oil	1526-123355	1
Taoasis	Rosemary oil	26057-119164	1
Taoasis	Rosemary oil	1526-125088	1
Caelo	Rosemary oil	15442017	1
Taoasis	Rosemary oil	26057-122996	1
Bombastus	Rosemary oil	301449	2

- 2778 spectra from 264 *Apo-Ident* customers from a total of 1454 batches from a further 115 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Eucalyptus oil* / *Rosemary 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 *Eucalyptus oil* / *Rosemary oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	16 019
Type B	0	149	43	16 112
Type C	0	18	3	2778

The substance/substance group *Eucalyptus oil* / *Rosemary 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 % (> 99.9463 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9400 %)	77.6042 % (> 76.0417 %)
Type C	100.0000 % (> 98.2298 %)	85.7143 % (> 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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	56.42
31551	31551	0.00	29.90
31691	31691	0.00	26.97
31694	31694	0.00	49.50
32903	32903	0.00	29.71
32933	32933	0.00	29.61

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Excipial® almond oil ointment**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30720-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Spirig Pharma	Excipial® almond...	M023	30720	40	not required
Spirig Pharma	Excipial® almond...	M031	31090	40	not required
Spirig Pharma	Excipial® almond...	N012	31278	40	not required
Spirig Pharma	Excipial® almond...	R012	31757	40	not required

Validation samples

A total of 35 362 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 *Excipial[®] almond oil ointment*. These samples are listed above in the [calibration samples](#) section.
- 16 099 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Excipial[®] almond oil ointment*.

Supplier	Substance	Batch	Sample ID	Spectra
Spirig Pharma	Excipial [®] almond oil ointment	R012	31757 [†]	20
Spirig Pharma	Excipial [®] almond oil ointment	S021	33209	40
Spirig Pharma	Excipial [®] almond oil ointment	T052	33210	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 22 spectra from 9 *Apo-Ident* customers from 18 batches from the substance/substance group *Excipial[®] almond oil ointment*.

[†]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*.

Supplier	Substance	Batch	Spectra
Galderma/Now	Excipial [®] almond oil ointment	LOTS021	1
Spirig/Noweda	Excipial [®] almond oil ointment	R043	1
Galderma (Spirig Pharma...	Excipial [®] almond oil ointment	R043	1
Galderma	Excipial [®] almond oil ointment	R043	1
Spirig	Excipial [®] almond oil ointment	S011	1
Galderma/Noweda	Excipial [®] almond oil ointment	S012	1
Spirig	Excipial [®] almond oil ointment	S032	1
Spirig	Excipial [®] almond oil ointment	LOTM023	1
Spirig / Gehe	Excipial [®] almond oil ointment	LOTN022	1
Caelo	Excipial [®] almond oil ointment	lotno32	1
Spirig	Excipial [®] almond oil ointment	M023	1
Spirig	Excipial [®] almond oil ointment	N031	1
Spirig	Excipial [®] almond oil ointment	N032	1
Spirig Pharma/Nowed	Excipial [®] almond oil ointment	N022	1
Spirig	Excipial [®] almond oil ointment	R012	1
Spirig /Noweda	Excipial [®] almond oil ointment	R012	1
Spirig /Noweda	Excipial [®] almond oil ointment	r021	1
Spirig/Sanacorp	Excipial [®] almond oil ointment	LOTN011	1
Caelo	Excipial [®] almond oil ointment	LOTN022	2
Spirig	Excipial [®] almond oil ointment	M032	1
Spirig/AHD	Excipial [®] almond oil ointment	N011	1

- 2777 spectra from 265 *Apo-Ident* customers from a total of 1462 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	160	0	16 099
Type B	0	100	0	16 204
Type C	0	22	0	2777

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2297 %)	100.0000 % (> 72.7273 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30720	30720	0.00	30.06
31090	31090	0.00	24.85
31278	31278	0.00	24.53
31757	31757	0.00	21.90

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Fat ointments
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	30881-2017-09-08
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Fat ointments; Asche Basis[®] fatty ointment; Cottonwood ointment; Marjoram ointment; Neribas[®] fatty ointment; Protegin[®] XN; Unguentum majoranae; Unguentum Populi

Special notes

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

no information

Applicable documents

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Caelo	Marjoram ointment	12123001	30881	40	not required
Henry Lamotte	Marjoram ointment	5322500	30926	40	not required
Chiesi	Asche Basis [®] fat...	23014A	31013	40	not required
Caelo	Protegin [®] XN	13081901	31112	40	not required

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Marjoram ointment	14089901	31443	40	not required
Caelo	Protegin [®] XN	13344402	31475	40	not required
Jenapharm	Neribas [®] fatty o...	32032C	31489	40	not required
Chiesi	Asche Basis [®] fat...	41017A	31858	40	not required
Jenapharm	Neribas [®] fatty o...	YY00K7C	31872	40	not required
Caelo	Cottonwood ointm...	161175	32473	40	20160607*
Caelo	Cottonwood ointm...	170572	33130	40	20170307*
Caelo	Cottonwood ointm...	170573	33131	40	20170308*

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 480 spectra of 12 reference samples from the substance/substance group *Fat ointments*. These samples are listed above in the [calibration samples](#) section.
- 15 779 spectra from a total of 363 batches from further 139 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 870 spectra of 21 reference samples from the substance/substance group *Fat ointments*.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Protegin [®] XN	11022410	30422	40
Caelo	Protegin [®] XN	10079803	30435	40
Caelo	Protegin [®] XN	11196702	30469	40
Caelo	Protegin [®] XN	11196801	30471	40
Caelo	Protegin [®] XN	11196801	30472	70
Caelo	Protegin [®] XN	11196703	30500	40
Caelo	Protegin [®] XN	11196702	30511	40
Chiesi	Asche Basis [®] fatty ointment	41017A	31858 [†]	20
Jenapharm	Neribas [®] fatty ointment	YY00K7C	31872 [†]	20
Caelo	Marjoram ointment	153533	31990	60
Caelo	Marjoram ointment	153540	31991	60
Caelo	Protegin [®] XN	161645	32340	40

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

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Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Marjoram ointment	160687	32516	40
Chiesi	Asche Basis [®] fatty ointment	53021A	32716	40
Jenapharm	Neribas [®] fatty ointment	YY011K0	32764	40
Caelo	Marjoram ointment	162575	32872	40
Caelo	Marjoram ointment	162576	32873	40
Chiesi	Asche Basis [®] fatty ointment	53021A	32925	40
Caelo	Cottonwood ointment	170534	33162	40
Caelo	Cottonwood ointment	170574	33163	40
Jenapharm	Neribas [®] fatty ointment	YY019KR	33290	40

- 15 434 spectra from a total of 408 batches from further 172 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 353 spectra from 111 *Apo-Ident* customers from 117 batches from the substance/substance group *Fat ointments*.

Supplier	Substance	Batch	Spectra
Chiese	Asche Basis [®] fatty ointment	33016A	1
Chiesi/Gehe	Asche Basis [®] fatty ointment	41017A	1
CHiesi	Asche Basis [®] fatty ointment	41018A	3
Chiesi/Gehe	Asche Basis [®] fatty ointment	51020A	1
Chiesi	Asche Basis [®] fatty ointment	51020A	1
Chiese	Asche Basis [®] fatty ointment	63023A	1
Caelo	Marjoram ointment	2021506	1
Caelo	Marjoram ointment	10111402	1
Caelo	Marjoram ointment	13382903	3
Caelo	Marjoram ointment	13383001	1
Fagron	Marjoram ointment	13A16-T04-000208	1
Caelo	Marjoram ointment	13e10-t04-003550	1
Fagron	Marjoram ointment	13F27-T03-004962	3
Caelo	Marjoram ointment	140020101	1
Caelo	Marjoram ointment	14002101	15
Caelo	Marjoram ointment	14089901	8
Gehe	Marjoram ointment	14089901	1
Euro OTC	Marjoram ointment	14089901	1
Caelo	Marjoram ointment	14090002	8
Fagron	Marjoram ointment	14090002	1
Caelo	Marjoram ointment	14332101	8
Fagron	Marjoram ointment	14A07-T04-009079	3
Caelo	Marjoram ointment	14332202	1
Fagron	Marjoram ointment	14A07-T05-009082	1
Fagron	Marjoram ointment	14A07-T06-009085	3
Caelo	Marjoram ointment	15038303	1

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

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Supplier	Substance	Batch	Spectra
Caelo	Marjoram ointment	15038401	2
Caelo	Marjoram ointment	15038501	3
VDL	Marjoram ointment	15354001	2
Caelo	Marjoram ointment	15353303	1
Caelo	Marjoram ointment	15354001	3
Caelo	Marjoram ointment	15392402	2
Fagron	Marjoram ointment	15K10-T10-027644	1
Caelo	Marjoram ointment	16068801	1
Caelo	Marjoram ointment	16068901	2
Fagron	Marjoram ointment	16E02-T02-032846	1
Fagron	Marjoram ointment	16K07-T20-038496	1
Henry Lamotte Oils GmbH	Marjoram ointment	5563400	1
Caelo	Marjoram ointment	27031505	1
Henry Lamotte/Sanacorp	Marjoram ointment	5563400	4
Caelo	Marjoram ointment	2011405	1
Caelo	Marjoram ointment	7121203	1
Caelo	Marjoram ointment	8031304	1
Caelo	Marjoram ointment	11061201	1
Caelo	Marjoram ointment	11274603	2
Gehe	Marjoram ointment	11327501	1
Caelo	Marjoram ointment	11327501	2
Caelo	Marjoram ointment	12018001	7
Phönix 06.10.2012	Marjoram ointment	12018001	1
Phönix	Marjoram ointment	12018001	1
Caelo	Marjoram ointment	12018101	3
Caelo	Marjoram ointment	12081002	6
Fagron	Marjoram ointment	12081002	1
Sanacorp	Marjoram ointment	12081002	1
Caelo	Marjoram ointment	12123001	7
Euro OTC	Marjoram ointment	12123001	1
Caelo	Marjoram ointment	12123101	2
Caelo	Marjoram ointment	1225402	1
Caelo	Marjoram ointment	12295402	7
Fagron	Marjoram ointment	12D24-T01	2
Caelo	Marjoram ointment	13028301	2
Phönix 10.12.12	Marjoram ointment	12D24-T02	1
Caelo	Marjoram ointment	13028302	3
Jenne	Marjoram ointment	13028302	2
Cealo	Marjoram ointment	13028401	2
Caelo	Marjoram ointment	13028401	8
Phoenix	Marjoram ointment	13028401	1
Gehe	Marjoram ointment	13028401	1
Caelo	Marjoram ointment	13051304	1
Caelo	Marjoram ointment	13095401	5
Sanacorp	Marjoram ointment	13095401	1
Caelo	Marjoram ointment	13307102	6
Gehe	Marjoram ointment	13307102	1
Caelo	Marjoram ointment	13382901	1
Caelo	Marjoram ointment	13382902	2
Fagron	Marjoram ointment	13A16-T02	1
Caelo	Marjoram ointment	1513E-02536	1
Caelo	Marjoram ointment	15101205	1
Erika apotheke	Marjoram ointment	5067400	1
Caelo	Marjoram ointment	20290312-1	1
Henry Lamotte Oils GmbH...	Marjoram ointment	5067400	1
Lamotte / Gehe	Marjoram ointment	5322500	1
Lamotte/ Noweda	Marjoram ointment	5322500	1
Noweda	Marjoram ointment	5322500	1
Henry Lamotte Oils GmbH	Marjoram ointment	5322500	1
Henry Lamotte Oils GmbH...	Marjoram ointment	5322500	1

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Supplier	Substance	Batch	Spectra
Caelo	Neribas [®] fatty ointment	yy00k7C	1
GP Grenzach Produktions...	Neribas [®] fatty ointment	YY00K7C	1
/ AHD	Neribas [®] fatty ointment	YY016LP	2
Jenapharm/Ahd	Neribas [®] fatty ointment	YYo11Ko	1
Jenapharm/Phönix	Neribas [®] fatty ointment	YY00K7C	1
Phoenix	Neribas [®] fatty ointment	YY00K7C	1
Caelo	Protegin [®] XN	14220202	4
Caelo	Protegin [®] XN	14220205	6
Caelo	Protegin [®] XN	14220206	1
Caelo	Protegin [®] XN	14220208	4
Caelo	Protegin [®] XN	14220209	3
Caelo	Protegin [®] XN	14341301	3
Caelo	Protegin [®] XN	14341302	2
Caelo	Protegin [®] XN	15252702	1
Caelo	Protegin [®] XN	15252703	4
Caelo	Protegin [®] XN	16026701	5
Gehe	Protegin [®] XN	16026701	2
Caelo	Protegin [®] XN	16026702	3
Caelo	Protegin [®] XN	16026703	2
Caelo	Protegin [®] XN	16026704	1
Caelo	Protegin [®] XN	16026707	1
Caelo	Protegin [®] XN	13081905	12
Caelo	Protegin [®] XN	13081906	7
Caelo	Protegin [®] XN	13344401	8
Caelo	Protegin [®] XN	13344402	11
Caelo	Protegin [®] XN	14220201	1
Caelo	Protegin [®] XN	14220203	2
Caelo	Protegin [®] XN	14220204	3
Caelo	Protegin [®] XN	26031509	1
Caelo	Protegin [®] XN	3091208	1
Caelo	Protegin [®] XN	6012014A	1
Caelo	Protegin [®] XN	8031305	1
Caelo	Protegin [®] XN	11022403	1
Caelo	Protegin [®] XN	11196702	2
Caelo	Protegin [®] XN	11196703	1
Phönix	Protegin [®] XN	11196706	1
Caelo	Protegin [®] XN	11196707	1
Caelo	Protegin [®] XN	11196801	1
Kehr	Protegin [®] XN	11196803	1
Großhandel	Protegin [®] XN	11196801	1
Caelo	Protegin [®] XN	11196805	1
Caelo	Protegin [®] XN	12229201	5
Phönix	Protegin [®] XN	12229201	1
Gehe	Protegin [®] XN	12229201	2
Anzag	Protegin [®] XN	12229205	1
Phönix 12.03.2013	Protegin [®] XN	12229205	1
Caelo	Protegin [®] XN	12229209	1
Caelo	Protegin [®] XN	12229210	1
Phönix, 07.11.13	Protegin [®] XN	12229210	1
Caelo	Protegin [®] XN	12229211	6
Gehe	Protegin [®] XN	12229211	1
Großhandel	Protegin [®] XN	12229211	1
Caelo	Protegin [®] XN	122910	1
Caelo	Protegin [®] XN	13081901	6
Phönix	Protegin [®] XN	13081901	3
Caelo	Protegin [®] XN	13081902	6
Caelo	Protegin [®] XN	13081903	1
Caelo	Protegin [®] XN	13081904	2
Großhandel	Protegin [®] XN	13081905	1
Caelo	Protegin [®] XN	13081907	3

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Supplier	Substance	Batch	Spectra
Caelo	Protegin [®] XN	13081908	1
Caelo	Protegin [®] XN	20011402	1
Caelo	Protegin [®] XN	25061301	1
	Protegin [®] XN	2711E-03598	1
VDL	Marjoram ointment	14090002	1
Sanacorp, 21.03.17, 5,73EUR	Marjoram ointment	16068602	1
Sanacorp	Marjoram ointment	12295402	1
Henry Lamotte GmbH/Hold...	Marjoram ointment	5067400	1
Caelo	Marjoram ointment	5322500	1

- 2446 spectra from 243 *Apo-Ident* customers from a total of 1357 batches from a further 113 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	480	0	15 779
Type B	0	870	0	15 394
Type C	0	331	22	2446

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9462 %)	100.0000 % (> 98.7500 %)
Type B	100.0000 % (> 99.9408 %)	100.0000 % (> 99.3103 %)
Type C	100.0000 % (> 98.2261 %)	93.7677 % (> 92.9178 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	36.20
30926	30926	0.00	46.30
31013	31013	0.00	41.68
31112	31112	0.00	42.13
31443	31443	0.00	36.95
31475	31475	0.00	41.42
31489	31489	0.00	45.45
31858	31858	0.00	48.83
31872	31872	0.00	50.69
32473	32473	0.00	32.74
33130	33130	0.00	32.23
33131	33131	0.00	33.52

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Fenistil® Gel**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31045-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Novartis	Fenistil® Gel	N00927A	31045	40	not required
Novartis	Fenistil® Gel	R02021A	31767	40	not required

Validation samples

A total of 35 362 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 *Fenistil® Gel*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Fenistil® Gel*.

Supplier	Substance	Batch	Sample ID	Spectra
Novartis	Fenistil® Gel	R02021A	31767 [†]	20
Euro OTC	Fenistil® Gel	T02415A	32787	40
Euro OTC	Fenistil® Gel	T02416A	32825	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	90	10	16 204
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	90.0000 % (> 87.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	19.14
31767	31767	0.00	21.90

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Fennel oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31140-2017-09-08
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:

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Fennel oil	1806-125039	32795	40	not required

Validation samples

A total of 35 362 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 *Fennel oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Fennel oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Fennel oil	L35513DN-119762	31693 [†]	20
Taoasis	Fennel oil	1806-127213	32952	40

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Fennel oil*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	60	0	16 244
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31140	31140	0.00	94.80
31693	31693	0.00	91.61
32795	32795	0.00	19.27

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Fitalite™**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31492-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fitalite™

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Fitalite™	14B18-T01-010352	31492	40	not required
Fagron	Fitalite™	14B18-T01-010352	31639	40	not required
Fagron	Fitalite™	1503259	32779	40	not required

Validation samples

A total of 35 362 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 *FitaliteTM*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *FitaliteTM*.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Fitalite TM	14B18-T01-010352	31492 [†]	20
Fagron	Fitalite TM	14B18-T01-010352	31639 [†]	20
Fagron	Fitalite TM	1503259	32823	40

- 16 224 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *FitaliteTM*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the

[†]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*.

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

Validation results

The validation runs checked whether the substance/substance group *Fitalite*TM can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Fitalite*TM and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	16 139
Type B	0	80	0	16 211
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9412 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31492	31492	0.00	15.38
31639	31639	0.00	14.84
32779	32779	0.00	10.59

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Frankincense oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30843-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Frankincense oil; Oleum boswellia serrata; Oleum olibanum

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Frankincense oil	15181-119714	31633	40	not required
Taoasis	Frankincense oil	1509-122197	31820	40	not required
Taoasis	Frankincense oil	1509-125625	33052	40	not required

Validation samples

A total of 35 362 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 *Frankincense oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 120 spectra of 4 reference samples from the substance/substance group *Frankincense oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Frankincense oil	pending	30298	40
Taoasis	Frankincense oil	3.26550	30843	40
Taoasis	Frankincense oil	15181-119714	31633 [†]	20
Taoasis	Frankincense oil	1509-122197	31820 [†]	20

- 16 184 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Apoth.Bauer&Co/Noweda	Frankincense oil		1
Apoth.Bauer&Co/Noweda	Frankincense oil	3175391505	1
Taoasis	Frankincense oil	549702-112299	1

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

- 2796 spectra from 265 *Apo-Ident* customers from a total of 1471 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Frankincense 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 *Frankincense oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	40	80	16 184
Type C	0	2	1	2796

The substance/substance group *Frankincense 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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9401 %)	33.3333 % (> 30.8333 %)
Type C	100.0000 % (> 98.2539 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31633	31633	0.00	75.79
31820	31820	0.00	11.09
33052	33052	0.00	16.64

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe

mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Ginger oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30451-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ginger oil; Oleum zingiber officinalis; Zingiber officinalis oleum

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
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 35 362 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 *Ginger oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

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

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Ginger oil	6454-92725	30451	40
Bombastus	Ginger oil	300690	32569	40
Bombastus	Ginger oil	300690	33014	40

- 16 184 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Taoasis	Ginger oil	6454-92725	1

- 2798 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	80	40	16 184
Type C	0	0	1	2798

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9401 %)	66.6667 % (> 64.1667 %)
Type C	100.0000 % (> 98.3099 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30958	30958	0.00	20.35
31142	31142	0.00	22.02
32270	32270	0.00	30.26

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das

alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Grapefruit oil organic / Orange oil
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	30960-2017-09-08
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Grapefruit oil organic / Orange oil; Citrus sinensis oleum; Grapefruit oil, organic; Oleum citrus paradisi; Oleum citrus sinensis; Orange oil

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Orange oil	121109-110685BAG90451	30960	40	not required
Taoasis	Grapefruit oil, ...	31564-119383	31634	80	not required

continued on the next page

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Orange oil	33732-12088	31679	40	not required
Taoasis	Grapefruit oil, ...	38755-122181	31781	40	not required
Apotheker Bau...	Grapefruit oil, ...	7.99615.16.02	31853	40	not required

Validation samples

A total of 35 362 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 *Grapefruit oil organic / Orange oil*. These samples are listed above in the [calibration samples](#) section.
- 16 019 spectra from a total of 370 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 300 spectra of 9 reference samples from the substance/substance group *Grapefruit oil organic / Orange oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Grapefruit oil, organic	pending	30538	40
Taoasis	Grapefruit oil, organic	31564-119383	31634 [†]	40
Taoasis	Orange oil	33732-12088	31679 [†]	20
Taoasis	Grapefruit oil, organic	38755-122181	31781 [†]	20
Apotheker Bauer & Cie	Grapefruit oil, organic	7.99615.16.02	31853 [†]	20
Taoasis	Orange oil	43829C-124974	32790	40
Taoasis	Orange oil	44583A-126780	32902	40
Taoasis	Grapefruit oil, organic	44040A-124468	32979	40
Apotheker Bauer & Cie	Grapefruit oil, organic	7.68413.17.012018-03	33019	40

- 16 004 spectra from a total of 418 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B*

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

section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 12 batches from the substance/substance group *Grapefruit oil organic / Orange oil*.

Supplier	Substance	Batch	Spectra
Taoasis	Grapefruit oil, organic	31564-120540	1
Taoasis	Grapefruit oil, organic	40038-123110	1
Taoasis	Grapefruit oil, organic	44040A-124468	1
Taoasis	Orange oil	140129-116983	1
Taoasis	Orange oil	140129-118141	1
Taoasis	Orange oil	140129-118420	1
Taoasis	Orange oil	122650-123643	1
Taoasis	Orange oil	140129-118790	1
Bombastus	Orange oil	302428	1
Taoasis	Orange oil	42861A-121691	1
Taoasis	Orange oil	42861A-122532	1
Taoasis	Orange oil	43829C-125351	1

- 2787 spectra from 265 *Apo-Ident* customers from a total of 1462 batches from a further 115 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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* can clearly be 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* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	16 019
Type B	0	260	40	16 004
Type C	0	12	0	2787

The substance/substance group *Grapefruit oil organic / 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 % (> 99.9463 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9399 %)	86.6667 % (> 85.6667 %)
Type C	100.0000 % (> 98.2328 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30960	30960	0.00	46.21
31634	31634	0.00	45.87
31679	31679	0.00	47.93
31781	31781	0.00	47.66
31853	31853	0.00	40.83

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Hans Karrer Lipolotion MicroSilver**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31730-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hans Karrer Lipolotion MicroSilver

Special notes

When selecting the *Hans Karrer Lipolotion MicroSilver* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hans Karrer G...	Hans Karrer Lipo...	15003	31730	40	not required
Hans Karrer G...	Hans Karrer Lipo...	15008	31873	40	not required

Validation samples

A total of 35 362 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 *Hans Karrer Lipolotion MicroSilver*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 374 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Hans Karrer Lipolotion MicroSilver*.

Supplier	Substance	Batch	Sample ID	Spectra
Hans Karrer GmbH	Hans Karrer Lipolotion Micro...	15003	31730 [†]	20
Hans Karrer GmbH	Hans Karrer Lipolotion Micro...	15008	31873 [†]	20
Hans Karrer GmbH	Hans Karrer Lipolotion Micro...	16005	32753	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 batches from the substance/substance group *Hans Karrer Lipolotion MicroSilver*.

Supplier	Substance	Batch	Spectra
Hans Karrer/Gehe	Hans Karrer Lipolotion Micro...	17002	20

[†]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*.

- 2779 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hans Karrer Lipolotion 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 *Hans Karrer Lipolotion MicroSilver* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	80	0	16 224
Type C	0	9	11	2779

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9403 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2300 %)	45.0000 % (> 30.0000 %)

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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31730	31730	0.00	13.28
31873	31873	0.00	14.53

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Labor-

prüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Hydrophilic ointments
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	30634-2017-09-08
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Hydrophilic ointments; Abitima[®] clinic body cream; Abitima[®] clinic body lotion; Abitima[®] clinic face cream; Asche Basis[®] cream; Asche Basis[®] lotion; Base cream Taoasis; Dermatop[®] base cream; Dermifant[®] kids lotion; DMS[®] base cream classic; DMS[®] base cream high classic; DMS[®] base cream high classic plus; Eucerinum O/W basis; Eucerinum W/O basis; Excipial[®] hydro cream; Excipial[®] U Lipolotio; Excipial[®] U10 Lipolotio; Hans Karrer Lipocream MicroSilver; Linola[®] body milk; Lipoderm[®] lotion; Neribas[®] cream; Thrombocid[®] ointment; VersatileTM Rich

Special notes

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

no information

Applicable documents

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Bayer	Neribas [®] cream	21076A	30634	40	not required
Spirig Pharma	Lipoderm [®] lotion	K057	30635	40	not required
Chiesi	Asche Basis [®] cream	03117A	30713	40	not required
Spirig Pharma	Excipial [®] hydro ...	I013	30725	40	not required
Spirig Pharma	Excipial [®] U Lipo...	M042	30732	60	not required
Spirig Pharma	Excipial [®] U10 Li...	M021	30733	60	not required
benel	Thrombocid [®] oint...	410B113	30772	40	not required
Chiesi	Asche Basis [®] cream	22197A	30775	40	not required
Chiesi	Asche Basis [®] lot...	21042A	30828	40	not required
Actavis	Abitima [®] clinic ...	46820	30845	40	not required
Actavis	Abitima [®] clinic ...	145054	30847	40	not required
Allergika	Dermifant [®] kids ...	1301020	30971	80	not required
Beiersdorf	Eucerinum W/O ba...	31230108WA	30993	31	not required
Taoasis	Base cream Taoasis	121205-2276	31041	80	not required
Intendis	Neribas [®] cream	21076A	31050	40	not required
Actavis	Abitima [®] clinic ...	110712	31058	40	not required
Actavis	Abitima [®] clinic ...	051112	31061	40	not required
Allergika	Dermifant [®] kids ...	1306020	31064	40	not required
Spirig Pharma	Excipial [®] U10 Li...	N025	31066	40	not required
Spirig Pharma	Excipial [®] U Lipo...	N031	31067	40	not required
Chiesi	Asche Basis [®] lot...	24049A	31068	40	not required
Spirig Pharma	Lipoderm [®] lotion	M065	31072	40	not required
Chiesi	Asche Basis [®] cream	24220A	31085	40	not required
Spirig Pharma	Excipial [®] hydro ...	N013	31089	40	not required
Bayer	Neribas [®] cream	21076A	31095	40	not required
Bene	Thrombocid [®] oint...	410B113	31098	40	not required
Taoasis	Base cream Taoasis	130124-3021	31115	40	not required
Sanofi aventis	Dermatop [®] base c...	3F031A	31234	40	not required
Koko	DMS [®] base cream ...	L010K13	31236	70	not required
Spirig Pharma	Excipial [®] U Lipo...	N085	31280	40	not required
Spirig Pharma	Excipial [®] U10 Li...	N047	31281	40	not required
Koko	DMS [®] base cream ...	L026G13	31307	40	not required
Koko	DMS [®] base cream ...	L032A14	31308	40	not required
Koko	DMS [®] base cream ...	L014L13	31309	40	not required
Fagron	Versatile [™] Rich	14B19-T08-101395	31494	40	not required
Dr. Wolff	Linola [®] body milk	433240	31511	40	not required
Spirig Pharma	Lipoderm [®] lotion	R023	31535	40	not required
Beiersdorf	Eucerinum O/W ba...	41830108WA	31539	40	not required
Taoasis	Base cream Taoasis	141222-4350	31578	40	not required
Fagron	Versatile [™] Rich	14B19-T04-010395	31868	40	not required
Koko	DMS [®] base cream ...	L034H15	31869	40	not required
Koko	DMS [®] base cream ...	L041K15	31870	40	not required
Dr. Wolff	Linola [®] body milk	511750	31874	40	not required
Sanofi aventis	Dermatop [®] base c...	5F056A	32177	40	not required
Koko	DMS [®] base cream ...	L003L15	32178	40	not required
Actavis	Abitima [®] clinic ...	158584	32179	40	not required
Beiersdorf	Eucerinum W/O ba...	53430208WA	32767	40	not required
Koko	DMS [®] base cream ...	L003H16	32916	40	not required
Actavis	Abitima [®] clinic ...	159997	32942	40	not required
Actavis	Abitima [®] clinic ...	070915	32997	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
Spirig Pharma	Excipial [®] hydro ...	T052	33208	40	not required
Beiersdorf	Eucerinum O/W ba...	64030208WA	33213	40	not required
Galderma Labo...	Excipial [®] U Lipo...	T122	33270	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 2341 spectra of 55 reference samples from the substance/substance group *Hydrophilic ointments*. These samples are listed above in the [calibration samples](#) section.
- 13918 spectra from a total of 325 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 1749 spectra of 49 reference samples from the substance/substance group *Hydrophilic ointments*.

Supplier	Substance	Batch	Sample ID	Spectra
Beiersdorf	Eucerinum O/W basis	pending	30409	40
Beiersdorf	Eucerinum W/O basis	21430108WA	30494	40
Beiersdorf	Eucerinum O/W basis	930108WA	30565	40
Actavis	Abitima [®] clinic body cream	72013	30736	39
Spirig Pharma	Excipial [®] hydro cream	I013	30836	40
Taoasis	Base cream Taoasis	121205-2276	31041 [†]	20
Spirig Pharma	Excipial [®] hydro cream	N013	31277	40
Fagron	Versatile [™] Rich	14B19-T08-101395	31494 [†]	20
Dr. Wolff	Linola [®] body milk	433240	31511 [†]	20
Spirig Pharma	Lipoderm [®] lotion	R023	31535 [†]	20
Beiersdorf	Eucerinum O/W basis	41830108WA	31539 [†]	20
Taoasis	Base cream Taoasis	141222-4350	31578 [†]	20
Fagron	Versatile [™] Rich	14B19-T04-010395	31868 [†]	20
Koko	DMS [®] base cream classic	L034H15	31869 [†]	20
Koko	DMS [®] base cream high classic	L041K15	31870 [†]	20
Dr. Wolff	Linola [®] body milk	511750	31874 [†]	20
Actavis	Abitima [®] clinic body lotion	159997	32171	30
Chiesi	Asche Basis [®] lotion	53075A	32715	40
Sanofi aventis	Dermatop [®] base cream	5F057A	32717	40
Actavis	Abitima [®] clinic face cream	158584	32723	40
Fagron	Versatile [™] Rich	1503257	32735	40
Bene	Thrombocid [®] ointment	408C141	32742	40
Allergika	Dermifant [®] kids lotion	1607080	32755	40
Dr. Wolff	Linola [®] body milk	606430	32765	40
Koko	DMS [®] base cream classic	L003E16	32788	40
Koko	DMS [®] base cream high classic	L003H16	32789	40
Koko	DMS [®] base cream classic	L003E16	32826	40
Koko	DMS [®] base cream high classic...	L018D16	32827	40
Fagron	Versatile [™] Rich	1503257	32841	40

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Supplier	Substance	Batch	Sample ID	Spectra
Bene	Thrombocid [®] ointment	409A151	32915	40
Chiesi	Asche Basis [®] lotion	53075A	32926	40
Chiesi	Asche Basis [®] cream	63351A	32928	40
Taoasis	Base cream Taoasis	161124-6322	32944	40
Taoasis	Base cream Taoasis	161124-6322	32945	40
Actavis	Abitima [®] clinic face cream	158584	32998	40
Actavis	Abitima [®] clinic body cream	40116	32999	40
Hans Karrer GmbH	Hans Karrer Lipocream MicroS...	17001	33196	40
Hans Karrer GmbH	Hans Karrer Lipocream MicroS...	16002	33197	40
Spirig Pharma	Excipial [®] U Lipolotio	T122	33204	40
Spirig Pharma	Excipial [®] U10 Lipolotio	T072	33205	40
Beiersdorf	Eucerinum O/W basis	64030208WA	33212	40
Spirig Pharma	Lipoderm [®] lotion	V012	33248	40
Dr. Wolff	Linola [®] body milk	609202	33258	40
Galderma Laboratorium G...	Excipial [®] U Lipolotio	T122	33269	40
Jenapharm	Neribas [®] cream	YY01FX3	33289	40
Galderma Laboratorium G...	Excipial [®] U Lipolotio	V011	33298	40
Koko	DMS [®] base cream high classic	L037K16	33433	40
Koko	DMS [®] base cream high classic	L037K16	33434	40
Chiesi	Asche Basis [®] cream	63354A	33435	40

- 14555 spectra from a total of 385 batches from further 155 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 652 spectra from 104 *Apo-Ident* customers from 334 batches from the substance/substance group *Hydrophilic ointments*.

Supplier	Substance	Batch	Spectra
Actavis	Abitima [®] clinic body cream	10915	2
Actavis/Noweda	Abitima [®] clinic body cream	21015	1
Actavis Deutschland GmbH	Abitima [®] clinic body cream	31015	1
Actavis	Abitima [®] clinic body cream	31015	2
Actavis	Abitima [®] clinic body cream	31114	1
Actavis/Gehe	Abitima [®] clinic body cream	81013	1
Actavis Deutschland GmbH	Abitima [®] clinic body cream	121115	1
Actavis/Phönix	Abitima [®] clinic face cream	159274	2
Actavis	Abitima [®] clinic face cream	160670	1
Actavis/Noweda	Abitima [®] clinic face cream	161423	1
Caelo	Abitima [®] clinic face cream	161468	2
A.H.D.	Abitima [®] clinic body cream	260515	2
Actavis/Noweda	Abitima [®] clinic body cream	260515	2
Persano/Gehe	Abitima [®] clinic face cream	57792	1
actavis	Abitima [®] clinic body cream	60513	2

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

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Supplier	Substance	Batch	Spectra
actavis/Gehe	Abitima [®] clinic body cream	60513	1
actavis	Abitima [®] clinic body cream	70513	1
Caelo	Abitima [®] clinic body cream	110712	2
actavis	Abitima [®] clinic body cream	140113	1
Actavis/Noweda	Abitima [®] clinic body cream	140113	1
Fagron	Abitima [®] clinic face cream	150203	2
Fagron	Abitima [®] clinic face cream	150204	1
Actavis/Noweda	Abitima [®] clinic face cream	150204	1
Actavis / Anzag	Abitima [®] clinic face cream	150237	1
Astellas Pharma	Abitima [®] clinic body cream	190213	1
Actavis Deutschland GmbH	Abitima [®] clinic body cream	350313	2
Actavis / Noweda	Abitima [®] clinic face cream	142371	1
Noweda	Abitima [®] clinic face cream	146735	1
Caelo	Abitima [®] clinic face cream	146735	1
Actavis / Anzag	Abitima [®] clinic face cream	148024	1
Actavis/GEHE	Abitima [®] clinic face cream	148051	1
Phoenix/actavis	Abitima [®] clinic face cream	148460	1
actavis	Abitima [®] clinic face cream	148495	1
Actavis/Noweda	Abitima [®] clinic face cream	148417	1
actavis	Abitima [®] clinic face cream	148496	2
Actavis/ Noweda	Abitima [®] clinic face cream	148496	1
Actavis/Gehe	Abitima [®] clinic face cream	148495	1
Actavis / Anzag	Abitima [®] clinic face cream	148503	1
Caelo	Abitima [®] clinic face cream	149666	2
actavis	Abitima [®] clinic face cream	150202	1
Sanacorp	Abitima [®] clinic body cream	12015/110/12	1
actavis	Abitima [®] clinic body cream	20912	2
Actavis	Abitima [®] clinic body cream	20912	1
Actavis/Gehe	Abitima [®] clinic body cream	51112	1
Sanacorp	Abitima [®] clinic body cream	51112	1
Abitima	Abitima [®] clinic body cream	52015/051112	1
Actavis/ Gehe	Abitima [®] clinic body cream	60513	1
Sanacorp	Abitima [®] clinic body cream	70512	1
Actavis/Sanacorp	Abitima [®] clinic body cream	110712	1
Actavis / Gehe	Abitima [®] clinic body cream	110712	1
actavis/ebert	Abitima [®] clinic body cream	110712	1
actavis/Gehe	Abitima [®] clinic body cream	112015	1
Sanacorp	Abitima [®] clinic body cream	140113	1
Roche/AHD	Abitima [®] clinic body cream	142620	1
Sanacorp	Abitima [®] clinic body cream	210612	1
Actavis/Noweda	Abitima [®] clinic body cream	370313	1
Chiesi	Asche Basis [®] cream	30102014A	1
Caelo	Asche Basis [®] lotion	32054A	1
Chiesi	Asche Basis [®] lotion	32054A	1
Chiesi	Asche Basis [®] cream	32233A	5
Chiesi/Noweda	Asche Basis [®] cream	32312A	1
Caelo	Asche Basis [®] lotion	33055A	3
chiesi/gehe	Asche Basis [®] lotion	33056A	2
Chiesi	Asche Basis [®] cream	33239A	2
Chiesi GmbH / Anzag	Asche Basis [®] cream	33244A	1
chiesi/gehe	Asche Basis [®] cream	33246A	2
Chiesi / Noweda	Asche Basis [®] cream	33246A	1
Chiesi	Asche Basis [®] lotion	333056A	2
chiesi/gehe	Asche Basis [®] lotion	34058A	1
Chiesi/AHD	Asche Basis [®] cream	34247A	1
Chiesi/Noweda	Asche Basis [®] cream	34247A	1
Chiesi GmbH / Sanacorp	Asche Basis [®] cream	34247A	1
Chiesi/Gehe	Asche Basis [®] cream	34248A	1
Chiesi	Asche Basis [®] cream	34248A	1
Chiesi	Asche Basis [®] cream	34249A	1

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Supplier	Substance	Batch	Spectra
Chiesi GmbH / Anzag	Asche Basis [®] cream	34249A	1
Chiesi	Asche Basis [®] cream	34250A	1
Chiesi/V.d.L.	Asche Basis [®] cream	34250A	1
Chiesi	Asche Basis [®] cream	34251A	3
Chiesi / Gehe	Asche Basis [®] cream	34252A	1
chiesi / Noweda	Asche Basis [®] cream	34250A	1
Chiesi	Asche Basis [®] lotion	41059A	1
Chiese	Asche Basis [®] lotion	41060A	1
Chiesi/Noweda	Asche Basis [®] cream	41255A	2
Chiesi	Asche Basis [®] cream	41258A	2
Chiesi/Noweda	Asche Basis [®] cream	41258A	2
Chiese	Asche Basis [®] cream	41259A	1
Chiesi/ Now	Asche Basis [®] cream	41259A	1
Chiesi GmbH / Anzag	Asche Basis [®] cream	41260A	1
Chiesi/Gehe	Asche Basis [®] cream	41260A	1
Chiesi	Asche Basis [®] cream	41260A	2
Chiesi	Asche Basis [®] cream	41261A	1
Caelo	Asche Basis [®] cream	41261A	1
Chiesi GmbH / Anzag	Asche Basis [®] cream	41261A	1
Chiesi/Gehe	Asche Basis [®] cream	41262A	1
Chiesi / Gehe	Asche Basis [®] cream	41265A	1
CHiesi	Asche Basis [®] cream	41264A	1
Chiesi/	Asche Basis [®] cream	41266A	1
Caelo	Asche Basis [®] cream	41265B	1
Chiesi GmbH / Anzag	Asche Basis [®] cream	42268A	2
Anzag/ Chiesi	Asche Basis [®] cream	42269A	1
Chiesi	Asche Basis [®] cream	42270A	1
Chiesi/Gehe	Asche Basis [®] cream	42271A	1
Chiesi	Asche Basis [®] cream	42271A	2
Chiesi	Asche Basis [®] cream	42272A	1
Anzag/ Chiesi GmbH	Asche Basis [®] cream	42272A	1
Anzag/ Chiesi GmbH	Asche Basis [®] cream	42273A	1
Chiesi/ Now	Asche Basis [®] cream	42273A	1
Chiesi/Noweda	Asche Basis [®] cream	42275A	2
Chiesi	Asche Basis [®] cream	42275A	1
Chiesi/ Phönix	Asche Basis [®] lotion	43066A	1
gehe/Chiesi	Asche Basis [®] lotion	43066A	1
Chiesi	Asche Basis [®] lotion	43066A	1
Chiesi/Phoenix	Asche Basis [®] cream	43278A	1
Chiesi	Asche Basis [®] cream	43279A	1
Chiesi	Asche Basis [®] cream	43278A	1
Chiesi	Asche Basis [®] cream	43280A	1
Chiesi/Noweda	Asche Basis [®] cream	43280A	1
Chiesi / Gehe	Asche Basis [®] cream	43281A	1
Chiesi/ Now	Asche Basis [®] cream	43282A	1
Chiesi/ Now	Asche Basis [®] cream	43283A	2
Chiesi/Noweda	Asche Basis [®] cream	43284A	1
Chiesi	Asche Basis [®] cream	43287A	1
Chiesi/Noweda	Asche Basis [®] cream	44288A	1
Chiesi/Alliance Healthc...	Asche Basis [®] cream	44290A	4
Chiesi GmbH / Phönix	Asche Basis [®] lotion	51067A	1
Chiesi/ Noweda	Asche Basis [®] cream	51292A	1
Chiesi/ Noweda	Asche Basis [®] cream	51294a	1
Chiesi	Asche Basis [®] cream	51294A	1
Chiesi	Asche Basis [®] cream	51296A	1
Gehe/Chiesi	Asche Basis [®] cream	51296A	1
Chiesi	Asche Basis [®] cream	51300A	4
Chiesi / Phoenix	Asche Basis [®] cream	51300A	1
Chiesi/Gehe	Asche Basis [®] cream	51301A	1
Chiesi	Asche Basis [®] cream	51305A	2

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Supplier	Substance	Batch	Spectra
Phoenix	Asche Basis [®] lotion	52069A	1
Gehe20.10.15	Asche Basis [®] lotion	52070A	1
Chiesi/Phoenix	Asche Basis [®] lotion	52070A	1
Caelo	Asche Basis [®] cream	52306A	3
noweda/chiesi	Asche Basis [®] cream	52306A	1
Chiesi	Asche Basis [®] cream	52307A	1
Chiesi/Gehe	Asche Basis [®] cream	52307A	1
Chiesi	Asche Basis [®] cream	52308A	2
Chiesi	Asche Basis [®] cream	52309A	1
Chiesi/Noweda	Asche Basis [®] cream	52316A	1
Chiesi/Noweda	Asche Basis [®] cream	52318a	1
Chiesi/Noweda	Asche Basis [®] cream	52318A	1
Chiesi GmbH	Asche Basis [®] cream	52319A	1
Chiesi/Noweda	Asche Basis [®] cream	52321A	1
Caelo	Asche Basis [®] cream	52322A	3
Chiesi / Phoenix	Asche Basis [®] cream	52323A	2
Chiesi	Asche Basis [®] cream	52322A	1
Fagron	Asche Basis [®] cream	52323A	4
Chiesi/Phönix	Asche Basis [®] lotion	53071A	1
Chiesi/Phoenix	Asche Basis [®] lotion	53071A	1
Caelo	Asche Basis [®] lotion	53072A	1
Caelo	Asche Basis [®] lotion	53073A	1
Chiesi/Fiebig	Asche Basis [®] lotion	53073A	2
Chiesi	Asche Basis [®] lotion	53075A	1
Chiesi/Anzag	Asche Basis [®] cream	53327A	1
Chiesi/Alliance Healthc...	Asche Basis [®] cream	53329A	1
Chiesi/Phönix	Asche Basis [®] cream	53329A	1
Chiesi	Asche Basis [®] cream	53330A	1
Caelo	Asche Basis [®] cream	53330A	1
Chiesi	Asche Basis [®] cream	53331A	2
Phoenix	Asche Basis [®] cream	53331A	1
Phoenix	Asche Basis [®] cream	54332A	1
Chiesi	Asche Basis [®] cream	54332A	1
Chiesi/Noweda	Asche Basis [®] lotion	61077A	1
Chiesi GmbH	Asche Basis [®] cream	61335A	1
Caelo	Asche Basis [®] cream	61341A	2
Caelo	Asche Basis [®] cream	61338A	1
PHÖNIX	Asche Basis [®] cream	62343A	1
Chiesi	Asche Basis [®] cream	63347A	3
Chiesi/Fiebig	Asche Basis [®] lotion	63980A	1
Noweda	Asche Basis [®] lotion	63980A	1
Chiesi	Asche Basis [®] lotion	64082A	1
Chiesi	Asche Basis [®] cream	64357A	3
Gehe	Asche Basis [®] cream	64358A	2
Chiesi	Asche Basis [®] cream	64360A	1
Chiesi GmbH / Anzag	Asche Basis [®] cream	22196A	1
Chiesi	Asche Basis [®] cream	14178A	1
Chisi	Asche Basis [®] cream	23203A	1
Anzag	Asche Basis [®] cream	23204A	1
Chiesi	Asche Basis [®] cream	23204A	1
Chiesi	Asche Basis [®] cream	23206A	1
chiesi / Noweda	Asche Basis [®] cream	23213A	1
Chiesi	Asche Basis [®] cream	24214A	2
Chiesi GmbH	Asche Basis [®] cream	24214A	2
Chiesi/Phoenix	Asche Basis [®] cream	24215A	1
Chiesi	Asche Basis [®] cream	24217A	1
Chiesi/Gehe	Asche Basis [®] cream	24218A	1
All.Heal./Chiesi	Asche Basis [®] cream	24218A	1
Chiesi	Asche Basis [®] cream	24219A	1
Chiesi	Asche Basis [®] cream	24220A	2

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Supplier	Substance	Batch	Spectra
Chiesi/Anzag	Asche Basis [®] cream	24221A	1
Chiesi/Gehe	Asche Basis [®] cream	24221A	4
Ichthyol/Sanacorp	Asche Basis [®] cream	24221A	1
Chiese	Asche Basis [®] cream	24221A	1
Chiesi/AHD	Asche Basis [®] cream	31222A	1
chiesi / Noweda	Asche Basis [®] cream	31222A	1
Chiesi GmbH / Anzag	Asche Basis [®] cream	31222A	1
Chiesi/AHD	Asche Basis [®] cream	31223A	1
Chiesi/Ebert	Asche Basis [®] cream	31224A	1
Chiesi/AHD	Asche Basis [®] cream	31224A	1
Chiesi/Noweda	Asche Basis [®] cream	31224A	1
Chiesi/Gehe	Asche Basis [®] cream	31224A	2
Caelo	Asche Basis [®] cream	31226A	1
chiesi / Jenne	Asche Basis [®] cream	31227a	1
Chiesi/Phoenix	Asche Basis [®] cream	31227A	2
Chiesi/Phoenix	Asche Basis [®] cream	31225A	1
chiesi / Noweda	Asche Basis [®] cream	31225A	1
Caelo	Asche Basis [®] cream	31227A	1
Chiesi/Sanacorp	Asche Basis [®] cream	31227A	1
Chiesi	Asche Basis [®] cream	31227A	2
Chiesi/AHD	Asche Basis [®] cream	31228A	2
Chiesi/Noweda	Asche Basis [®] cream	31229A	1
chiesi/gehe	Asche Basis [®] cream	31228A	1
Chiesi/Phoenix	Asche Basis [®] cream	31229A	1
Chiesi GmbH / Anzag	Asche Basis [®] cream	31229A	1
Chiesi GmbH / Anzag	Asche Basis [®] cream	31231A	2
Chiesi GmbH / Anzag	Asche Basis [®] cream	31230A	1
Chiesi	Asche Basis [®] cream	31232A	1
Chiesi/Noweda	Asche Basis [®] cream	31232A	2
Chiesi/Gehe	Asche Basis [®] cream	32233A	1
Gehe/Chiesi	Asche Basis [®] cream	32233A	1
Chiesi/Phoenix	Asche Basis [®] cream	32233A	1
Phönix	Asche Basis [®] cream	32234A	1
Chiesi/AHD	Asche Basis [®] cream	32234A	1
Chiesi/AHD	Asche Basis [®] cream	32235A	1
Chiesi	Asche Basis [®] cream	32235A	1
chiesi/gehe	Asche Basis [®] cream	32236A	1
Chiesi	Asche Basis [®] cream	32236A	1
Gehe	Asche Basis [®] cream	32236A	1
Euro OTC	Asche Basis [®] cream	3229A	2
Chiesi/ Noweda	Asche Basis [®] cream	33237A	1
Chiesi	Asche Basis [®] cream	33237A	1
Alliance Healthcare	Asche Basis [®] cream	33237A	1
Chiesi/Noweda	Asche Basis [®] cream	33237A	1
Chiesi/AHD	Asche Basis [®] cream	33238A	1
Chiesi / Noweda	Asche Basis [®] cream	33238A	1
Chiesi/ phoenix	Asche Basis [®] cream	33239A	1
Alliance Healthcare	Asche Basis [®] cream	33240A	1
Chiesi/ Now	Asche Basis [®] cream	33240A	1
Chiesi	Asche Basis [®] cream	33240A	1
Chiesi/ Noweda	Asche Basis [®] cream	33241A	1
Chiesi	Asche Basis [®] cream	33243A	1
Chiesi/AHD	Asche Basis [®] cream	33242A	1
Chiesi / Gehe	Asche Basis [®] cream	33244A	1
Gehe	Asche Basis [®] cream	33244A	1
Phoenix/Chiesi	Asche Basis [®] cream	33246A	1
Lamotte / Gehe	Asche Basis [®] cream	34247A	1
Chiesi/Gehe	Asche Basis [®] cream	34253A	1
Chiesi/AHD	Asche Basis [®] lotion	24049A	1
Chiesi/Noweda	Asche Basis [®] cream	53329A	1

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Supplier	Substance	Batch	Spectra
Chiesi/Gehe	Asche Basis [®] lotion	23047A	1
Chiesi/Noweda	Asche Basis [®] lotion	24049A	1
Chiesi/Anzag	Asche Basis [®] lotion	32054A	1
Taoasis	Base cream Taoasis	150219-4350	1
Taoasis	Base cream Taoasis	150326-5079	1
Taoasis	Base cream Taoasis	161124-6322	1
Taoasis	Base cream Taoasis	160201-6027	1
Taoasis	Base cream Taoasis	170110-6322	1
Sanofi/Gehe	Dermatop [®] base cream	4F050A	1
Sanofi/Noweda	Dermatop [®] base cream	5F056A	1
Sanofi/Noweda	Dermatop [®] base cream	5F055A	2
Sanofi/Anzag	Dermatop [®] base cream	5F056A	1
Sanofi	Dermatop [®] base cream	4F046A	1
Sanofi/Noweda	Dermatop [®] base cream	4F045A	1
Sanofi Aventis	Dermatop [®] base cream	4F046A	1
Sanofi/Anzag	Dermatop [®] base cream	5F051A	1
Allergika/Kehr	Dermifant [®] kids lotion	1604060	1
KOKO GmbH & Co. KG	DMS [®] base cream high classic...	L018D16	1
Caelo	DMS [®] base cream high classic	L010J15	1
KOKO GmbH & Co. KG	DMS [®] base cream high classic	L054B16	1
Koko GmbH & Co.Kg	DMS [®] base cream high classic	L060A15	1
KOKO GMBH	DMS [®] base cream high classic	L008I14	1
KOKO GMBH	DMS [®] base cream high classic	L031A14	1
Koko GmbH	DMS [®] base cream high classic	L031A14	1
KOKO	DMS [®] base cream high classic	L031A14	1
Beiersdorf AG	Eucerinum W/O basis	32930208WA	3
Beiersdorf	Eucerinum W/O basis	24072015A	1
Beiersdorf	Eucerinum W/O basis	34930308WA	5
Beiersdorf/Phoenix	Eucerinum W/O basis	34930308WA	1
Beiersdorf AG	Eucerinum W/O basis	34930308WA	1
Beiersdorf/Noweda	Eucerinum W/O basis	34930308WA	1
Beiersdorf/ Vedono	Eucerinum W/O basis	34930308WA	1
Beiersdorf/ Sanacorp	Eucerinum W/O basis	418301087WA	1
Beiersdorf/Noweda	Eucerinum W/O basis	41830108WA	2
Beiersdorf AG	Eucerinum W/O basis	41830108WA	1
Beiersdorf	Eucerinum W/O basis	41830108WA	2
Caelo	Eucerinum W/O basis	41830108WA	3
Beiersdorf/Noweda	Eucerinum W/O basis	41830108wa	1
BDF	Eucerinum W/O basis	41830108WA	1
Ph.Eur.8.0	Eucerinum W/O basis	41830108WA	1
Baiersdorf	Eucerinum W/O basis	41839108WA	1
Baiersdorf	Eucerinum W/O basis	43430208WA	1
BDF / Noweda	Eucerinum W/O basis	43430208WA	1
Gehe/Beiersdorf	Eucerinum W/O basis	51630108WA	1
Beiersdorf	Eucerinum W/O basis	51630108WA	4
Beiersdorf/Noweda	Eucerinum W/O basis	51630108wa	1
Beiersdorf/Noweda	Eucerinum W/O basis	51630108WA	2
Noweda/BDF	Eucerinum W/O basis	51630108WA	1
Rondell Apotheke	Eucerinum W/O basis	51630108WA	1
Beiersdorf AG	Eucerinum W/O basis	51630108WA	2
Caelo	Eucerinum W/O basis	51630108WA	1
Beiersdorf/AHD	Eucerinum O/W basis	51630108WA	1
Beiersdorf AG/Noweda	Eucerinum O/W basis	53430208WA	1
Caelo	Eucerinum W/O basis	53430208WA	4
Beiersdorf	Eucerinum W/O basis	53430208WA	1
Beiersdorf/Kehr	Eucerinum O/W basis	53430208WA	3
Beiersdorf/Kehr	Eucerinum O/W basis	61130108WA	1
Beiersdor	Eucerinum W/O basis	541830108WA	1
Beiersdorf/ Noweda	Eucerinum W/O basis	64030108WA	1
Caelo	Eucerinum W/O basis	64030108WA	2

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Supplier	Substance	Batch	Spectra
Beiersdorf/Kehr	Eucerinum W/O basis	64030108WA	1
Beiersdorf/AHD	Eucerinum O/W basis	64030208WA	1
Beiersdorf/VDL	Eucerinum O/W basis	64030208WA	1
Caelo	Eucerinum O/W basis	13730308WA	1
Beiersdorf AG	Eucerinum O/W basis	2483030308WA	1
Beiersdorf	Eucerinum O/W basis	24830308WA	1
Hersteller: Beiersdorf/...	Eucerinum O/W basis	24830308WA	1
Beiersdorf AG	Eucerinum O/W basis	24830308WA	1
Beiersdorf	Eucerinum O/W basis	319030108WA	1
Caelo	Eucerinum O/W basis	31930108WA	1
Beiersdorf/Gehe	Eucerinum O/W basis	31930108WA	1
Beiersdorf	Eucerinum O/W basis	51630108WA	1
Beiersdorf	Eucerinum O/W basis	53430208WA	1
Noweda	Eucerinum W/O basis	4730308WA	1
Beiersdorf	Eucerinum W/O basis	21430108WA	2
Beiersdorf	Eucerinum W/O basis	24830208WA	1
beiersdorf	Eucerinum W/O basis	24830208WA	1
BDF / Sanacorp	Eucerinum W/O basis	21430108WA	1
Baiersdorf	Eucerinum W/O basis	24830208WA	1
Beiersdorf/Sanacorp	Eucerinum W/O basis	31230108WA	1
Beiersdorf/Anzag	Eucerinum W/O basis	31230108WA	1
BDF	Eucerinum W/O basis	31230108WA	1
beiersdorf	Eucerinum W/O basis	31230108WA	1
Beiersdorf/Noweda	Eucerinum W/O basis	31230108WA	1
Beiersdorf	Eucerinum W/O basis	31230108wa	1
BeiersdorfPhoenix	Eucerinum W/O basis	31230108WA	1
Beiersdorf	Eucerinum W/O basis	32930208WA	4
Beiersdorf AG/Noweda	Eucerinum W/O basis	31230108WA	1
Beiersdorf	Eucerinum W/O basis	31230108WA	1
Gehe	Eucerinum W/O basis	32930208WA	1
eucerinum	Eucerinum W/O basis	41830108WA	1
Beiersdorf	Eucerinum W/O basis	516301328wa	1
Spirig Pharma AG	Excipial [®] hydro cream	813993/12	1
galderma/G	Excipial [®] U Lipolotio	L0TS202	1
Spierig/Gehe	Excipial [®] hydro cream	R014	1
Spirig	Excipial [®] hydro cream	R014	2
Spirig	Excipial [®] U Lipolotio	R047	1
Caelo	Excipial [®] hydro cream	R045	1
Galderma (Spirig Pharma...	Excipial [®] U Lipolotio	R061	1
Spirig/Galderma	Excipial [®] U Lipolotio	R146	1
Spirig/Galderma	Excipial [®] U Lipolotio	R156	2
Galderma	Excipial [®] U Lipolotio	R167	2
Galderma / Kehr	Excipial [®] U Lipolotio	R167	1
Galderma	Excipial [®] U Lipolotio	R168	1
Galderma / Kehr	Excipial [®] U Lipolotio	R171	1
Galderma	Excipial [®] U Lipolotio	R171	1
Caelo	Excipial [®] U Lipolotio	R186	1
Galderma/Gehe	Excipial [®] U Lipolotio	R189	1
Spirig/Gehe	Excipial [®] U Lipolotio	R262	1
Sprig (Galderma)/ G	Excipial [®] U Lipolotio	S123	1
Galderma/Galderma	Excipial [®] U Lipolotio	s017	1
Galderma/Galderma	Excipial [®] U Lipolotio	S017	1
Galderma/Galderma	Excipial [®] hydro cream	S024	2
Galderma/ Sana	Excipial [®] hydro cream	S024	1
Spirig	Excipial [®] hydro cream	S025	6
Galderma/ Sana	Excipial [®] hydro cream	S025	1
spirig	Excipial [®] hydro cream	s025	1
Jenne	Excipial [®] hydro cream	S041	1
Galderma	Excipial [®] hydro cream	S054	1
Galderma/Phönix	Excipial [®] hydro cream	S045	1

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Supplier	Substance	Batch	Spectra
Spirig Pharma/ G	Excipial [®] hydro cream	S053	1
Galderma/Noweda	Excipial [®] hydro cream	S054	1
Galderma/Galderma	Excipial [®] hydro cream	S054	1
Galderma	Excipial [®] U Lipolotio	S064	1
Galderma/Kehr	Excipial [®] U Lipolotio	S071	1
Galderma	Excipial [®] U Lipolotio	S091	1
Phoenix	Excipial [®] U Lipolotio	S091	1
Spirig Pharma	Excipial [®] U Lipolotio	S122	1
Gehe	Excipial [®] U Lipolotio	S132	1
Phoenix	Excipial [®] U Lipolotio	S138	2
Galderma/Galderma	Excipial [®] U Lipolotio	S142	1
Gehe	Excipial [®] U Lipolotio	S143	1
Spirig/Fiebig	Excipial [®] U Lipolotio	S143	1
Galderma	Excipial [®] U Lipolotio	S147	1
Phoenix	Excipial [®] U Lipolotio	S148	1
Galderma/Kehr	Excipial [®] U Lipolotio	S203	1
Galderma/Anzag	Excipial [®] U Lipolotio	S206	1
Caelo	Excipial [®] U Lipolotio	S206	1
Galderma/Alliance Healt...	Excipial [®] hydro cream	S025	1
Galderma/Galderma	Excipial [®] hydro cream	so25	1
Spirig (Galderma)	Excipial [®] hydro cream	T011	1
Spirig (Galderma)	Excipial [®] hydro cream	T012	2
Galderma / Kehr	Excipial [®] U Lipolotio	T029	2
PHÖNIX	Excipial [®] U Lipolotio	T063	1
Kehr/Galderma	Excipial [®] U Lipolotio	T029	1
Spirig (Galderma)	Excipial [®] hydro cream	V011	2
Spirig Pharma/Gehe	Excipial [®] hydro cream		1
Spirig/Noweda	Excipial [®] U Lipolotio	LOTN113	1
Spirig Pharma AG/ Anzag	Excipial [®] hydro cream	LOTN034	1
Spirig / Anzag	Excipial [®] hydro cream	LOTN043	1
Spirig /Gehe	Excipial [®] hydro cream	LOTN044	1
Spirig/AHD	Excipial [®] U Lipolotio	lotno86	1
Spirig Pharma AG/ Anzag	Excipial [®] hydro cream	LOTR013	1
Phoenix/Spirig	Excipial [®] hydro cream	N044	1
Fischar	Excipial [®] U Lipolotio	LOTN085	1
Spirig / Gehe	Excipial [®] hydro cream	N011	1
spirig	Excipial [®] hydro cream	N034	2
Spirig / Noweda	Excipial [®] hydro cream	N035	1
Spirig/Noweda	Excipial [®] U10 Lipolotio	N043	1
spirig	Excipial [®] hydro cream	N043	2
Spirig	Excipial [®] hydro cream	N043	1
Spirig/Noweda	Excipial [®] hydro cream	N043	1
spirig	Excipial [®] hydro cream	N045	2
spirig	Excipial [®] U Lipolotio	N058	3
Spirig/Noweda	Excipial [®] U Lipolotio	N061	1
Spirig	Excipial [®] U Lipolotio	N123	1
Fagron	Excipial [®] U Lipolotio	N168	2
spirig	Excipial [®] hydro cream	No14	1
Spirig	Excipial [®] U Lipolotio	N086	1
Spirig Pharma	Excipial [®] hydro cream	N044	1
AHD	Excipial [®] hydro cream	R011	1
Spirig	Excipial [®] hydro cream	R013	1
spirig	Excipial [®] hydro cream	R013	2
spirig	Excipial [®] U Lipolotio	R037	1
Spirig / Sanacorp	Excipial [®] U Lipolotio	R041	1
Galderma / Galderma	Excipial [®] U Lipolotio	R086	1
Galderma	Excipial [®] U Lipolotio	R111	1
Galderma/Noweda	Excipial [®] U Lipolotio	R124	1
Spirig Pharma	Excipial [®] hydro cream	813993/10	1
Spirig / Anzag	Excipial [®] hydro cream	813993/09	1

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Supplier	Substance	Batch	Spectra
Spirig / Anzag	Excipial [®] hydro cream	813993/10	1
spirig	Excipial [®] hydro cream	813993/10	1
Spirig	Excipial [®] hydro cream	K013	1
Spirig Pharma	Excipial [®] hydro cream	LON014	1
Sanacorp	Excipial [®] hydro cream	LOTN011	1
Spirig/Anzag	Excipial [®] hydro cream	LOTM041	1
Spirig/Gehe	Excipial [®] hydro cream	M012	1
spirig	Excipial [®] hydro cream	M014	2
Phoenix/Spirig	Excipial [®] hydro cream	M015	1
spirig	Excipial [®] hydro cream	M041	1
spirig	Excipial [®] hydro cream	M034	1
Spirig Pharma	Excipial [®] hydro cream	N011	1
Sanacorp	Excipial [®] hydro cream	N011	1
Spirig / Anzag	Excipial [®] hydro cream	N034	1
Phoenix/Spirig	Excipial [®] hydro cream	N034	1
Spirig/Anzag	Excipial [®] hydro cream	N035	1
Spirig Pharma	Excipial [®] hydro cream	N013	1
Spirig	Excipial [®] hydro cream	N035	1
Alliance/Spirig	Excipial [®] hydro cream	N043	1
Spirig Pharma AG/GEHE	Excipial [®] hydro cream	R011	1
Spirig/ Noweda	Excipial [®] U Lipolotio	LOTN027	1
Spirig Pharma	Excipial [®] U Lipolotio	LOTK131	1
Spirig Pharma	Excipial [®] U Lipolotio	LOTN013	1
Spirig/ Noweda	Excipial [®] U Lipolotio	LOTN056	1
Spirig/AHD	Excipial [®] U Lipolotio	M085	1
Spirig	Excipial [®] U Lipolotio	M091	1
Spirig/Gehe	Excipial [®] U Lipolotio	M102	2
Spirig Pharma	Excipial [®] U Lipolotio	M134	1
spirig	Excipial [®] U Lipolotio	M142	1
Spirig/Gehe	Excipial [®] U Lipolotio	M146	1
Spirig/Gehe	Excipial [®] U Lipolotio	M182	1
Spirig / Anzag	Excipial [®] U Lipolotio	M182	1
Spirig/Noweda	Excipial [®] U Lipolotio	N027	1
Spirig / Anzag	Excipial [®] U Lipolotio	N032	1
Spirig / Anzag	Excipial [®] U Lipolotio	N041	1
Phoenix/Spirig	Excipial [®] U Lipolotio	N041	1
Spirig/AHD	Excipial [®] U Lipolotio	N058	1
spirig	Excipial [®] U Lipolotio	N061	1
spirig	Excipial [®] U Lipolotio	N013	1
Phoenix	Excipial [®] U Lipolotio	N105	1
Spirig/Noweda	Excipial [®] U Lipolotio	N032	1
spirig	Excipial [®] U Lipolotio	N086	1
Spirig/AHD	Excipial [®] U10 Lipolotio	M025	1
Galderma	Lipoderm [®] lotion	R044	2
Spirig Pharma / Allianc...	Lipoderm [®] lotion	R044	3
Galderma/Kehr	Lipoderm [®] lotion	S021	2
Spirig/AllianceHC	Lipoderm [®] lotion	S021	3
Galderma	Lipoderm [®] lotion	S021	1
Galderma/Phoenix	Lipoderm [®] lotion	S041	1
Spirig	Lipoderm [®] lotion	S041	2
Galderma/AllianceHC	Lipoderm [®] lotion	T011	2
Jenne	Lipoderm [®] lotion	T011	1
Galderma	Lipoderm [®] lotion	T011	1
Spirig Pharma AG/Allian...	Lipoderm [®] lotion	R011	4
Spirig Pharma AG/Allian...	Lipoderm [®] lotion	N041	1
Galderma /AllianceHC	Lipoderm [®] lotion	T043	2
Spirig/AHD	Lipoderm [®] lotion	LOTN041	1
Spirig	Lipoderm [®] lotion	LOTR011	1
Spirig	Lipoderm [®] lotion	R011	2
Spirig Pharma AG/Allian...	Lipoderm [®] lotion	R023	8

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Supplier	Substance	Batch	Spectra
Spirig	Lipoderm [®] lotion	R023	2
Spirig/Phoenix	Lipoderm [®] lotion	M065	4
Spirig Pharma AG	Lipoderm [®] lotion	N041	1
Spirig/AHD	Lipoderm [®] lotion	N041	1
Spirig Pharma AG/Allian...	Lipoderm [®] lotion	N041	1
Jenapharm/Gehe	Neribas [®] cream	YY005HT	1
Jenapharm/Gehe	Neribas [®] cream	YY006KY	1
Intendis / Sanacorp	Neribas [®] cream	24105A	1
Jenapharm/Alliance	Neribas [®] cream	YY000C3	1
Jenapharm/Alliance	Neribas [®] cream	YY001HS	1
Bayer/ Sanacorp	Neribas [®] cream	YY002L6	1
Intendis GmbH	Neribas [®] cream	24089A	1
Intendis / Gehe	Neribas [®] cream	21076A	1
Chiesi / Gehe	Neribas [®] cream	32097A	1
Jenapharm / Gehe	Neribas [®] cream	34104C	1

- 2147 spectra from 259 *Apo-Ident* customers from a total of 1148 batches from a further 101 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	2341	0	13 918
Type B	0	1696	53	14 296
Type C	0	602	50	2140

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9461 %)	100.0000 % (> 99.7437 %)
Type B	100.0000 % (> 99.9443 %)	96.9697 % (> 96.7982 %)
Type C	100.0000 % (> 98.2353 %)	92.3313 % (> 91.8712 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	33.80
30635	30635	0.00	29.36
30713	30713	0.00	38.11
30725	30725	0.00	36.31
30732	30732	0.00	35.83
30733	30733	0.00	41.24
30772	30772	0.00	27.09
30775	30775	0.00	39.63
30828	30828	0.00	22.93
30845	30845	0.00	16.04
30847	30847	0.00	17.68
30971	30971	0.00	13.57
30993	30993	0.00	43.80
31041	31041	0.00	20.05
31050	31050	0.00	37.41
31058	31058	0.00	35.62
31061	31061	0.00	31.46
31064	31064	0.00	14.80
31066	31066	0.00	37.84
31067	31067	0.00	34.09
31068	31068	0.00	20.10
31072	31072	0.00	40.14
31085	31085	0.00	36.34
31089	31089	0.00	20.99
31095	31095	0.00	38.41
31098	31098	0.00	25.90
31115	31115	0.00	16.79
31234	31234	0.00	30.75
31236	31236	0.00	33.64
31280	31280	0.00	30.57
31281	31281	0.00	40.69
31307	31307	0.00	14.36
31308	31308	0.00	45.75
31309	31309	0.00	33.19
31494	31494	0.00	30.64
31511	31511	0.00	27.14
31535	31535	0.00	38.71
31539	31539	0.00	29.75
31578	31578	0.00	19.46
31868	31868	0.00	33.58
31869	31869	0.00	12.23
31870	31870	0.00	42.49
31874	31874	0.00	28.96
32177	32177	0.00	30.26
32178	32178	0.00	33.47
32179	32179	0.00	16.59
32767	32767	0.00	36.09
32916	32916	0.00	35.03

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32942	32942	0.00	17.81
32997	32997	0.00	30.44
33194	33194	0.00	26.64
33195	33195	0.00	29.34
33208	33208	0.00	25.04
33213	33213	0.00	30.79
33270	33270	0.00	35.78

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Hyssop oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30537-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hyssop oil; Oleum hyssopus officinalis

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Hyssop oil	31823-118643	31649	40	not required
Taoasis	Hyssop oil	33065-122200	31782	40	not required
Apotheker Bau...	Hyssop oil	13.201345120.16.02	31850	40	not required
Taoasis	Hyssop oil	1616260-125049	32980	40	not required

Validation samples

A total of 35 362 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 *Hyssop oil*. These samples are listed above in the [calibration samples](#) section.
- 16 099 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 140 spectra of 5 reference samples from the substance/substance group *Hyssop oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Hyssop oil	pending	30537	40
Taoasis	Hyssop oil	31823-118643	31649 [†]	20
Taoasis	Hyssop oil	33065-122200	31782 [†]	20
Apotheker Bauer & Cie	Hyssop oil	13.201345120.16.02	31850 [†]	20
Apotheker Bauer & Cie	Hyssop oil	13.201604082.17.01	32923	40

- 16 164 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Hyssop oil	31095-105392	1

- 2798 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *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 *Hyssop oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	16 099
Type B	0	140	0	16 164
Type C	0	1	0	2798

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 98.3099 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31649	31649	0.00	33.88
31782	31782	0.00	31.77
31850	31850	0.00	29.62
32980	32980	0.00	20.42

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Immortelle oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30450-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Immortelle oil	L24113D-113148BAG90451	31138	40	not required
Taoasis	Immortelle oil	L24415DN-122092BAG90451	32069	40	not required

Validation samples

A total of 35 362 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 *Immortelle oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 140 spectra of 4 reference samples from the substance/substance group *Immortelle oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Immortelle oil	L03111DN-102431	30450	40
Taoasis	Immortelle oil	L24415DN-122092BAG90451	32069 [†]	20
Taoasis	Immortelle oil	L17716DN-126770	32975	40
Taoasis	Immortelle oil	L17716DN-124955	33021	40

- 16 164 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 6 spectra from 3 *Apo-Ident* customers from 5 batches from the substance/substance group *Immortelle oil*.

Supplier	Substance	Batch	Spectra
Taoasis	Immortelle oil	L03111DN	1

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

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Supplier	Substance	Batch	Spectra
Taoasis	Immortelle oil	L38914DN-118878	2
Taoasis	Immortelle oil	33111D	1
Taoasis	Immortelle oil	L13613DN	1
Fagron	Immortelle oil	L10712D-111673	1

- 2793 spectra from 265 *Apo-Ident* customers from a total of 1469 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	140	0	16 164
Type C	0	4	2	2793

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 98.2399 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31138	31138	0.00	39.82
32069	32069	0.00	38.59

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Juniper oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31559-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Juniper oil; Juniperi aetheroleum; Oleum juniperi e baccararum

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Juniper oil	4155-120900	31687	40	not required
Taoasis	Juniper oil	02JB0B-126047	32809	40	not required

Validation samples

A total of 35 362 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 *Juniper oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Juniper oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Juniper oil	4155-116757	31559 [†]	20
Taoasis	Juniper oil	4155-120900	31687 [†]	20
Taoasis	Juniper oil	2JB0B-127283	32932	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Juniper oil	155-118896	1
Caelo	Juniper oil	16160706	1

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	80	0	16 224
Type C	0	2	0	2797

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31559	31559	0.00	22.28
31687	31687	0.00	24.37
32809	32809	0.00	21.44

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **La Roche-Posay Cold Cream Naturel**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30829-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

La Roche-Posay Cold Cream Naturel

Special notes

When selecting the *La Roche-Posay Cold Cream Naturel* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required

Validation samples

A total of 35 362 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 Cold Cream Naturel*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *La Roche-Posay Cold Cream Naturel*.

Supplier	Substance	Batch	Sample ID	Spectra
La Roche-Posay	La Roche-Posay Cold Cream Na...	54LN1P	31765 [†]	20
La Roche-Posay	La Roche-Posay Cold Cream Na...	54M51P	33262	40

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 3 spectra from 1 *Apo-Ident* customers from 3 batches from the substance/substance group *La Roche-Posay Cold Cream Naturel*.

Supplier	Substance	Batch	Spectra
La Roche-Posay	La Roche-Posay Cold Cream Na...	54M01P	1
La Roche-Posay	La Roche-Posay Cold Cream Na...	54M11P	1
La Roche-Posay	La Roche-Posay Cold Cream Na...	54M91P	1

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

- 2796 spectra from 265 *Apo-Ident* customers from a total of 1471 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	60	0	16 244
Type C	0	3	0	2796

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.2539 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30829	30829	0.00	95.96
31074	31074	0.00	90.47
31765	31765	0.00	86.58

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe

mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **La Roche-Posay Toleriane**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30827-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

La Roche-Posay Toleriane

Special notes

When selecting the *La Roche-Posay Toleriane* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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 35 362 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.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 40 spectra of 1 reference samples from the substance/substance group *La Roche-Posay Toleriane*.

Supplier	Substance	Batch	Sample ID	Spectra
La Roche-Posay	La Roche-Posay Toleriane	54N600	32759	40

- 16 264 spectra from a total of 425 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *La Roche-Posay Toleriane*.

Supplier	Substance	Batch	Spectra
Caelo	La Roche-Posay Toleriane	54J500	1
Roche/AHD	La Roche-Posay Toleriane	54J800	1

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	40	0	16 264
Type C	0	2	0	2797

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	24.59
31094	31094	0.00	14.08
32563	32563	0.00	18.41

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR

bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Lavender oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30961-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lavender oil; Lavendula officinalis oleum; Oleum lavendula officinalis

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Lavender oil	L16812DN-108661BAG90451	30961	40	not required
Taoasis	Lavender oil	110186BAG90451	30962	40	not required
Taoasis	Lavender oil	22015-121843	31756	40	not required

Validation samples

A total of 35 362 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 *Lavender oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 112 spectra of 4 reference samples from the substance/substance group *Lavender oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Lavender oil	22015-121843	31756 [†]	20
Taoasis	Lavender oil	2/2015-125808I09	33015	40
Taoasis	Lavender oil	22015-125925I10	33016	40
Taoasis	Lavender oil	2/2015-125808I09	not required	12

- 16 192 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 5 spectra from 4 *Apo-Ident* customers from 5 batches from the substance/substance group *Lavender oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis/Noweda	Lavender oil	16716-126380/11	1
Bombastus	Lavender oil	300666	1
Taoasis	Lavender oil	22015-125927	1
Taoasis	Lavender oil	34/151/16	1
Bergland	Lavender oil	K502790	1

- 2794 spectra from 264 *Apo-Ident* customers from a total of 1469 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lavender 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 *Lavender oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	112	0	16 192
Type C	0	3	2	2794

The substance/substance group *Lavender 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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 94.6429 %)
Type C	100.0000 % (> 98.2427 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30961	30961	0.00	28.93
30962	30962	0.00	16.93
31756	31756	0.00	12.17

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Lemon grass oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30661-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required

Validation samples

A total of 35 362 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 *Lemon grass oil*. These samples are listed above in the [calibration samples](#) section.
- 16 099 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Lemon grass oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Lemon grass oil	130930-116754	31549 [†]	20
Taoasis	Lemon grass oil	1448-127048	32977	40
Bombastus	Lemon grass oil	294338	33012	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 6 *Apo-Ident* customers from 8 batches from the substance/substance group *Lemon grass oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Bombastus	Lemon grass oil	270423	1
Taoasis	Lemon grass oil	130930-115336	1
Taoasis	Lemon grass oil	FFL457-123568	1
Taoasis	Lemon grass oil	8911011-121890	1
Taoasis	Lemon grass oil	1663-125423	1
Taoasis	Lemon grass oil	13131-112982	1
Primavera	Lemon grass oil	11401144	1
Taoasis	Lemon grass oil	532897-111140	1

- 2791 spectra from 265 *Apo-Ident* customers from a total of 1466 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	160	0	16 099
Type B	0	96	4	16 204
Type C	0	7	1	2791

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9402 %)	96.0000 % (> 93.0000 %)
Type C	100.0000 % (> 98.2363 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	47.19
31185	31185	0.00	41.19
31187	31187	0.00	38.86
31549	31549	0.00	46.35

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Lime oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31544-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lime oil; Oleum citrus aurantifolia

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Lime oil	059-117571	31544	40	not required
Taoasis	Lime oil	867-124956	32976	40	not required

Validation samples

A total of 35 362 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 *Lime oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

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

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Lime oil	59-117571	31544 [†]	20
Taoasis	Lime oil	59-117571	31654	60
Taoasis	Lime oil	867-124956	32800	40

- 16 184 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Taoasis	Lime oil	867-124956	1

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

- 2798 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	120	0	16 184
Type C	0	1	0	2798

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.3099 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31544	31544	0.00	67.98
32976	32976	0.00	70.09

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das

alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Liniment ointments**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30731-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Liniment ointments; Amciderm[®] Base cream; Excipial[®] U Hydrolotio; Linola[®] Ö/W cream; Linola[®] Sept; Nourivan[™] Antiox

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Spirig Pharma	Excipial [®] U Hydr...	M016	30731	40	not required
Dr. Wolff	Linola [®] Ö/W cream	238482	30834	40	not required
Spirig Pharma	Excipial [®] U Hydr...	M063	31073	40	not required
Dr. Wolff	Linola [®] Sept	334080	31079	40	not required

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Dr. Wolff	Linola [®] Ö/W cream	334010	31133	40	not required
Spirig Pharma	Excipial [®] U Hydr...	N013	31279	40	not required
Dr. Wolff	Linola [®] Ö/W cream	432480	31312	40	not required
Fagron	Nourivan [™] Antiox	14C11-T09-010959	31495	40	not required
Almirall	Amciderm [®] Base c...	313311	31509	40	not required
Spirig Pharma	Excipial [®] U Hydr...	R014	31536	40	not required
Almirall	Amciderm [®] Base c...	313311	31628	55	not required
Dr. Wolff	Linola [®] Sept	509361	31856	40	not required
Fagron	Nourivan [™] Antiox	1503258	31958	30	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 525 spectra of 13 reference samples from the substance/substance group *Liniment ointments*. These samples are listed above in the [calibration samples](#) section.
- 15 734 spectra from a total of 364 batches from further 139 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 410 spectra of 13 reference samples from the substance/substance group *Liniment ointments*.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Nourivan [™] Antiox	14C11-T09-010959	31495 [†]	20
Almirall	Amciderm [®] Base cream	313311	31509 [†]	20
Spirig Pharma	Excipial [®] U Hydrolotio	R014	31536 [†]	20
Almirall	Amciderm [®] Base cream	313311	31628 [†]	20
Dr. Wolff	Linola [®] Sept	509361	31856 [†]	20
Fagron	Nourivan [™] Antiox	1503258	31958 [†]	30
Almirall	Amciderm [®] Base cream	538331	32758	40
Dr. Wolff	Linola [®] Sept	603190	32760	40
Fagron	Nourivan [™] Antiox	1503258	32778	40
Fagron	Nourivan [™] Antiox	1503258	32822	40
Spirig Pharma	Excipial [®] U Hydrolotio	S061	33206	40
Dr. Wolff	Linola [®] Sept	603190	33257	40
Dr. Wolff	Linola [®] Ö/W cream	610960	33259	40

- 15 894 spectra from a total of 417 batches from further 172 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 30 *Apo-Ident* customers from 57 batches from the substance/substance group *Liniment ointments*.

Supplier	Substance	Batch	Spectra
Caelo	Excipial [®] U Hydrolotio	L0TR092	1
Galderma/Noweda	Excipial [®] U Hydrolotio	R054	1
Spirig Pharma AG/ NOWEDA	Excipial [®] U Hydrolotio	L0TN022	1
Galderma	Excipial [®] U Hydrolotio	L0TR054	1
Spirig	Excipial [®] U Hydrolotio	N013	1
Spirig	Excipial [®] U Hydrolotio	N013	1
Phoenix/Spirig	Excipial [®] U Hydrolotio	M016	1
Dr. Wolff	Linola [®] Ö/W cream	610960	1
Dr. Wolff	Linola [®] Ö/W cream	505200	4
Dr. August Wolff	Linola [®] Ö/W cream	505560	1
Dr. Wolff	Linola [®] Ö/W cream	510792	1
Dr. Wolff	Linola [®] Ö/W cream	602190	3
Sanofi/Noweda	Linola [®] Ö/W cream	602300	1
Caelo	Linola [®] Ö/W cream	602310	1
Dr. August Wolff	Linola [®] Ö/W cream	605560	1
Dr. Wolff/Gehe	Linola [®] Ö/W cream	606100	1
Dr. Wolff GmbH / Phoenix	Linola [®] Ö/W cream	606100	1
Dr. August Wolff	Linola [®] Ö/W cream	607140	1
Dr. August Wolff	Linola [®] Ö/W cream	608900	1
Dr. Wolff/Gehe	Linola [®] Ö/W cream	138350	1
Dr. Wolff	Linola [®] Ö/W cream	434430	3
Dr. Wolff	Linola [®] Ö/W cream	438200	2
Dr. Wolff/Gehe	Linola [®] Ö/W cream	438360	1
Dr. Wolff	Linola [®] Ö/W cream	438200	1
Dr. Wolff	Linola [®] Ö/W cream	504100	1
Dr. Wolff/Noweda	Linola [®] Ö/W cream	505280	1
Dr. Wolff/Malteser	Linola [®] Ö/W cream	338990	1
Wolff / Noweda	Linola [®] Ö/W cream	431120	4
Wolff / Gehe	Linola [®] Ö/W cream	431130	3
Dr. Wolff/Noweda	Linola [®] Ö/W cream	431130	2
Dr. Wolff	Linola [®] Ö/W cream	431200	3
Dr. August Wolff/Ebert	Linola [®] Ö/W cream	431250	1
Dr. Wolff	Linola [®] Ö/W cream	432480	1
Dr. Wolff/Gehe	Linola [®] Ö/W cream	432490	2
Dr. August Wolff/Ebert	Linola [®] Ö/W cream	432970	1
Dr. Wolff	Linola [®] Ö/W cream	432490	1
wolff	Linola [®] Ö/W cream	434320	1
Dr. Wolff/Gehe	Linola [®] Ö/W cream	434320	2

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

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Supplier	Substance	Batch	Spectra
AHD	Linola [®] Ö/W cream	437110	1
Dr. Wolff	Linola [®] Ö/W cream	435530	1
Dr. Wolff	Linola [®] Ö/W cream	437120	1
Dr. August Wolff	Linola [®] Ö/W cream	233140	1
Dr. Wolff/Noweda	Linola [®] Ö/W cream	438350	2
Dr. Wolff	Linola [®] Ö/W cream	233200	1
Dr. Wolff/Noweda	Linola [®] Ö/W cream	233200	1
Caelo	Linola [®] Ö/W cream	438350	1
DR. WOLFF	Linola [®] Ö/W cream	234192	1
Dr. Wolff/ Anzag	Linola [®] Ö/W cream	234193	1
Caelo	Linola [®] Ö/W cream	236281	1
Dr. Wolff	Linola [®] Ö/W cream	238482	1
Dr. Wolff	Linola [®] Ö/W cream	236290	1
Caelo	Linola [®] Ö/W cream	238484	1
Dr. Wolff	Linola [®] Ö/W cream	238484	1
Wolff/AHD	Linola [®] Ö/W cream	238520	2
Dr. Wolff/Gehe	Linola [®] Ö/W cream	238520	1
Dr. Wolff	Linola [®] Ö/W cream	238520	2
Dr. Wolff/Anzag	Linola [®] Ö/W cream	238520	2
Caelo	Linola [®] Ö/W cream	238530	2
Dr. Wolff	Linola [®] Ö/W cream	238530	1
Dr. Wolff	Linola [®] Ö/W cream	238530	4
Caelo	Linola [®] Ö/W cream	239181	1
Dr. Wolff/Malteser	Linola [®] Ö/W cream	330751	1
Caelo	Linola [®] Ö/W cream	330760	2
chiesi / Noweda	Linola [®] Ö/W cream	331460	1
Wolff/Sanacorp	Linola [®] Ö/W cream	333630	2
Phoenix/Wolff	Linola [®] Ö/W cream	333640	1
Dr. Wolff	Linola [®] Ö/W cream	333640	1
Dr. August Wolff/Ebert	Linola [®] Ö/W cream	333640	2
Euro OTC	Linola [®] Ö/W cream	333730	1
Dr. Wolff/Malteser	Linola [®] Ö/W cream	333880	1
Dr. Wolff	Linola [®] Ö/W cream	334003	1
Dr. Wolff / Sanacorp	Linola [®] Ö/W cream	338990	3
Dr. Wolff	Linola [®] Ö/W cream	435080	1
Dr. Wolff/GEHE	Linola [®] Ö/W cream	437110	1

- 2694 spectra from 265 *Apo-Ident* customers from a total of 1420 batches from a further 115 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	525	0	15 734
Type B	0	341	69	15 883
Type C	0	104	1	2694

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9462 %)	100.0000 % (> 98.8571 %)
Type B	100.0000 % (> 99.9404 %)	83.1707 % (> 82.4390 %)
Type C	100.0000 % (> 98.2266 %)	99.0476 % (> 96.1905 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30731	30731	0.00	12.53
30834	30834	0.00	16.35
31073	31073	0.00	12.21
31079	31079	0.00	21.16
31133	31133	0.00	16.86
31279	31279	0.00	12.16
31312	31312	0.00	22.83
31495	31495	0.00	19.90
31509	31509	0.00	25.50
31536	31536	0.00	12.22
31628	31628	0.00	26.08
31856	31856	0.00	18.87
31958	31958	0.00	21.56

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Linola[®] fat creme / Linola[®] H fat N / Alfason[®] R...**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30724-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Linola[®] fat creme / Linola[®] H fat N / Alfason[®] Repair; Alfason[®] Repair; Linola[®] fat cream;
Linola[®] H fat N

Special notes

When selecting the *Linola[®] fat creme / Linola[®] H fat N / Alfason[®] Repair* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Linola[®] fat creme / Linola[®] H fat N / Alfason[®] Repair*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Astellas Pharma	Alfason [®] Repair	12F18/77	30724	50	not required
Dr. Wolff	Linola [®] fat cream	235260	30771	40	not required
Astellas Pharma	Alfason [®] Repair	13E16/76	31069	40	not required
Dr. Wolff	Linola [®] H fat N	333080	31092	40	not required

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Dr. Wolff	Linola [®] fat cream	337280	31096	40	not required
Astellas Pharma	Alfason [®] Repair	16G60/75	32993	40	not required
Dr. Wolff	Linola [®] H fat N	611060	33211	40	not required
Dr. Wolff	Linola [®] fat cream	611011	33243	40	not required
Dr. Wolff	Linola [®] fat cream	612211	33260	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 370 spectra of 9 reference samples from the substance/substance group *Linola[®] fat creme / Linola[®] H fat N / Alfason[®] Repair*. These samples are listed above in the [calibration samples](#) section.
- 15 889 spectra from a total of 366 batches from further 141 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 205 spectra of 6 reference samples from the substance/substance group *Linola[®] fat creme / Linola[®] H fat N / Alfason[®] Repair*.

Supplier	Substance	Batch	Sample ID	Spectra
Dr. Wolff	Linola [®] H fat N	231610	30576	40
Astellas Pharma	Alfason [®] Repair	12F18/77	30724 [†]	5
Dr. Wolff	Linola [®] H fat N	603230	32560	40
Dr. Wolff	Linola [®] fat cream	603820	32561	40
Astellas Pharma	Alfason [®] Repair	15K07/77	32562	40
Dr. Wolff	Linola [®] H fat N	611060	33038	40

- 16 099 spectra from a total of 420 batches from further 174 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B*

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

section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 14 *Apo-Ident* customers from 18 batches from the substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair*.

Supplier	Substance	Batch	Spectra
Phoenix	Alfason® Repair	15/03/75	1
Phönix	Alfason® Repair	15J09/75	1
Astellas	Alfason® Repair	13H02/76	1
Sanofi/Noweda	Linola® fat cream	501000	1
Wolff/Noweda	Linola® fat cream	501230	1
dr.wolff	Linola® fat cream	337770	1
Dr. Wolff / Gehe	Linola® fat cream	337860	1
Wolff / Wolff	Linola® fat cream	431190	1
Dr.Wolff/NOW	Linola® fat cream	435160	1
Caelo	Linola® fat cream	435161	1
Dr. Wolff	Linola® fat cream	437270	1
Caelo	Linola® fat cream	438070	1
Löwen City-Apotheke Bar...	Linola® fat cream	231060	1
Dr. Wolff /Anzag	Linola® fat cream	237710	1
Dr. Wolff	Linola® fat cream	237920	1
Caelo	Linola® fat cream	238540	1
Phönix	Linola® fat cream	238540	1
dr.wolff	Linola® fat cream	337760	1
Dr. Wolff	Linola® fat cream	432591	1
Wolff/Phönix	Linola® fat cream	337770	1

- 2779 spectra from 265 *Apo-Ident* customers from a total of 1456 batches from a further 115 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	370	0	15 889
Type B	0	203	2	16 081
Type C	0	19	1	2779

The substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair* can be clearly distinguished from all other substances. In order to make these figures comparable, the

weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9462 %)	100.0000 % (> 98.3784 %)
Type B	100.0000 % (> 99.9409 %)	99.0244 % (> 97.5610 %)
Type C	100.0000 % (> 98.2300 %)	95.0000 % (> 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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30724	30724	0.00	20.04
30771	30771	0.00	19.90
31069	31069	0.00	8.23
31092	31092	0.00	20.30
31096	31096	0.00	22.23
32993	32993	0.00	14.44
33211	33211	0.00	25.98
33243	33243	0.00	25.98
33260	33260	0.00	24.56

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Lipolotio urea 5% F body lotion**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30973-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required

Validation samples

A total of 35 362 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 *Lipolotio urea 5% F body lotion*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Lipolotio urea 5% F body lotion*.

Supplier	Substance	Batch	Sample ID	Spectra
Allergika	Lipolotio urea 5% F body lot...	13112021	31766 [†]	20
Allergika	Lipolotio urea 5% F body lot...	1502011	32766	40

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Lipolotio urea 5% F body lotion*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	60	0	16 244
Type C	0	0	0	2799

The substance/substance group *Lipolotio urea 5% F body lotion* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30973	30973	0.00	26.82
31766	31766	0.00	41.55

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Lygal® head ointment N 3%**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31049-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lygal® head ointment N 3%*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taurus	Lygal® head oint...	124311	31049	40	not required
Taurus	Lygal® head oint...	143710	31763	40	not required
Taurus	Lygal® head oint...	160732	33261	40	not required

Validation samples

A total of 35 362 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 *Lygal[®] head ointment N 3%*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Lygal[®] head ointment N 3%*.

Supplier	Substance	Batch	Sample ID	Spectra
Taurus	Lygal [®] head ointment N 3%	143710	31763 [†]	20
Taurus	Lygal [®] head ointment N 3%	160732	32763	40

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Lygal[®] head ointment N 3%*.

Supplier	Substance	Batch	Spectra
TaurusPharma/Noweda	Lygal [®] head ointment N 3%	141703	1
Taurus Pharma	Lygal [®] head ointment N 3%	134507	1

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

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lygal*[®] *head ointment N 3%* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lygal*[®] *head ointment N 3%* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	60	0	16 244
Type C	0	2	0	2797

The substance/substance group *Lygal*[®] *head ointment N 3%* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31049	31049	0.00	35.00
31763	31763	0.00	33.48
33261	33261	0.00	32.03

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe

mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Lygal[®] ointment base**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31014-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lygal[®] ointment base

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taurus	Lygal [®] ointment ...	121302P	31014	40	not required
Taurus	Lygal [®] ointment ...	124904P	31704	40	not required
Taurus	Lygal [®] ointment ...	154841	32749	40	not required
Taurus	Lygal [®] ointment ...	164201	32772	40	not required
Taurus	Lygal [®] ointment ...	164201	33244	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Lygal[®] ointment base*. These samples are listed above in the [calibration samples](#) section.
- 16 059 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Lygal[®] ointment base*.

Supplier	Substance	Batch	Sample ID	Spectra
Taurus	Lygal [®] ointment base	124904P	31704 [†]	20
Taurus	Lygal [®] ointment base	164201	33297	40

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 6 *Apo-Ident* customers from 10 batches from the substance/substance group *Lygal[®] ointment base*.

Supplier	Substance	Batch	Spectra
Taurus/ Phönix	Lygal [®] ointment base	133401T	1

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

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Supplier	Substance	Batch	Spectra
TAUROS PHARMA	Lygal [®] ointment base	141601P	1
Caelo	Lygal [®] ointment base	141601P	1
Taurus	Lygal [®] ointment base	141601T	1
TAUROS PHARMA	Lygal [®] ointment base	141602T	1
Taurus	Lygal [®] ointment base	141603	2
Taurus	Lygal [®] ointment base	133402	1
TAUROS PHARMA	Lygal [®] ointment base	154841	1
TAUROS PHARMA	Lygal [®] ointment base		1
TAUROS PHARMA	Lygal [®] ointment base	124803	1
Taurus	Lygal [®] ointment base	124803	2
Taurus Pharma	Lygal [®] ointment base	133401P	1
Taurus Pharma	Lygal [®] ointment base	133401T	2
Taurus	Lygal [®] ointment base	133401T	2

- 2781 spectra from 265 *Apo-Ident* customers from a total of 1464 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	200	0	16 059
Type B	0	50	10	16 244
Type C	0	18	0	2781

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9464 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9404 %)	83.3333 % (> 78.3333 %)
Type C	100.0000 % (> 98.2305 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31014	31014	0.00	21.89
31704	31704	0.00	20.27
32749	32749	0.00	26.46
32772	32772	0.00	34.02
33244	33244	0.00	29.25

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Manuka oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31545-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Manuka oil	14286-119821	31655	40	not required

Validation samples

A total of 35 362 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 *Manuka oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 120 spectra of 4 reference samples from the substance/substance group *Manuka oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Manuka oil	1235-116650	31545 [†]	20
Taoasis	Manuka oil	14286-119821	31655 [†]	20
Taoasis	Manuka oil	42798-125299	32799	40
Taoasis	Manuka oil	42798-125299	33198	40

- 16 184 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 4 batches from the substance/substance group *Manuka oil*.

Supplier	Substance	Batch	Spectra
Taoasis	Manuka oil	23694-122415	1

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

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Supplier	Substance	Batch	Spectra
Taoasis	Manuka oil	23694-123569	1
Taoasis	Manuka oil	36968-121509	1
Taoasis	Manuka oil	42798-125299	2

- 2794 spectra from 265 *Apo-Ident* customers from a total of 1470 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	110	10	16 184
Type C	0	4	1	2794

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 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	91.6667 % (> 89.1667 %)
Type C	100.0000 % (> 98.2427 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	35.16
31655	31655	0.00	34.92

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Marjoram oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30454-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Marjoram oil; Majoranae aetheroleum; Oleum Majoranae

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Marjoram oil	130312-111991BAG90451	31137	40	not required
Taoasis	Marjoram oil	3701004-121123	32067	40	not required
Caelo	Marjoram oil	16170005	32819	40	not required

Validation samples

A total of 35 362 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 *Marjoram oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 140 spectra of 4 reference samples from the substance/substance group *Marjoram oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Marjoram oil	29293-98717	30454	40
Taoasis	Marjoram oil	3701004-121123	32067 [†]	20
Taoasis	Marjoram oil	1838-125624	32478	40
Caelo	Marjoram oil	16170005	32919	40

- 16 164 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 25 spectra from 8 *Apo-Ident* customers from 16 batches from the substance/substance group *Marjoram oil*.

Supplier	Substance	Batch	Spectra
Caelo	Marjoram oil	12041602	7

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

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Supplier	Substance	Batch	Spectra
Taoasis	Marjoram oil	130312-111347	1
Taoasis	Marjoram oil	130312-111870	1
Caelo	Marjoram oil	13041601	1
Taoasis	Marjoram oil	130910-116960	1
Taoasis	Marjoram oil	130910-117430	1
Caelo	Marjoram oil	13121301	1
Caelo	Marjoram oil	15051505	1
Taoasis	Marjoram oil	1631-122347	1
Taoasis	Marjoram oil	1631-124621	1
Taoasis/Gehe	Marjoram oil	29293-98717	1
Taoasis	Marjoram oil	3701004-119994	2
Caelo	Marjoram oil	13041603	2
Caelo	Marjoram oil	13041606	1
Caelo	Marjoram oil	14198304	1
Taoasis	Marjoram oil	29293-98717	1
Bombastus	Marjoram oil	278279	1

- 2774 spectra from 265 *Apo-Ident* customers from a total of 1458 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	120	0	16 139
Type B	0	138	2	16 164
Type C	0	17	8	2774

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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9401 %)	98.5714 % (> 96.4286 %)
Type C	100.0000 % (> 98.2292 %)	68.0000 % (> 56.0000 %)

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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	70.04
32067	32067	0.00	51.98
32819	32819	0.00	45.77

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Matricaria oil, morrocan**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30844-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Matricaria oil, morrocan; Oleum ormenis multicaulis; Ormenis multicaulis oleum

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Matricaria oil, ...	6121017-122184	31841	40	not required
Taoasis	Matricaria oil, ...	1629-124596	32269	40	not required

Validation samples

A total of 35 362 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 *Matricaria oil, morrocan*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 160 spectra of 5 reference samples from the substance/substance group *Matricaria oil, morrocan*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Matricaria oil, morrocan	6982-1074109BAC90451	30844	40
Taoasis	Matricaria oil, morrocan	140124-116959	31579 [†]	20
Taoasis	Matricaria oil, morrocan	6121017-122184	31841 [†]	20
Taoasis	Matricaria oil, morrocan	1629-125295	32480	40
Taoasis	Matricaria oil, morrocan	1814-126707	33020	40

- 16 144 spectra from a total of 421 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Matricaria oil, morrocan*.

[†]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*.

Supplier	Substance	Batch	Spectra
	Matricaria oil, morrocan	6995	1
Taoasis	Matricaria oil, morrocan	6159-93239	1
Taoasis	Matricaria oil, morrocan	6631-104465	1

- 2796 spectra from 265 *Apo-Ident* customers from a total of 1471 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	140	20	16 144
Type C	0	1	2	2796

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9400 %)	87.5000 % (> 85.6250 %)
Type C	100.0000 % (> 98.2539 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31579	31579	0.00	60.10
31841	31841	0.00	59.55
32269	32269	0.00	54.35

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Matricaria oil, roman**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31254-2017-09-08
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:

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Matricaria oil, ...	8941-125875	32796	40	not required

Validation samples

A total of 35 362 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 *Matricaria oil, roman*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Matricaria oil, roman*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Matricaria oil, roman	1850119-119823	31686 [†]	20
Taoasis	Matricaria oil, roman	8941-125875	32978	40

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 7 batches from the substance/substance group *Matricaria oil, roman*.

Supplier	Substance	Batch	Spectra
Taoasis	Matricaria oil, roman	1511-122183	1

continued on the next page

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

continued from previous page

Supplier	Substance	Batch	Spectra
Taoasis	Matricaria oil, roman	1850119-116753	1
Taoasis	Matricaria oil, roman	1850119-119451	1
Taoasis	Matricaria oil, roman	1850119-118138	1
Taoasis	Matricaria oil, roman	1850119-121467	1
Taoasis	Matricaria oil, roman	1638-123706	1
Taoasis	Matricaria oil, roman	8941-125875	1

- 2792 spectra from 265 *Apo-Ident* customers from a total of 1467 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	60	0	16 244
Type C	0	7	0	2792

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.2379 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31254	31254	0.00	27.50
31686	31686	0.00	27.04
32796	32796	0.00	34.98

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Mountain pine oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31542-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mountain pine oil; Oleum pini pumilionis; Pini pumilionis aetherolum

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Mountain pine oil	586-116867	31542	40	not required
Taoasis	Mountain pine oil	25599-120877	31689	40	not required
Taoasis	Mountain pine oil	8783-127273	32937	40	not required

Validation samples

A total of 35 362 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 *Mountain pine oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 85 spectra of 4 reference samples from the substance/substance group *Mountain pine oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Mountain pine oil	586-116867	31542 [†]	20
Taoasis	Mountain pine oil	25599-120877	31689 [†]	20
Taoasis	Mountain pine oil	8783-125163	32811	40
Taoasis	Mountain pine oil	8783-125163	not required	5

- 16 219 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 3 spectra from 1 *Apo-Ident* customers from 3 batches from the substance/substance group *Mountain pine oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Mountain pine oil	6635-122703	1
Taoasis	Mountain pine oil	8238-124968	1
Taoasis	Mountain pine oil	8238-126318	1

- 2796 spectra from 265 *Apo-Ident* customers from a total of 1471 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mountain 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 *Mountain pine oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	70	15	16 219
Type C	0	1	2	2796

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9402 %)	82.3529 % (> 78.8235 %)
Type C	100.0000 % (> 98.2539 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31542	31542	0.00	27.30
31689	31689	0.00	27.65
32937	32937	0.00	33.30

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Myrrh oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30748-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Myrrh oil	41197-124418BAG90451	32271	40	not required
Taoasis	Myrrh oil	41197-126694	33051	40	not required

Validation samples

A total of 35 362 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 *Myrrh oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Myrrh oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Myrrh oil	22920-105398BAG90451	30748	40
Taoasis	Myrrh oil	30007-120958	31692 [†]	20
Taoasis	Myrrh oil	41197-126694	33050	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Taoasis	Myrrh oil	2067-107953	1

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

- 2798 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	60	40	16 204
Type C	0	0	1	2798

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9402 %)	60.0000 % (> 57.0000 %)
Type C	100.0000 % (> 98.3099 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	145.09
32271	32271	0.00	198.57
33051	33051	0.00	185.98

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Labor-

prüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Neroli oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31260-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Neroli oil; Oleum citrus aurantium var. amara; Oleum neroli

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Neroli oil	91029-115714	31260	40	not required
Taoasis	Neroli oil	6142-120057BAG90451	31695	40	not required
Taoasis	Neroli oil	125052-124958	32805	40	not required

Validation samples

A total of 35 362 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 *Neroli oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 60 spectra of 2 reference samples from the substance/substance group *Neroli oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Neroli oil	6142-120057BAG90451	31695 [†]	20
Taoasis	Neroli oil	125052-124958	33042	40

- 16 244 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	60	0	16 244
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	54.18
31695	31695	0.00	69.01
32805	32805	0.00	26.17

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Neuroderm[®] care lotion / moisturising cream**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30722-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Neuroderm[®] care lotion / moisturising cream; Neuroderm[®] care lotion; Neuroderm[®] moisturising cream

Special notes

When selecting the *Neuroderm[®] care lotion / moisturising cream* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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[®] care lotion / moisturising cream*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Infectopharm	Neuroderm [®] moist...	S041214.1	30722	40	not required
Infectopharm	Neuroderm [®] care ...	S041204.1	31070	40	not required
Infectopharm	Neuroderm [®] moist...	S021307.1	31102	40	not required
Infectopharm	Neuroderm [®] moist...	S101428.1	31761	40	not required
Infectopharm	Neuroderm [®] care ...	S031505.1	31772	40	not required

Validation samples

A total of 35 362 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 *Neuroderm[®] care lotion / moisturising cream*. These samples are listed above in the [calibration samples](#) section.
- 16 059 spectra from a total of 370 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 200 spectra of 6 reference samples from the substance/substance group *Neuroderm[®] care lotion / moisturising cream*.

Supplier	Substance	Batch	Sample ID	Spectra
Infectopharm	Neuroderm [®] moisturising cream	S101428.1	31761 [†]	20
Infectopharm	Neuroderm [®] care lotion	S031505.1	31772 [†]	20
Infectopharm	Neuroderm [®] care lotion	S111514.1	32740	40
Infectopharm	Neuroderm [®] moisturising cream	S051612.1	32905	40
Infectopharm	Neuroderm [®] moisturising cream	S051612.1	32906	40
Infectopharm	Neuroderm [®] care lotion	S081610.1	33286	40

- 16 104 spectra from a total of 421 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Neuroderm[®] care lotion / moisturising cream*.

[†]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*.

Supplier	Substance	Batch	Spectra
Infectopharm	Neuroderm [®] moisturising cream		6
Infectopharm/Kehr	Neuroderm [®] moisturising cream		1
Infectopharm/Gehe	Neuroderm [®] moisturising cream	S0315081	1
Infectopharm/Fiebig	Neuroderm [®] moisturising cream		1
Bombastus	Neuroderm [®] moisturising cream		1
Noweda	Neuroderm [®] moisturising cream		1
Infectopharm/Noweda	Neuroderm [®] care lotion		2
Sanacorp	Neuroderm [®] moisturising cream		1
infectopharm	Neuroderm [®] moisturising cream		1
Infectpharm/ Noweda	Neuroderm [®] moisturising cream		1

- 2783 spectra from 265 *Apo-Ident* customers from a total of 1459 batches from a further 115 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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[®] care lotion / moisturising 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 *Neuroderm[®] care lotion / moisturising cream* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	16 059
Type B	0	200	0	16 089
Type C	0	16	0	2782

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9464 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9409 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 98.2404 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30722	30722	0.00	17.21
31070	31070	0.00	24.26
31102	31102	0.00	15.35
31761	31761	0.00	17.02
31772	31772	0.00	21.80

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Neuroderm[®] moisturising cream lipo**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30721-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Infectopharm	Neuroderm [®] moist...	S031202.1	30721	40	not required
Infectopharm	Neuroderm [®] moist...	S031506.1	31672	40	not required

Validation samples

A total of 35 362 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 *Neuroderm[®] moisturising cream lipo*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Neuroderm[®] moisturising cream lipo*.

Supplier	Substance	Batch	Sample ID	Spectra
Infectopharm	Neuroderm [®] moisturising crea...	S031506.1	31672 [†]	20
Infectopharm	Neuroderm [®] moisturising crea...	S071617.2	32739	40
Infectopharm	Neuroderm [®] moisturising crea...	S021706.1	33287	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Infectopharm	Neuroderm [®] moisturising crea...		1
Infectopharm/AHD	Neuroderm [®] moisturising crea...		1

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

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	100	0	16 204
Type C	0	2	0	2797

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	30.35
31672	31672	0.00	23.99

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Labor-

prüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Nicotine**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31019-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	1410523
Roth	Nicotine	194210173	31518	40	not required
Roth	Nicotine	116210173	31948	30	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 130 spectra of 4 reference samples from the substance/substance group *Nicotine*. These samples are listed above in the [calibration samples](#) section.
- 16 129 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 65 spectra of 4 reference samples from the substance/substance group *Nicotine*.

Supplier	Substance	Batch	Sample ID	Spectra
Roth	Nicotine	451178717	30376	10
Roth	Nicotine	194210173	31508 [†]	20
Roth	Nicotine	194210173	31518 [†]	20
Roth	Nicotine	116210173	31948 [†]	15

- 16 239 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	130	0	16 129
Type B	0	65	0	16 239
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.3846 %)
Type B	100.0000 % (> 99.9404 %)	100.0000 % (> 90.7692 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	172.94
31508	31508	0.00	171.00
31518	31518	0.00	172.03
31948	31948	0.00	172.89

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe

von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Ointment ash basis / Neribas®**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30774-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ointment ash basis / Neribas®; Asche Basis® ointment; Neribas® ointment

Special notes

When selecting the *Ointment ash basis / Neribas®* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

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

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Ointment ash basis / Neribas®*. These samples are listed above in the [calibration samples](#) section.
- 16 019 spectra from a total of 372 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 200 spectra of 5 reference samples from the substance/substance group *Ointment ash basis / Neribas®*.

Supplier	Substance	Batch	Sample ID	Spectra
Jenapharm	Neribas [®] ointment	YY00TJ0	32564	40
Chiesi	Asche Basis [®] ointment	61067A	32590	40
Chiesi	Asche Basis [®] ointment	61067A	32924	40
Chiesi	Asche Basis [®] ointment	61067A	32927	40
Jenapharm	Neribas [®] ointment	YY016EC	33288	40

- 16 104 spectra from a total of 423 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 54 spectra from 20 *Apo-Ident* customers from 30 batches from the substance/substance group *Ointment ash basis / Neribas®*.

Supplier	Substance	Batch	Spectra
Chiese	Asche Basis [®] ointment	31045A	4
Chiesi/AHD	Asche Basis [®] ointment	32048A	2
Chiesi / Gehe	Asche Basis [®] ointment	33050A	1
Chiesi	Asche Basis [®] ointment	41052A	1
Chiesi/Noweda	Asche Basis [®] ointment	41053A	1
Chiesi/Sanacorp	Asche Basis [®] ointment	41053A	1
Chiesi	Asche Basis [®] ointment	41054A	3
chiesi	Asche Basis [®] ointment	42055A	1
Chiesi/Gehe	Asche Basis [®] ointment	42056A	1
chiesi	Asche Basis [®] ointment	44057A	1
Chiesi/Phönix	Asche Basis [®] ointment	51059A	1
Chiesi	Asche Basis [®] ointment	51060A	1
CHIESI/ NOWEDA	Asche Basis [®] ointment	51060A	2
Chiesi	Asche Basis [®] ointment	52062A	2
Chiesi GmbH	Asche Basis [®] ointment	53065A	1
Caelo	Asche Basis [®] ointment	61067A	1
Caelo	Asche Basis [®] ointment	63068A	2
Chiesi GmbH	Asche Basis [®] ointment	21039A	1
Anzag/Ichtyol-Gesellsch. . .	Asche Basis [®] ointment	23043A	1
Chiesi/Phoenix	Asche Basis [®] ointment	23042A	1
Phönix	Asche Basis [®] ointment	31047A	1
Chiesi/AHD	Asche Basis [®] ointment	31047A	1
Caelo	Asche Basis [®] ointment	31047A	1
Chiesi	Asche Basis [®] ointment	32048A	1
Chiesi/AHD	Asche Basis [®] ointment	33049A	1
Chiesi / Gehe	Asche Basis [®] ointment	33049A	1
Chiesi	Asche Basis [®] ointment	33049A	1
Chiesi	Asche Basis [®] ointment	34051A	1
Jenapharm/ Sanacorp	Neribas [®] ointment	YY006JT	3
Jenapharm	Neribas [®] ointment	YY006JT	1
Caelo	Neribas [®] ointment	YY00CC8	1
Jenapharm/ Anzag	Neribas [®] ointment	YY00K7E	2
Jenapharm / Anzag	Neribas [®] ointment	YY00THL	1
Jenapharm/ Sanacorp	Neribas [®] ointment	YY00THL	1
Jenapharm/Noweda	Neribas [®] ointment	YY00THL	1
Caelo	Neribas [®] ointment	YY00TJ0	1
Jenapharm/ Anzag	Neribas [®] ointment	YY00XEH	2
Caelo	Neribas [®] ointment	YY00XEH	1
Jenapharm	Neribas [®] ointment	YY00XEH	1
Caelo	Neribas [®] ointment	YY016LN	1
Jenapharm	Neribas [®] ointment	YY017LF	1

- 2745 spectra from 263 *Apo-Ident* customers from a total of 1444 batches from a further 115 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	240	0	16 019
Type B	0	198	2	16 064
Type C	0	52	2	2745

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9463 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9409 %)	99.0000 % (> 97.5000 %)
Type C	100.0000 % (> 98.2274 %)	96.2963 % (> 90.7407 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	35.23
30833	30833	0.00	36.47
30969	30969	0.00	34.23
30994	30994	0.00	30.69
31080	31080	0.00	35.41
31093	31093	0.00	25.91

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Orange aroma**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31190-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Orange aroma

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Fagron	Orange aroma	13H23-B41-295530	31510	40	not required
Caelo	Orange aroma	163470	33100	40	20161221*

Validation samples

A total of 35 362 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 *Orange aroma*. These samples are listed above in the [calibration samples](#) section.
- 16 099 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 140 spectra of 4 reference samples from the substance/substance group *Orange aroma*.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Orange aroma	11069914	30335	40
Symrise	Orange aroma	113	30414	40
Fagron	Orange aroma	13H23-B41-295530	31510 [†]	20
Caelo	Orange aroma	162063	32331	40

- 16 164 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 52 spectra from 25 *Apo-Ident* customers from 29 batches 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.

[†]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*.

Supplier	Substance	Batch	Spectra
Caelo	Orange aroma	13330207	1
Caelo	Orange aroma	13406101	2
Caelo	Orange aroma	13406104	1
Caelo	Orange aroma	13406108	3
Caelo	Orange aroma	14150703	1
Caelo	Orange aroma	14150706	6
Caelo	Orange aroma	14150707	3
Caelo	Orange aroma	14150714	1
Caelo	Orange aroma	14352903	1
Caelo	Orange aroma	14352904	2
Fagron	Orange aroma	14352904	1
Caelo	Orange aroma	15215401	1
Caelo	Orange aroma		1
Caelo	Orange aroma	15215402	3
Caelo	Orange aroma	15215403	2
Caelo	Orange aroma	15215408	1
Caelo	Orange aroma	15215410	1
Audor Pharma	Orange aroma	15215409	1
Caelo	Orange aroma	16056105	3
Allergika/Kehr	Orange aroma	16056107	1
Caelo	Orange aroma	16056108	1
Caelo	Orange aroma	12149707	1
Caelo	Orange aroma	12216712	2
Caelo	Orange aroma	12356503	2
Caelo	Orange aroma	12356502	2
Sanacorp	Orange aroma	12356503	1
Caelo	Orange aroma	13123305	2
Caelo	Orange aroma	13123309	2
Caelo	Orange aroma	13330206	1
Caelo	Orange aroma	23051201	1
Caelo	Orange aroma	25031304	1

- 2747 spectra from 263 *Apo-Ident* customers from a total of 1445 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	160	0	16 099
Type B	0	124	16	16 164
Type C	0	51	1	2747

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 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9401 %)	88.5714 % (> 86.4286 %)
Type C	100.0000 % (> 98.2275 %)	98.0769 % (> 92.3077 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	90.55
31402	31402	0.00	87.54
31510	31510	0.00	168.06
33100	33100	0.00	91.07

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Oregano oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31554-2017-09-08
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:

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Oregano oil	0131022-117999	31554	40	not required
Taoasis	Oregano oil	7921018-119483	31779	40	not required
Taoasis	Oregano oil	43878A-125814	32769	40	not required

Validation samples

A total of 35 362 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 *Oregano oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Oregano oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Oregano oil	131022-117999	31554 [†]	20
Taoasis	Oregano oil	7921018-119483	31779 [†]	20
Taoasis	Oregano oil	43878A-123201	32939	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Oregano oil*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	80	0	16 224
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	101.21
31779	31779	0.00	134.74
32769	32769	0.00	44.44

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Palmarosa oil, organic**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30597-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Palmarosa oil, organic; Oleum cymbopogon martinii; 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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Palmarosa oil, o...	4941003-126708	33043	40	not required

Validation samples

A total of 35 362 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 *Palmarosa oil, organic*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 140 spectra of 4 reference samples from the substance/substance group *Palmarosa oil, organic*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Palmarosa oil, organic	17524-105015BAG90451	30597	40
Taoasis	Palmarosa oil, organic	17524-105015BAG90451	30671	40
Taoasis	Palmarosa oil, organic	2461021-121891	31828 [†]	20
Taoasis	Palmarosa oil, organic	4941003-126708	33044	40

- 16 164 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 4 spectra from 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Palmarosa oil, organic*.

Supplier	Substance	Batch	Spectra
Taoasis/Taoasis	Palmarosa oil, organic	121018-111872	1

continued on the next page

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

continued from previous page

Supplier	Substance	Batch	Spectra
Taoasis	Palmarosa oil, organic	121018-111094	1
Taoasis	Palmarosa oil, organic	121018-111872	2

- 2795 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	139	1	16 164
Type C	0	4	0	2795

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	99.2857 % (> 97.1429 %)
Type C	100.0000 % (> 98.2469 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31828	31828	0.00	158.62
33043	33043	0.00	149.31

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Panthenol ointment Lichtenstein**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30727-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required

Validation samples

A total of 35 362 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 *Panthenol ointment Lichtenstein*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Panthenol ointment Lichtenstein*.

Supplier	Substance	Batch	Sample ID	Spectra
Zentiva Pharma GmbH	Panthenol ointment Lichtenst...	EH4594	31764 [†]	20
Zentiva Pharma GmbH	Panthenol ointment Lichtenst...	GC5567	33284	40
Zentiva Pharma GmbH	Panthenol ointment Lichtenst...	GD5661	33425	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	100	0	16 204
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30727	30727	0.00	287.78
31091	31091	0.00	280.84
31764	31764	0.00	229.98

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Patchouli oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31547-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Patchouli oil	130930-112789	31547	40	not required
Caelo	Patchouli oil	14167204	31619	40	not required
Taoasis	Patchouli oil	FFL735-123003	32172	40	not required
Taoasis	Patchouli oil	1633-126207	33031	40	not required

Validation samples

A total of 35 362 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 *Patchouli oil*. These samples are listed above in the [calibration samples](#) section.
- 16 099 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Patchouli oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Patchouli oil	130930-112789	31547 [†]	20
Caelo	Patchouli oil	14167204	31619 [†]	20
Taoasis	Patchouli oil	1633-126207	33032	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Patchouli oil	130930-116684	1
Taoasis	Patchouli oil	33474-119161	1

- 2797 spectra from 265 *Apo-Ident* customers from a total of 1472 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	160	0	16 099
Type B	0	80	0	16 224
Type C	0	1	1	2797

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9403 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2679 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	26.97
31619	31619	0.00	32.68
32172	32172	0.00	35.65
33031	33031	0.00	27.17

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Peppermint oil
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	30930-2017-09-08
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Peppermint oil; Menthae piperitae aetheroleum; Oleum menthae piperitae dopp. rectific.

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
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 35 362 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 *Peppermint oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 2 reference samples from the substance/substance group *Peppermint oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Peppermint oil	2016104277-126375	32804	40
Taoasis	Peppermint oil	104277-126684	33030	40

- 16 224 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 6 *Apo-Ident* customers from 12 batches from the substance/substance group *Peppermint oil*.

Supplier	Substance	Batch	Spectra
Caelo	Peppermint oil	12114225	1
Taoasis/Kehr	Peppermint oil	127711	1
Fagron	Peppermint oil	15B11-B08-304117	1
Taoasis	Peppermint oil	24699-117643	1

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Supplier	Substance	Batch	Spectra
Taoasis	Peppermint oil	40076-120885	1
Bombastus	Peppermint oil	286204	1
Taoasis/ Kehr	Peppermint oil	41798-120746H08	1
Taoasis	Peppermint oil	41798-121607	1
Taoasis	Peppermint oil	52216-123564	1
Taoasis	Peppermint oil	63561-125104	1
Taoasis	Peppermint oil	63561-125729	1
Taoasis	Peppermint oil	63561-126008	1

- 2787 spectra from 264 *Apo-Ident* customers from a total of 1462 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	120	0	16 139
Type B	0	79	1	16 224
Type C	0	12	0	2787

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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	98.7500 % (> 95.0000 %)
Type C	100.0000 % (> 98.2328 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	87.73
30965	30965	0.00	95.85
32481	32481	0.00	74.50

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Ravensara**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30386-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ravensara

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Ravensara	231012-118739	31635	40	not required
Taoasis	Ravensara	1687-125316	32803	40	not required

Validation samples

A total of 35 362 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 *Ravensara*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Ravensara*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Ravensara	T170I11	30386	40
Taoasis	Ravensara	231012-118739	31635 [†]	20
Taoasis	Ravensara	1687-125316	33029	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 13 spectra from 1 *Apo-Ident* customers from 8 batches from the substance/substance group *Ravensara*.

Supplier	Substance	Batch	Spectra
Taoasis	Ravensara	231012-119831	1
Taoasis	Ravensara	1687-125316	1

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

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Supplier	Substance	Batch	Spectra
Taoasis	Ravensara	2101005-116830	3
Taoasis	Ravensara	231012-118738	1
Taoasis	Ravensara	231012-118739	2
Taoasis	Ravensara	231012-118892	1
Taoasis	Ravensara	231012-120291	1
Taoasis	Ravensara	9331006-121650	3

- 2786 spectra from 265 *Apo-Ident* customers from a total of 1466 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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* can clearly be 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* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	16 179
Type B	0	100	0	16 204
Type C	0	13	0	2786

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.2323 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	25.73
32803	32803	0.00	23.99

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Rose-geranium oil, organic**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30536-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Rose-geranium oi...	21027-121893	31776	40	not required
Taoasis	Rose-geranium oi...	21027-121893	31951	40	not required
Taoasis	Rose-geranium oi...	1616008-125056	33036	40	not required

Validation samples

A total of 35 362 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 *Rose-geranium oil, organic*. These samples are listed above in the [calibration samples](#) section.
- 16 099 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 140 spectra of 5 reference samples from the substance/substance group *Rose-geranium oil, organic*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Rose-geranium oil, organic	pending	30536	40
Taoasis	Rose-geranium oil, organic	21027-119997	31698 [†]	20
Taoasis	Rose-geranium oil, organic	21027-121893	31776 [†]	20
Taoasis	Rose-geranium oil, organic	21027-121893	31951 [†]	20
Taoasis	Rose-geranium oil, organic	1616008-125056	33037	40

- 16 164 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 13 spectra from 7 *Apo-Ident* customers from 12 batches from the substance/substance group *Rose-geranium oil, organic*.

[†]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*.

Supplier	Substance	Batch	Spectra
Bombastus	Rose-geranium oil, organic	22625-106677	1
Taoasis	Rose-geranium oil, organic	21027-119121	1
Taoasis	Rose-geranium oil, organic	21027-120292	1
Taoasis	Rose-geranium oil, organic	401011-117806	2
Taoasis	Rose-geranium oil, organic	1500969-123554	1
Primavera	Rose-geranium oil, organic	8304131	1
Taoasis	Rose-geranium oil, organic	130729-113060	1
Taoasis	Rose-geranium oil, organic	21027-121337	1
Taoasis	Rose-geranium oil, organic	130111-112615	1
Taoasis	Rose-geranium oil, organic	401011-117641	1
Taoasis	Rose-geranium oil, organic	130111-110467	1
Taoasis/Taoasis	Rose-geranium oil, organic	22625-104463	1

- 2786 spectra from 265 *Apo-Ident* customers from a total of 1462 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	160	0	16 099
Type B	0	140	0	16 164
Type C	0	13	0	2786

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 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 98.2323 %)	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.

Identity according to identity test using NIR spectroscopy

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

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	30.66
31776	31776	0.00	33.91
31951	31951	0.00	34.68
33036	33036	0.00	42.14

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Rosewood oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31556-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Rosewood oil	4381004-120355	31688	40	not required

Validation samples

A total of 35 362 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 *Rosewood oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 120 spectra of 4 reference samples from the substance/substance group *Rosewood oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Rosewood oil	11572-116545	31556 [†]	20
Taoasis	Rosewood oil	4381004-120355	31688 [†]	20
Taoasis	Rosewood oil	5101015-124967	32801	40
Taoasis	Rosewood oil	5101015-124967	33048	40

- 16 184 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 7 batches from the substance/substance group *Rosewood oil*.

Supplier	Substance	Batch	Spectra
Taoasis	Rosewood oil	4381004-1200355	1

continued on the next page

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

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Supplier	Substance	Batch	Spectra
Taoasis	Rosewood oil	4381004-121143	2
Taoasis	Rosewood oil	4381004-122041	2
Taoasis	Rosewood oil	5101017-122566	2
Taoasis	Rosewood oil	5101015-124967	2
Taoasis	Rosewood oil	5101015-123299	1
Taoasis	Rosewood oil	5101015-124243	1

- 2788 spectra from 265 *Apo-Ident* customers from a total of 1467 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	120	0	16 184
Type C	0	11	0	2788

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.2335 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31556	31556	0.00	62.30
31688	31688	0.00	66.40

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Sage oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31139-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sage oil; Oleum salviae; Salvia officinalis oleum

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required

Validation samples

A total of 35 362 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 *Sage oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 140 spectra of 4 reference samples from the substance/substance group *Sage oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Sage oil	8461016-122272	31783 [†]	20
Taoasis	Sage oil	8461016-126496	33034	40
Taoasis	Sage oil	8461016-126496	33035	40
Taoasis	Sage oil	24858-79297	36005	40

- 16 164 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 5 batches from the substance/substance group *Sage oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Sage oil	13988-117449	1
Taoasis	Sage oil	21190-118009	1
Taoasis	Sage oil	21190-119239	1
Taoasis	Sage oil	29944-120889	1
Taoasis	Sage oil	29944-120965	1

- 2794 spectra from 265 *Apo-Ident* customers from a total of 1469 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	99	41	16 164
Type C	0	2	3	2794

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9401 %)	70.7143 % (> 68.5714 %)
Type C	100.0000 % (> 98.2427 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31139	31139	0.00	36.71
31257	31257	0.00	21.18
31783	31783	0.00	34.35

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Salicylic white paraffin 10%**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31521-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Bombastus	Salicylic white ...	291886	31629	55	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 95 spectra of 2 reference samples from the substance/substance group *Salicylic white paraffin 10%*. These samples are listed above in the [calibration samples](#) section.
- 16 164 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 120 spectra of 4 reference samples from the substance/substance group *Salicylic white paraffin 10%*.

Supplier	Substance	Batch	Sample ID	Spectra
Bombastus	Salicylic white paraffin 10%	287820	31521 [†]	20
Bombastus	Salicylic white paraffin 10%	291886	31629 [†]	20
Bombastus	Salicylic white paraffin 10%	302737	32741	40
Bombastus	Salicylic white paraffin 10%	309004	33416	40

- 16 184 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 6 spectra from 4 *Apo-Ident* customers from 6 batches from the substance/substance group *Salicylic white paraffin 10%*.

[†]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*.

Supplier	Substance	Batch	Spectra
Eigenrezeptur	Salicylic white paraffin 10%	150702	1
Caelo	Salicylic white paraffin 10%	15394702	1
Caelo	Salicylic white paraffin 10%	16120701	1
Caelo	Salicylic white paraffin 10%	16214202	1
Caelo	Salicylic white paraffin 10%	16214203	1
Bombastus	Salicylic white paraffin 10%	293212	1

- 2793 spectra from 264 *Apo-Ident* customers from a total of 1468 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Salicylic white paraffin 10%* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Salicylic white paraffin 10%* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	95	0	16 164
Type B	0	120	0	16 184
Type C	0	6	0	2793

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 % (> 99.9468 %)	100.0000 % (> 93.6842 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.2399 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	93.58
31629	31629	0.00	93.95

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Sebexol® formula basis / Sebexol® cream lotion / ...**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30839-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

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

Special notes

When selecting the *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Devesa	Sebexol® cream l...	1220	30839	40	1403097

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Kesla Pharma	Wofacutan wash l...	0974.12	30972	80	not required
Kesla Pharma	Wofacutan wash l...	0389.13	31065	40	not required
Devesa	Sebexol [®] cream l...	1317	31103	40	not required
Devesa	Sebexol [®] basic p...	1307	31104	40	1403098
Devesa	Sebexol [®] cream l...	1412	31592	30	not required
Devesa	Sebexol [®] cream l...	1531	31839	40	not required
Devesa	Sebexol [®] basic p...	1522	31961	40	not required
Devesa	Sebexol [®] cream l...	1552.2	32743	40	not required
Devesa	Sebexol [®] basic p...	1638124	32744	40	not required
Hans Karrer G...	Hans Karrer Hydr...	16001	33190	40	not required
Hans Karrer G...	Hans Karrer Hydr...	16002	33191	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 510 spectra of 12 reference samples from the substance/substance group *Sebexol[®] formula basis / Sebexol[®] cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver*. These samples are listed above in the [calibration samples](#) section.
- 15 749 spectra from a total of 363 batches from further 140 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 415 spectra of 12 reference samples from the substance/substance group *Sebexol[®] formula basis / Sebexol[®] cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver*.

Supplier	Substance	Batch	Sample ID	Spectra
Devesa	Sebexol [®] basic pH 5 formula ...	1131	30521	40
Devesa	Sebexol [®] cream lotion pH 5	1412	31592 [†]	15
Devesa	Sebexol [®] cream lotion pH 5	1531	31839 [†]	20
Devesa	Sebexol [®] basic pH 5 formula ...	1522	31961 [†]	20
Devesa	Sebexol [®] cream lotion pH 5	1605101	32907	40
Devesa	Sebexol [®] cream lotion pH 5	1605101	32908	40
Kesla Pharma	Wofacutan wash lotion	729.16	32913	40
Kesla Pharma	Wofacutan wash lotion	729.16	32914	40
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

- 15 889 spectra from a total of 416 batches from further 173 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 149 spectra from 39 *Apo-Ident* customers from 62 batches from the substance/substance group *Sebexol[®] formula basis* / *Sebexol[®] cream lotion* / *Wofacutan washing lotion* / *Hans Karrer Hydrocream MicroSilver*.

Supplier	Substance	Batch	Spectra
Devesa	Sebexol [®] basic pH 5 formula ...	1440	4
DEVESA	Sebexol [®] basic pH 5 formula ...	1440	1
Devesa	Sebexol [®] basic pH 5 formula ...	1511	2
DEVESA	Sebexol [®] basic pH 5 formula ...	1511	1
Devesa/Noweda	Sebexol [®] basic pH 5 formula ...	1511	1
Devesa	Sebexol [®] basic pH 5 formula ...	1522	2
Devesa	Sebexol [®] basic pH 5 formula ...	1543	1
Devesa	Sebexol [®] basic pH 5 formula ...	1604127	2
Devesa/Noweda	Sebexol [®] basic pH 5 formula ...	1604127	1
Devesa / Noweda	Sebexol [®] basic pH 5 formula ...	1620117	1
Devesa	Sebexol [®] basic pH 5 formula ...	1638124	1
Caelo	Sebexol [®] cream lotion pH 5	1417	1
Devesa/Noweda	Sebexol [®] cream lotion pH 5	1447	3
Astellas	Sebexol [®] cream lotion pH 5	1504	2
Caelo	Sebexol [®] cream lotion pH 5	1504	1
Devesa/NOW	Sebexol [®] cream lotion pH 5	1504	2
Devesa/Gehe	Sebexol [®] cream lotion pH 5	1504	1
Devesa/Noweda	Sebexol [®] cream lotion pH 5	1504	1
Devesa/NOW	Sebexol [®] cream lotion pH 5	1504/01	1
DEVESA	Sebexol [®] cream lotion pH 5	1505	1
Devesa	Sebexol [®] cream lotion pH 5	1510	4
Caelo	Sebexol [®] cream lotion pH 5	1511	2
DEVESA	Sebexol [®] cream lotion pH 5	1510	1
Devesa/Phoenix	Sebexol [®] cream lotion pH 5	1511	1
Fagron	Sebexol [®] cream lotion pH 5	1517	1
DEVESA	Sebexol [®] cream lotion pH 5	1523	1
Devesa/NOW	Sebexol [®] cream lotion pH 5	1523	1
Devesa	Sebexol [®] cream lotion pH 5	1523	2
Devesa/Sanacorp	Sebexol [®] cream lotion pH 5	1530	1
Rondell Apotheke	Sebexol [®] cream lotion pH 5	1523	1
Caelo	Sebexol [®] cream lotion pH 5	1531	1
Devesa/ Phoenix	Sebexol [®] cream lotion pH 5	1524	1
Devesa / Noweda	Sebexol [®] cream lotion pH 5	1531	1
DEVESA	Sebexol [®] cream lotion pH 5	1531	1
Dr. Wolff	Sebexol [®] cream lotion pH 5		1
Caelo	Sebexol [®] cream lotion pH 5		2
Devesa/Noweda	Sebexol [®] cream lotion pH 5		1
Devesa/fiebig	Sebexol [®] cream lotion pH 5		1

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

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Supplier	Substance	Batch	Spectra
Devesa/NOW	Sebexol [®] cream lotion pH 5		1
Devesa/NOW	Sebexol [®] cream lotion pH 5	1552	1
Devesea	Sebexol [®] cream lotion pH 5	1604128	1
Phönix	Sebexol [®] cream lotion pH 5	1604129	1
Devesa/NOW	Sebexol [®] cream lotion pH 5	1604129	1
Devesa/NOW	Sebexol [®] cream lotion pH 5	1604228	1
sanacorp, 27.9.16,4,312EUR	Sebexol [®] cream lotion pH 5	1604328	1
Devesa/Noweda	Sebexol [®] cream lotion pH 5	1605201	3
Devesa/NOW	Sebexol [®] cream lotion pH 5	1644102	1
Devesa/Noweda	Sebexol [®] cream lotion pH 5	1651120	1
Noweda	Sebexol [®] cream lotion pH 5	1651120	1
Devesa	Sebexol [®] cream lotion pH 5	1651121	1
Devesa	Sebexol [®] cream lotion pH 5	1708120	2
Caelo	Sebexol [®] cream lotion pH 5	1712223	1
Devesa	Sebexol [®] basic pH 5 formula ...	1307	4
Caelo	Sebexol [®] basic pH 5 formula ...	1328	4
Devesa	Sebexol [®] basic pH 5 formula ...	1328	8
DEVESA	Sebexol [®] basic pH 5 formula ...	1328	2
DEVESA Dr.Reingraber GmbH	Sebexol [®] basic pH 5 formula ...	1328	1
Devesa	Sebexol [®] basic pH 5 formula ...	1335	2
Devesa/ Fiebig	Sebexol [®] basic pH 5 formula ...	1338	1
devesa/gehe	Sebexol [®] basic pH 5 formula ...	1346	1
Bombastus	Sebexol [®] basic pH 5 formula ...	1346	2
devesa/gehe	Sebexol [®] basic pH 5 formula ...	1356	1
Sebexol/ Noweda	Sebexol [®] basic pH 5 formula ...	1403	1
Devesa	Sebexol [®] basic pH 5 formula ...	1404	1
Phoenix/Devesa	Sebexol [®] basic pH 5 formula ...	1407	1
Devesa	Sebexol [®] basic pH 5 formula ...	1407	2
Devesa/Kehr	Sebexol [®] basic pH 5 formula ...	1407	2
Phönix	Sebexol [®] basic pH 5 formula ...	1416	1
Devesa Dr.Reingraber GmbH	Sebexol [®] basic pH 5 formula ...	1425	1
Phönix	Sebexol [®] basic pH 5 formula ...	1425	2
Fagron	Sebexol [®] basic pH 5 formula ...	1425	1
Devesa/Noweda	Sebexol [®] basic pH 5 formula ...	1430	1
Sebexol/ Noweda	Sebexol [®] basic pH 5 formula ...	1430	1
Phoenix	Sebexol [®] basic pH 5 formula ...	1440	1
Devesa	Sebexol [®] basic pH 5 formula ...	1430	1
Devesa/Sanacorp	Sebexol [®] basic pH 5 formula ...	1440	1
Fagron	Sebexol [®] basic pH 5 formula ...	1510	2
Noweda/Devesa	Sebexol [®] basic pH 5 formula ...	2x1407	1
DEVESA	Sebexol [®] basic pH 5 formula ...	1318	2
Eigenherstellung	Sebexol [®] basic pH 5 formula ...	1328	1
Devesa	Sebexol [®] basic pH 5 formula ...		3
Caelo	Sebexol [®] basic pH 5 formula ...	1131	2
Phoenix/Devesa	Sebexol [®] basic pH 5 formula ...	1215	1
Dr.Reingraber GmbH	Sebexol [®] basic pH 5 formula ...	1232	1
Devesa	Sebexol [®] basic pH 5 formula ...	1232	3
Caelo	Sebexol [®] basic pH 5 formula ...	1239	1
Devesa	Sebexol [®] basic pH 5 formula ...	1239	1
Devesa Dr.Reingraber Gm...	Sebexol [®] basic pH 5 formula ...	1244	1
Devesa/AHD	Sebexol [®] basic pH 5 formula ...	1245	4
Sebexol/AHD	Sebexol [®] basic pH 5 formula ...	1303	2
Devesa Dr.Reingraber Gm...	Sebexol [®] basic pH 5 formula ...	1303	1
Phönix	Sebexol [®] basic pH 5 formula ...	1313	2
Sanacorp	Sebexol [®] basic pH 5 formula ...	1313	1
Sebexol	Sebexol [®] basic pH 5 formula ...	1313	1
Devesa/Gehe	Sebexol [®] basic pH 5 formula ...		1
Sebexol	Sebexol [®] basic pH 5 formula ...	1333	1
Devesa	Sebexol [®] basic pH 5 formula ...	1232	1
Devesa	Sebexol [®] basic pH 5 formula ...	1307	1

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Supplier	Substance	Batch	Spectra
Phönix Gotha	Wofacutan wash lotion	97913	1

- 2650 spectra from 262 *Apo-Ident* customers from a total of 1412 batches from a further 114 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	510	0	15 749
Type B	0	412	3	15 877
Type C	0	149	0	2650

The substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9462 %)	100.0000 % (> 98.8235 %)
Type B	100.0000 % (> 99.9405 %)	99.2771 % (> 98.5542 %)
Type C	100.0000 % (> 98.2264 %)	100.0000 % (> 95.9732 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	24.11
30972	30972	0.00	23.54
31065	31065	0.00	24.86
31103	31103	0.00	22.04
31104	31104	0.00	20.12
31592	31592	0.00	19.96
31839	31839	0.00	18.64
31961	31961	0.00	17.44
32743	32743	0.00	21.33
32744	32744	0.00	18.82
33190	33190	0.00	22.45
33191	33191	0.00	21.43

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Siam benzoin**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31490-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Primavera	Siam benzoin	00051M23	31844	40	not required
Primavera	Siam benzoin	00218C24	32184	40	not required

Validation samples

A total of 35 362 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 *Siam benzoin*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 40 spectra of 2 reference samples from the substance/substance group *Siam benzoin*.

Supplier	Substance	Batch	Sample ID	Spectra
Primavera	Siam benzoin	3602151	31490 [†]	20
Primavera	Siam benzoin	51M23	31844 [†]	20

- 16 264 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	40	0	16 264
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31490	31490	0.00	407.58
31844	31844	0.00	384.24
32184	32184	0.00	391.02

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Silvir fir oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31032-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Silvir fir oil; Oleum abies alba

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Silvir fir oil	120830-111781	31032	40	not required
Taoasis	Silvir fir oil	211-114751	31255	40	not required
Taoasis	Silvir fir oil	01A0B15-121623	31754	40	not required

Validation samples

A total of 35 362 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 *Silvir fir oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Silvir fir oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Silvir fir oil	1A0B15-121623	31754 [†]	20
Taoasis	Silvir fir oil	1A0B16-125623	33026	40
Taoasis	Silvir fir oil	1A0B16-125623	33027	40

- 16 204 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Taoasis	Silvir fir oil	212-120342	1

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

- 2798 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Silvir 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 *Silvir fir oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	87	13	16 204
Type C	0	1	0	2798

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9402 %)	87.0000 % (> 84.0000 %)
Type C	100.0000 % (> 98.3099 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31032	31032	0.00	25.21
31255	31255	0.00	12.84
31754	31754	0.00	13.83

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Labor-

prüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Solutio Cordes / Thrombocid gel**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30773-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Solutio Cordes / Thrombocid gel; Solutio Cordes®; Thrombocid® gel

Special notes

When selecting the *Solutio Cordes / Thrombocid gel* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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 / Thrombocid gel*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Bene	Thrombocid® gel	401B101	30773	40	not required
Ichthyol	Solutio Cordes®	12B006	30996	40	not required
Ichthyol	Solutio Cordes®	13B001	31076	40	not required
Bene	Thrombocid® gel	401B101	31099	40	not required
Ichthyol	Solutio Cordes®	15B005	32065	40	not required
Bene	Thrombocid® gel	403I143	32721	40	not required

Validation samples

A total of 35 362 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 *Solutio Cordes / Thrombocid gel*. These samples are listed above in the [calibration samples](#) section.
- 16 019 spectra from a total of 370 batches from further 142 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 180 spectra of 5 reference samples from the substance/substance group *Solutio Cordes / Thrombocid gel*.

Supplier	Substance	Batch	Sample ID	Spectra
Ichthyol	Solutio Cordes [®]	9B008	30224	40
Ichthyol	Solutio Cordes [®]	15B005	32065 [†]	20
Bene	Thrombocid [®] gel	403I143	32264	40
Ichthyol	Solutio Cordes [®]	15B005	32483	40
Bene	Thrombocid [®] gel	403I143	32847	40

- 16 124 spectra from a total of 423 batches from further 175 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 47 spectra from 15 *Apo-Ident* customers from 15 batches from the substance/substance group *Solutio Cordes / Thrombocid gel*.

[†]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*.

Supplier	Substance	Batch	Spectra
Ichthyol /Noweda	Solutio Cordes [®]	13B002	1
ICHTYOL-GESELLSCHAFT	Solutio Cordes [®]	13B001	1
Ichthyol/Phönix	Solutio Cordes [®]	13B002	3
Ichthyol / Gehe	Solutio Cordes [®]	14B006	1
Caelo	Solutio Cordes [®]	14B012	1
Phönix	Solutio Cordes [®]	13B002	1
Ichthyol/Phönix	Solutio Cordes [®]	14B011	1
Gehe/Ichthyol	Solutio Cordes [®]	14B006	1
Ichthyol Gesellschaft	Solutio Cordes [®]	14B006	1
Ichthyol Gesellschaft	Solutio Cordes [®]	14B012	1
Ichthyol / G	Solutio Cordes [®]	14B012	1
Ichthyol/Noweda	Solutio Cordes [®]	14B012	1
Ichthyol/Phönix	Solutio Cordes [®]	15B001	1
Ichthyol/Noweda	Solutio Cordes [®]	15B005	1
Ichthyol / E	Solutio Cordes [®]	15B005	3
Ichthyol-Gesellschaft	Solutio Cordes [®]	15B005	1
Ichthyol / G	Solutio Cordes [®]	16B005	2
Fiebig	Solutio Cordes [®]	22314	1
Ichthyol/Phönix	Solutio Cordes [®]	12B005	15
Ichthyol/Phönix	Solutio Cordes [®]	12B0005	1
Ichthyol	Solutio Cordes [®]	12B005	1
Ichthyol /Noweda	Solutio Cordes [®]	12B005	1
Ichtyol	Solutio Cordes [®]	12B006	2
Ichthyol	Solutio Cordes [®]	13B001	1
Ichthyol- Gesellschaft ...	Solutio Cordes [®]	13B001	1
Ichthyol	Solutio Cordes [®]	12B006	1
Ichtyol	Solutio Cordes [®]	13B002	1

- 2752 spectra from 265 *Apo-Ident* customers from a total of 1459 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 / Thrombocid 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 *Solutio Cordes / Thrombocid gel* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	16 019
Type B	0	150	30	16 124
Type C	0	32	15	2752

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9463 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9400 %)	83.3333 % (> 81.6667 %)
Type C	100.0000 % (> 98.2276 %)	68.0851 % (> 61.7021 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30773	30773	0.00	67.65
30996	30996	0.00	71.30
31076	31076	0.00	71.91
31099	31099	0.00	67.37
32065	32065	0.00	72.20
32721	32721	0.00	63.51

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Spearmint oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30453-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Spearmint oil	421012-126408	33200	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 110 spectra of 3 reference samples from the substance/substance group *Spearmint oil*. These samples are listed above in the [calibration samples](#) section.
- 16 149 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 100 spectra of 3 reference samples from the substance/substance group *Spearmint oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Spearmint oil	27537-96244	30453	40
Taoasis	Spearmint oil	946-120296	31685 [†]	20
Taoasis	Spearmint oil	421012-126408	33201	40

- 16 204 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Taoasis	Spearmint oil	27537-96244	1
Taoasis	Spearmint oil	421012-123260	1
Taoasis	Spearmint oil	421012-125373	1

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

- 2796 spectra from 265 *Apo-Ident* customers from a total of 1471 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	110	0	16 149
Type B	0	95	5	16 204
Type C	0	3	0	2796

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9467 %)	100.0000 % (> 94.5455 %)
Type B	100.0000 % (> 99.9402 %)	95.0000 % (> 92.0000 %)
Type C	100.0000 % (> 98.2539 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31135	31135	0.00	67.96
31685	31685	0.00	63.68
33200	33200	0.00	57.46

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe

mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Spruce needle oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30613-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Spruce needle oil; Oleum pini sibiricum; Piceae aetheroleum

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Spruce needle oil	29828-103169BAG90451	30672	40	not required
Taoasis	Spruce needle oil	1507-122520	31819	40	not required
Taoasis	Spruce needle oil	1719-124011	32066	40	not required

Validation samples

A total of 35 362 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 *Spruce needle oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 160 spectra of 5 reference samples from the substance/substance group *Spruce needle oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Spruce needle oil	11220801	30613	40
Taoasis	Spruce needle oil	29828-103169BAG90451	30652	40
Taoasis	Spruce needle oil	1507-122520	31819 [†]	20
Taoasis	Spruce needle oil	1719-124011	32066 [†]	20
Taoasis	Spruce needle oil	1769-124969	32479	40

- 16 144 spectra from a total of 421 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 11 *Apo-Ident* customers from 13 batches from the substance/substance group *Spruce needle oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Spruce needle oil	1769-124949	1
Taoasis	Spruce needle oil	1769-124969	2
Caelo	Spruce needle oil	11324401	4
Caelo	Spruce needle oil	10185604	1
Caelo	Spruce needle oil	13152001	2
Primavera	Spruce needle oil	1670814	1
Taoasis	Spruce needle oil	442-113922	1
Taoasis	Spruce needle oil	29828-107964	1
Taoasis	Spruce needle oil	534374-22869	1
Taoasis	Spruce needle oil	534474-111585	1
Taoasis	Spruce needle oil	531766-109893	1
Taoasis/Sanacorp	Spruce needle oil	534474-111869	1
Taoasis/Sanacorp	Spruce needle oil	534474-113171	1

- 2781 spectra from 265 *Apo-Ident* customers from a total of 1461 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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* can clearly be 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* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	16 139
Type B	0	80	80	16 144
Type C	0	3	15	2781

The substance/substance group *Spruce needle 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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9400 %)	50.0000 % (> 48.1250 %)
Type C	100.0000 % (> 98.2305 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30672	30672	0.00	26.50
31819	31819	0.00	11.57
32066	32066	0.00	13.71

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Stomahesive[®] adhesive paste**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30974-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Stomahesive[®] adhesive paste

Special notes

When selecting the *Stomahesive[®] adhesive paste* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	70	not required
ConvaTec Inc.	Stomahesive [®] adh...	2M084	31087	40	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 110 spectra of 2 reference samples from the substance/substance group *Stomahesive® adhesive paste*. These samples are listed above in the [calibration samples](#) section.
- 16 149 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 114 spectra of 4 reference samples from the substance/substance group *Stomahesive® adhesive paste*.

Supplier	Substance	Batch	Sample ID	Spectra
ConvaTec Inc.	Stomahesive® adhesive paste	2D117	30974 [†]	10
ConvaTec Inc.	Stomahesive® adhesive paste	6D079	32761	40
ConvaTec Inc.	Stomahesive® adhesive paste	5G062	32954	40
Convatec	Stomahesive® adhesive paste	5G062	not required	24

- 16 190 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Stomahesive® adhesive paste*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	110	0	16 149
Type B	0	114	0	16 190
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9467 %)	100.0000 % (> 94.5455 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 94.7368 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	69.09
31087	31087	0.00	70.07

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Swiss pine oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31553-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Swiss pine oil	3023-120087	31680	40	not required
Taoasis	Swiss pine oil	12069-127103	32934	40	not required

Validation samples

A total of 35 362 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 *Swiss pine oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Swiss pine oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Swiss pine oil	4892-117271	31553 [†]	20
Taoasis	Swiss pine oil	3023-120087	31680 [†]	20
Taoasis	Swiss pine oil	201610159-126370	32793	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Swiss pine oil*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	40	40	16 224
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	50.0000 % (> 46.2500 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31553	31553	0.00	16.11
31680	31680	0.00	17.38
32934	32934	0.00	32.50

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Tea tree oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30959-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tea tree oil; Melaleuca alternifolia oleum; Oleum melaleuca alternifolia

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required

Validation samples

A total of 35 362 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 *Tea tree oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 112 spectra of 4 reference samples from the substance/substance group *Tea tree oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Tea tree oil	44737-121997	31762 [†]	20
Taoasis	Tea tree oil	52642-125539	33017	40
Taoasis	Tea tree oil	52642-124527	33018	40
Taoasis	Tea tree oil	52642-125539BAG91303	not required	12

- 16 192 spectra from a total of 422 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 13 spectra from 3 *Apo-Ident* customers from 10 batches from the substance/substance group *Tea tree oil*.

[†]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*.

Supplier	Substance	Batch	Spectra
Taoasis	Tea tree oil	1469-117418	2
Caelo	Tea tree oil	15051806	1
Caelo	Tea tree oil	15337105	1
Taoasis	Tea tree oil	20269-116833	2
Taoasis	Tea tree oil	28348-119841	1
Taoasis	Tea tree oil	28348-121597	2
Taoasis	Tea tree oil	28348-121515	1
Taoasis	Tea tree oil	52642-124559	1
Taoasis	Tea tree oil	52642-12078	1
Taoasis	Tea tree oil	52642-124919	1

- 2786 spectra from 265 *Apo-Ident* customers from a total of 1464 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	120	0	16 139
Type B	0	112	0	16 192
Type C	0	13	0	2786

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 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 94.6429 %)
Type C	100.0000 % (> 98.2323 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	57.58
31134	31134	0.00	56.92
31762	31762	0.00	66.89

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Thyme oil, red**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30929-2017-09-08
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:

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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

Validation samples

A total of 35 362 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 *Thyme oil, red*. These samples are listed above in the [calibration samples](#) section.
- 16 099 spectra from a total of 371 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 40 spectra of 1 reference samples from the substance/substance group *Thyme oil, red*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Thyme oil, red	40517-121881	32472	40

- 16 264 spectra from a total of 425 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 11 batches from the substance/substance group *Thyme oil, red*.

Supplier	Substance	Batch	Spectra
Taoasis	Thyme oil, red	43637-122852	1
Taoasis	Thyme oil, red	43637-124964	1
Taoasis	Thyme oil, red	14381-117385	1
Taoasis	Thyme oil, red	25394-118296	1
Taoasis	Thyme oil, red	32444-118785	4

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Supplier	Substance	Batch	Spectra
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	9434-115525	1
Taoasis	Thyme oil, red	33092-111620	1

- 2784 spectra from 265 *Apo-Ident* customers from a total of 1463 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	160	0	16 099
Type B	0	40	0	16 264
Type C	0	13	2	2784

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 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.2314 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	57.39
31259	31259	0.00	49.42
32482	32482	0.00	71.72
32981	32981	0.00	65.12

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **VersatileTM**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31493-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

VersatileTM

Special notes

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

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Versatile TM	14B19-T02-010391	31493	40	not required
Fagron	Versatile TM	14B19-T02-010391	31832	30	not required

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 70 spectra of 2 reference samples from the substance/substance group *VersatileTM*. These samples are listed above in the [calibration samples](#) section.
- 16 189 spectra from a total of 374 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 130 spectra of 4 reference samples from the substance/substance group *VersatileTM*.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Versatile TM	14B19-T02-010391	31493 [†]	20
Fagron	Versatile TM	14B19-T02-010391	31832 [†]	30
Fagron	Versatile TM	1503256	32736	40
Fagron	Versatile TM	1503256	32844	40

- 16 174 spectra from a total of 424 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

Supplier	Substance	Batch	Spectra
Fagron	Versatile TM	14B19-T02-010391	1

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

- 2798 spectra from 265 *Apo-Ident* customers from a total of 1473 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	70	0	16 189
Type B	0	98	32	16 174
Type C	0	1	0	2798

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9470 %)	100.0000 % (> 91.4286 %)
Type B	100.0000 % (> 99.9401 %)	75.3846 % (> 73.0769 %)
Type C	100.0000 % (> 98.3099 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31493	31493	0.00	14.05
31832	31832	0.00	13.58

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe

mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Vetiver bourbon oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31546-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Vetiver bourbon ...	7141-119962	31684	40	not required

Validation samples

A total of 35 362 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 *Vetiver bourbon oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 120 spectra of 4 reference samples from the substance/substance group *Vetiver bourbon oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Vetiver bourbon oil	7141-116418	31546 [†]	20
Taoasis	Vetiver bourbon oil	7141-119962	31684 [†]	20
Taoasis	Vetiver bourbon oil	7141-124922	32810	40
Taoasis	Vetiver bourbon oil	7141-124922	33046	40

- 16 184 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 3 batches from the substance/substance group *Vetiver bourbon oil*.

Supplier	Substance	Batch	Spectra
Taoasis	Vetiver bourbon oil	7141-119174	1
Taoasis	Vetiver bourbon oil	7141-122195	2
Taoasis	Vetiver bourbon oil	7141-124600	2

[†]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*.

- 2794 spectra from 265 *Apo-Ident* customers from a total of 1471 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	120	0	16 184
Type C	0	5	0	2794

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9401 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.2427 %)	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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	30.78
31684	31684	0.00	33.86

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Labor-

prüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Wart ointment InfectoPharm® (NRF 11.31)**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30730-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Wart ointment InfectoPharm® (NRF 11.31)

Special notes

When selecting the *Wart ointment InfectoPharm® (NRF 11.31)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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...	S071602.1	32953	40	not required

Validation samples

A total of 35 362 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.
- 16 099 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 40 spectra of 1 reference samples from the substance/substance group *Wart ointment InfectoPharm*[®] (NRF 11.31).

Supplier	Substance	Batch	Sample ID	Spectra
Infectopharm	Wart ointment InfectoPharm [®] ...	S021601.1	32593	40

- 16 264 spectra from a total of 425 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 75 spectra from 39 *Apo-Ident* customers from 23 batches from the substance/substance group *Wart ointment InfectoPharm*[®] (NRF 11.31).

Supplier	Substance	Batch	Spectra
InfectoPharm/Anzag	Wart ointment InfectoPharm [®] ...	716A-03898	1
gehe/infecto	Wart ointment InfectoPharm [®] ...		1
Infectopharm	Wart ointment InfectoPharm [®] ...		24

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Supplier	Substance	Batch	Spectra
Euro OTC	Wart ointment InfectoPharm [®] ...		1
Infectopharm / Gehe	Wart ointment InfectoPharm [®] ...		1
Infectopharm/Phoenix Le...	Wart ointment InfectoPharm [®] ...		1
InfectopharmNoweda	Wart ointment InfectoPharm [®] ...		1
Infectopharm/Gehe	Wart ointment InfectoPharm [®] ...		1
Infectopharm Arzneimittel	Wart ointment InfectoPharm [®] ...		1
Infectopharm/Kehr	Wart ointment InfectoPharm [®] ...		1
Infectopharm/K	Wart ointment InfectoPharm [®] ...		1
InfectoPharm	Wart ointment InfectoPharm [®] ...	S0215011	1
PX/Infectop	Wart ointment InfectoPharm [®] ...	S0215011	3
Infectopharm/Noweda	Wart ointment InfectoPharm [®] ...		4
Infectopharm/Phönix	Wart ointment InfectoPharm [®] ...		2
Eigenherstellung	Wart ointment InfectoPharm [®] ...		1
InfectoPharm/Noweda	Wart ointment InfectoPharm [®] ...		2
Infectopharm/Alliance H...	Wart ointment InfectoPharm [®] ...		1
Infectopharm / Alliance...	Wart ointment InfectoPharm [®] ...		1
Infecto/Spangro	Wart ointment InfectoPharm [®] ...		1
Sanacorp	Wart ointment InfectoPharm [®] ...		2
Infectopharm/Phoenix	Wart ointment InfectoPharm [®] ...		1
Infectopharm/G	Wart ointment InfectoPharm [®] ...		1
InfectoPharm/Anzag	Wart ointment InfectoPharm [®] ...		2
Fagron	Wart ointment InfectoPharm [®] ...		1
Ichthyol-Gesellschaft C...	Wart ointment InfectoPharm [®] ...		1
InfectoPharm/AHD	Wart ointment InfectoPharm [®] ...		1
Infecto/Gehe	Wart ointment InfectoPharm [®] ...		1
Infect/PX	Wart ointment InfectoPharm [®] ...		2
Phönix Gotha	Wart ointment InfectoPharm [®] ...		1
infectopharm	Wart ointment InfectoPharm [®] ...		2
Löwen City-Apotheke Bar...	Wart ointment InfectoPharm [®] ...	8032013	1
Infectopharm	Wart ointment InfectoPharm [®] ...	3013I-07003	1
infectoPharm	Wart ointment InfectoPharm [®] ...		1
InfectoPharm	Wart ointment InfectoPharm [®] ...		1
InfectoPharm/ E	Wart ointment InfectoPharm [®] ...		1
infectipharm/Phönix	Wart ointment InfectoPharm [®] ...		1
Gehe	Wart ointment InfectoPharm [®] ...		1
Infectopharm (Phoenix)	Wart ointment InfectoPharm [®] ...		1
Caelo	Wart ointment InfectoPharm [®] ...		1
Infectopharm	Wart ointment InfectoPharm [®] ...	S111202	1

- 2724 spectra from 258 *Apo-Ident* customers from a total of 1452 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Wart ointment InfectoPharm[®]* (*NRF 11.31*) can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wart ointment InfectoPharm[®]* (*NRF 11.31*) and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	16 099
Type B	0	40	0	16 264
Type C	0	75	0	2724

The substance/substance group *Wart ointment InfectoPharm® (NRF 11.31)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9465 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.2270 %)	100.0000 % (> 92.0000 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30730	30730	0.00	263.92
30905	30905	0.00	256.41
30906	30906	0.00	251.24
32953	32953	0.00	239.74

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Water and aqueous solutions
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	31047-2017-09-08
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Water and aqueous solutions; Aloe Vera gel, 1:1; Aloe vera gel, 10x concentrated; Aqua; Bepanthen solution; Retterspitz external; SyrSpend® SF pH4 cherry aroma; SyrSpend® SF pH4 aroma free; Water

Special notes

When selecting the *Water and aqueous solutions* substance/substance group, the following information is displayed to the user:

- Advice for the identification of water: Preserved, purified and distilled water can not be conclusively distinguished by spectral analysis. An additional analysis of identity may be required.

Applicable documents

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Bayer	Bepanthen solution	KP08DR1	31047	40	not required
Caelo	Aloe Vera gel, 1:1	13025802	31145	40	not required

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Aloe vera gel, 1...	13045901	31146	40	not required
Hedinger	Water	219066	31623	40	not required
Fagron	SyrSpend® SF pH4...	1503D009	31670	40	not required
Fagron	SyrSpend® SF pH4...	1503D017	31671	40	not required
Caelo	Water	15068701	31675	40	not required
Fagron	SyrSpend® SF pH4...	1412D002	31722	40	not required
Fagron	SyrSpend® SF pH4...	1503D017	31723	40	not required
Bayer	Bepanthen solution	KP0ASHC	31857	40	not required
Caelo	Aloe vera gel, 1...	15185503	31862	40	not required
Caelo	Aloe Vera gel, 1:1	15329203	31866	40	not required
Caelo	Aloe Vera gel, 1:1	153292	31880	40	20151111*
Caelo	Aloe Vera gel, 1:1	153292	31881	40	20151111*
Caelo	Water	153943	32079	40	20151215*
Caelo	Aloe vera gel, 1...	161922	32313	40	20160707*
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

Validation samples

A total of 35 362 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 760 spectra of 19 reference samples from the substance/substance group *Water and aqueous solutions*. These samples are listed above in the [calibration samples](#) section.
- 15 499 spectra from a total of 358 batches from further 137 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 850 spectra of 27 reference samples from the substance/substance group *Water and aqueous solutions*.

Supplier	Substance	Batch	Sample ID	Spectra
Hedinger	Water	219066	31623 [†]	20
Fagron	SyrSpend® SF pH4 aroma free	1503D009	31670 [†]	20

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

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Supplier	Substance	Batch	Sample ID	Spectra
Fagron	SyrSpend [®] SF pH4 cherry aroma	1503D017	31671 [†]	20
Caelo	Water	15068701	31675 [†]	20
Fagron	SyrSpend [®] SF pH4 aroma free	1412D002	31722 [†]	20
Fagron	SyrSpend [®] SF pH4 cherry aroma	1503D017	31723 [†]	20
Bayer	Bepanthen solution	KP0ASHC	31857 [†]	20
Caelo	Aloe vera gel, 10x concentra...	15185503	31862 [†]	20
Caelo	Aloe Vera gel, 1:1	15329203	31866 [†]	20
Caelo	Aloe Vera gel, 1:1	153292	31880 [†]	20
Caelo	Aloe Vera gel, 1:1	153292	31881 [†]	20
Caelo	Water	153944	32081	40
Caelo	Water	153712	32083	40
Caelo	Aloe Vera gel, 1:1	162489	32580	40
Bayer	Bepanthen solution	KP0B60L	32719	40
Fagron	SyrSpend [®] SF pH4 aroma free	1507402	32737	40
Fagron	SyrSpend [®] SF pH4 cherry aroma	1503255	32738	40
Retterspitz GmbH	Retterspitz external	16179	32784	30
Fagron	SyrSpend [®] SF pH4 cherry aroma	1603252/2	32842	40
Fagron	SyrSpend [®] SF pH4 aroma free	1507402	32843	40
Caelo	Water	162553	32895	40
Caelo	Water	162867	32896	40
Caelo	Aloe Vera gel, 1:1	162912	32899	40
Bayer	Bepanthen solution	KP0BJ61	32949	40
Caelo	Water	163533	33176	40
Caelo	Water	170018	33177	40
Caelo	Aloe Vera gel, 1:1	171341	33411	40

- 15 454 spectra from a total of 402 batches from further 170 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 19 *Apo-Ident* customers from 20 batches from the substance/substance group *Water and aqueous solutions*.

Supplier	Substance	Batch	Spectra
Caelo	Aloe vera gel, 10x concentra...	15185512	1
Fagron	Water	15H25-T21-025683	1
Fagron	SyrSpend [®] SF pH4 aroma free	1410D020	1
Fagron	SyrSpend [®] SF pH4 cherry aroma	1503255	6
Fagron	SyrSpend [®] SF pH4 aroma free	1503D009	1
Fagron	SyrSpend [®] SF pH4 cherry aroma	1503D017	1
Caelo	SyrSpend [®] SF pH4 cherry aroma	1507318	1
Fagron	SyrSpend [®] SF pH4 aroma free	1605291	2
Fagron	Water	15H25-T14-025670	1
Fagron	Water	15H25-T18-025678	1

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

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Supplier	Substance	Batch	Spectra
Phoenix	Water	15L14-T14-028664	1
Fagron	Water	15L15-T01-028672	1
Fagron	Water	16F13-T16-034297	1
Euro OTC	Water	16F14-T07-034326	1
Fagron	Water	16C23-T06-031423	1
Caelo	Water		1
WEPA	Water	LOTAP0015	1
wepa	Water	LOTAP0019	1
Wepa/Wepa	Water	LOTAP0037	1
Wepa	Water	LOTAP0031	1

- 2773 spectra from 261 *Apo-Ident* customers from a total of 1454 batches from a further 113 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	760	0	15 499
Type B	0	849	1	15 114
Type C	0	26	0	2747

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 % (> 99.9461 %)	100.0000 % (> 99.2105 %)
Type B	100.0000 % (> 99.9409 %)	99.8824 % (> 99.5294 %)
Type C	100.0000 % (> 98.2434 %)	100.0000 % (> 76.9231 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	30.65
31145	31145	0.00	35.37
31146	31146	0.00	33.66
31623	31623	0.00	35.42
31670	31670	0.00	35.29
31671	31671	0.00	36.34
31675	31675	0.00	38.99
31722	31722	0.00	33.55
31723	31723	0.00	33.98
31857	31857	0.00	30.18
31862	31862	0.00	33.26
31866	31866	0.00	37.45
31880	31880	0.00	39.57
31881	31881	0.00	36.83
32079	32079	0.00	37.55
32313	32313	0.00	31.45
32785	32785	0.00	20.43
33430	33430	0.00	30.19
33431	33431	0.00	29.80

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group	Wax ointment (stabilised)
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	08/09/2017
Report number	31111-2017-09-08
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Wax ointment (stabilised); Unguentum cereum

Special notes

When selecting the *Wax ointment (stabilised)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-5416-7	<i>European Pharmacopoeia 8th Edition, Basic Version 2014</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>
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	20151217*
Caelo	Wax ointment (st...	154244	31912	40	20151217*

Validation samples

A total of 35 362 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 *Wax ointment (stabilised)*. These samples are listed above in the [calibration samples](#) section.
- 16 059 spectra from a total of 370 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 200 spectra of 6 reference samples from the substance/substance group *Wax ointment (stabilised)*.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Wax ointment (stabilised)	9361101	30267	40
Caelo	Wax ointment (stabilised)	12352501	30967	40
Caelo	Wax ointment (stabilised)	154243	31911 [†]	20
Caelo	Wax ointment (stabilised)	154244	31912 [†]	20
Caelo	Wax ointment (stabilised)	161215	32117	40
Caelo	Wax ointment (stabilised)	161334	32118	40

- 16 104 spectra from a total of 420 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

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

[†]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*.

- 187 spectra from 77 *Apo-Ident* customers from 45 batches from the substance/substance group *Wax ointment (stabilised)*.

Supplier	Substance	Batch	Spectra
Caelo	Wax ointment (stabilised)	13307802	11
VDL;6,45EUR;21.10.14	Wax ointment (stabilised)	14235901	1
Caelo	Wax ointment (stabilised)	14235901	10
Caelo	Wax ointment (stabilised)	15025801	12
Caelo	Wax ointment (stabilised)	15205402	7
Caelo	Wax ointment (stabilised)	15424301	7
Caelo	Wax ointment (stabilised)	16133401	7
Caelo	Wax ointment (stabilised)	12033701	6
Caelo	Wax ointment (stabilised)	12352501	4
Caelo	Wax ointment (stabilised)	1218702	2
Caelo	Wax ointment (stabilised)	1021303	1
Caelo	Wax ointment (stabilised)	7071204	1
Caelo	Wax ointment (stabilised)	11321302	2
Caelo	Wax ointment (stabilised)	11355202	1
Caelo	Wax ointment (stabilised)	12033602	2
Anzag 07.12.12	Wax ointment (stabilised)	12128702	1
Caelo	Wax ointment (stabilised)	12352051	1
Caelo	Wax ointment (stabilised)	12209402	1
Sanacorp	Wax ointment (stabilised)	12352501	1
Caelo	Wax ointment (stabilised)	12378701	8
Caelo	Wax ointment (stabilised)	13072102	11
Caelo	Wax ointment (stabilised)	13159302	7
Caelo	Wax ointment (stabilised)	13307701	16
Caelo	Wax ointment (stabilised)	14073701	12
Caelo	Wax ointment (stabilised)	20121305	1
Caelo	Wax ointment (stabilised)	20051012-1	1
Caelo	Wax ointment (stabilised)	14072801	1
Caelo	Wax ointment (stabilised)	1407301	1
AHD	Wax ointment (stabilised)	14073701	1
Sanacorp	Wax ointment (stabilised)	14073701	1
Caelo	Wax ointment (stabilised)	14073801	6
Caelo	Wax ointment (stabilised)	140737701	1
Caelo	Wax ointment (stabilised)	140737012	1
Caelo	Wax ointment (stabilised)	14236001	2
Caelo	Wax ointment (stabilised)	14236002	2
Caelo	Wax ointment (stabilised)	15025702	8
Sanacorp	Wax ointment (stabilised)	15205402	2
Caelo	Wax ointment (stabilised)	1524301	1
Henry Lamotte Olis GmbH...	Wax ointment (stabilised)	15424301	1
Caol/Phoenix	Wax ointment (stabilised)	15424301	1
Caelo	Wax ointment (stabilised)	15424401	1
Caelo	Wax ointment (stabilised)	15424402	1
Caelo	Wax ointment (stabilised)	16121501	4
Caelo	Wax ointment (stabilised)	17014901	1
Caelo	Wax ointment (stabilised)	2113Q-03212	1
Gehe	Wax ointment (stabilised)	16133401	1
Caelo	Wax ointment (stabilised)	28051511	1
Caelo	Wax ointment (stabilised)	1114E3212	1
Caelo	Wax ointment (stabilised)	17015001	1
Caelo	Wax ointment (stabilised)	11355201	2
Anzag	Wax ointment (stabilised)	12033701	1
Caelo	Wax ointment (stabilised)	12209401	3
Caesar & Loretz GmbH	Wax ointment (stabilised)	13072102	1
Gehe	Wax ointment (stabilised)	13072102	1
Caelo	Wax ointment (stabilised)	13159303	2
Celo	Wax ointment (stabilised)	15424402	1

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Supplier	Substance	Batch	Spectra
Caelo	Wax ointment (stabilised)	U-150513-2	1

- 2612 spectra from 258 *Apo-Ident* customers from a total of 1429 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	200	0	16 059
Type B	0	200	0	16 104
Type C	0	184	3	2612

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 % (> 99.9464 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9400 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 98.2263 %)	98.3957 % (> 96.7914 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31111	31111	0.00	36.68
31167	31167	0.00	39.10
31444	31444	0.00	42.60
31911	31911	0.00	43.46
31912	31912	0.00	41.68

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **White paraffin oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 32342-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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 35 362 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.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 2 reference samples from the substance/substance group *White paraffin oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	White paraffin oil	14338604	32454	40
Caelo	White paraffin oil	14338604	32846	40

- 16 224 spectra from a total of 425 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *White paraffin oil*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), 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.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	80	0	16 224
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9403 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32342	32342	0.00	26.33
32565	32565	0.00	28.10

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Wintergreen oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 30455-2017-09-08
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

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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	40	not required
Taoasis	Wintergreen oil	1828-125286	32807	40	not required

Validation samples

A total of 35 362 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 *Wintergreen oil*. These samples are listed above in the [calibration samples](#) section.
- 16 179 spectra from a total of 373 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 96 spectra of 3 reference samples from the substance/substance group *Wintergreen oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Wintergreen oil	423129090971	30455	40
Taoasis	Wintergreen oil	5411006-117696	31543 [†]	16
Taoasis	Wintergreen oil	1828-125286	32936	40

- 16 208 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 8 *Apo-Ident* customers from 9 batches from the substance/substance group *Wintergreen oil*.

Supplier	Substance	Batch	Spectra
Caelo	Wintergreen oil	15087406	1
Taoasis	Wintergreen oil	423121-90971	1

continued on the next page

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

continued from previous page

Supplier	Substance	Batch	Spectra
Taoasis	Wintergreen oil		1
Taoasis	Wintergreen oil	1303-121125	1
Caelo	Wintergreen oil	10318703	1
Caelo	Wintergreen oil	13099202	1
Caelo	Wintergreen oil	13099205	1
Taoasis	Wintergreen oil	97540	1
Caelo	Wintergreen oil	10318714	1

- 2790 spectra from 265 *Apo-Ident* customers from a total of 1465 batches from a further 116 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	16 179
Type B	0	72	24	16 208
Type C	0	6	3	2790

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9469 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9402 %)	75.0000 % (> 71.8750 %)
Type C	100.0000 % (> 98.2352 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31543	31543	0.00	406.28
32807	32807	0.00	406.78

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

VALIDATION REPORT

IdentModul 1.3-2017-05

Validated substance/substance group **Ylang-ylang oil**
Substance class APIs & excipients, liquid/semi-solid (other)
Report date 08/09/2017
Report number 31506-2017-09-08
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ylang-ylang oil; Oleum cananga odorata; Oleum ylang-ylang

Special notes

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

- Advice for the identification of essential oils : Some essential oils are listed in the class APIs & excipients, liquid/semi-solid (with analysis certificate) as well as in the class APIs & excipients, liquid/semi-solid (other).

Applicable documents

978-3-7692-5416-7 *European Pharmacopoeia 8th Edition, Basic Version 2014* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*
Anhang F [Zusatz zu den Modellen der zweiten Stufe](#)

Validation method

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Taoasis	Ylang-ylang oil	140114-115612	31506	40	not required
Taoasis	Ylang-ylang oil	07122-119828	31653	40	not required
Taoasis	Ylang-ylang oil	41813-124965	32808	40	not required

Validation samples

A total of 35 362 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 *Ylang-ylang oil*. These samples are listed above in the [calibration samples](#) section.
- 16 139 spectra from a total of 372 batches from further 143 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

These samples are allowed to originate from the same batch as calibration samples (*Type A*) as long as the package differs. In the following table spectra recorded from the same package as the corresponding calibration samples (*Type A*) are highlighted by [†].

- 80 spectra of 3 reference samples from the substance/substance group *Ylang-ylang oil*.

Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Ylang-ylang oil	140114-115612	31506 [†]	20
Taoasis	Ylang-ylang oil	7122-119828	31653 [†]	20
Taoasis	Ylang-ylang oil	43197-126348	33049	40

- 16 224 spectra from a total of 423 batches from further 176 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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*.
- 2799 spectra from 265 *Apo-Ident* customers from a total of 1474 batches from a further 117 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

[†]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*.

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

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	120	0	16 139
Type B	0	79	1	16 224
Type C	0	0	0	2799

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9466 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9403 %)	98.7500 % (> 95.0000 %)
Type C	100.0000 % (> 98.2258 %)	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.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31506	31506	0.00	89.71
31653	31653	0.00	40.13
32808	32808	0.00	82.16

Die Identität einer Probe wird mittels NIR bestätigt, wenn der Abstand zur nächsten Fremdprobe mindestens 50 % größer ist, als der Abstand zu einer Referenzprobe, deren Identität mittels Laborprüfung belegt wurde. Dieses Kriterium wird immer in dem chemometrischen Modell betrachtet, das alle Substanzen der Substanzklasse enthält, selbst dann wenn eine Zweite Stufe eine Untergruppe von ähnlichen Substanzen auflöst und dabei die Abstände untereinander vergrößert. Die mittels NIR bestätigten Proben untermauern die statistische Streuung der originalen Referenzsubstanz, können aber keine neuen Aspekte bzw. Ausprägungsformen der Substanz hinzufügen.

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 48 batches. From these 2031 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
Audor	Lipoid S 100	pending	40	not required
Bayer	Ultrabas [®]	33851A	40	not required
Bayer	Ultrapril [®]	22100A	40	not required
Bayer	Ultrasicc [®]	33614A	40	not required
Caelo	Base cream, dilu...	14242803	60	not required
Caelo	Milking grease S...	162049	40	20160711*
Caelo	Pine oil rubbing...	162091	40	20160713*
Caelo	Salmon oil	170345	40	20170213*
Caelo	Ultrasound conta...	12031301	40	not required
Caelo	Vario base cream	12077902	50	1405329
Caelo	Vario base cream	13257102	40	1405330
Dr. Wolff	Anefug [®] Simplex	237590	40	1407216
Dr. Wolff	Anefug [®] Simplex	234280	40	not required
Dr. Wolff	Linola [®] acute 0.5%	334620	40	not required
Dr. Wolff	Linola [®] sun prot...	134530	40	not required
Dyckerhoff	Regeneresen	150032Y-Na-5	40	not required
Dyckerhoff	Regeneresen	061211Art-2	40	not required
Dyckerhoff	Regeneresen	pending	40	not required
Dyckerhoff	Regeneresen	211111Rk-2	40	not required
Einhorn-Apoth...	Rizol raw material	200812174102290W	30	not required
Einhorn-Apoth...	Rizol raw material	AL0413-1	60	not required
Euro OTC	Capsaicin liquid...	2908036-01	41	not required
Fagron	Ora-Plus [®]	3334081	60	not required
Fagron	Ora-Sweet [®]	3062252	40	not required
Ichthyol	Milk Cordes [®] O/W...	10D032	40	not required
Koko	dermaviduals [®] ba...	L003L13	60	not required
Paddock	Ora-Blend [®]	2280130	40	not required
Paddock	Ora-Blend [®] SF	2038178	40	not required
Perrigo	Ora-Blend [®] SF	3112578	40	not required
Perrigo	Ora-Plus [®]	3334081	40	not required
Perrigo	Ora-Sweet [®]	3062252	40	not required
Pharmapol	Glycerol trinitr...	232961	60	not required
Pharmapol	Glycerol trinitr...	228718	40	not required
Pharmapol	Glycerol trinitr...	211528	50	not required
Phylak Sachse...	Skin cream, high...	pending	40	not required
Phylak Sachse...	Skin cream, ligh...	pending	40	not required
Primavera	Wild rose oil	94930-95763	40	not required
Spirig Pharma	Kerasal [®] base oi...	N011	40	not required
Spirig Pharma	Kerasal [®] base oi...	M031	40	not required
Stiefel	Physiogel [®] hypoa...	6940	40	not required
Stiefel	Physiogel [®] hypoa...	343P	40	not required
Stoko	Praecutan [®] lotio...	011657101571	40	not required
Stoko	Praecutan [®] lotio...	0915777806	40	not required
Taoasis	Angelica root ex...	21439-67783	40	not required
Taoasis	Black cumin oil	504511-115611	40	not required
Taoasis	Tolu res. 50% oil	493887-105383BAC90451	40	not required
Taoasis	Tolu res. 50% oil	pending	40	not required
Taoasis	Vanilla extract ...	789171-114788	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 91 batches. From these, 154 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
Anzag/Galderma	Kerasal [®] base ointment	S075	1
Arkeo Immun UG	Rizol raw material	1192HJ	2
Bombastus	Vario base cream	12375801	1
Caelo	Milk Cordes [®] O/W Emul...	13D002	1
Caelo	Milk Cordes [®] O/W Emul...	13D001	2
Caelo	Rizol raw material	15144304	1
Caelo	Vario base cream	16032402	1
Caelo	Vario base cream	13257102	2
Caelo	Vario base cream	13143401	1
Caelo	Vario base cream	12077902	1
Caelo	Vario base cream	14331902	4
Dr. Wolff	Anefug [®] Simplex	136840	1
Dyckerhoff	Regeneresen	1204620Le-2	1
Dyckerhoff	Regeneresen	120053NNR-2	1
Dyckerhoff	Regeneresen	120054Lu-2	1
Dyckerhoff	Regeneresen	120063ytfm-2	1
Dyckerhoff	Regeneresen	120073sy-2	1
Dyckerhoff	Regeneresen	120243pl-2	1
Dyckerhoff	Regeneresen	1202920v-2	1
Dyckerhoff	Regeneresen	120303Dü-2	1
Dyckerhoff	Regeneresen	120313Kn-2	1
Dyckerhoff	Regeneresen	120323Lu-2	1
Dyckerhoff	Regeneresen	120333NN-2	1
Dyckerhoff	Regeneresen	120453Pl-2	1
Dyckerhoff	Regeneresen	120023gh-2	1
Dyckerhoff	Regeneresen	120463GH-2	1
Dyckerhoff	Regeneresen	120502Ni-2	1
Dyckerhoff	Regeneresen	60611dü-2	1
Dyckerhoff	Regeneresen	150173th-2	1
Dyckerhoff	Regeneresen	1503839-Na	1
Dyckerhoff	Regeneresen	150403HZ-2	1
Dyckerhoff	Regeneresen	150423Ni-2	1
Dyckerhoff	Regeneresen	250511Ad-2	1
Dyckerhoff	Regeneresen	130111AU-2	1
Euro OTC	Capsaicin liquid extr...	6061204	1
Euro OTC	Capsaicin liquid extr...	1201010-01	1
Euro OTC	Capsaicin liquid extr...	1205038-01	2
Euro OTC	Capsaicin liquid extr...	12111205	1
Euro OTC	Capsaicin liquid extr...	1205038-02	2
Fagron	Ora-Blend [®] SF	3745164	1
Fagron	Ora-Blend [®] SF	4136370	1
Fagron	Ora-Sweet [®]	3414679	1
Fagron	Ora-Sweet [®]	4247427	1
Galderma/Gehe	Kerasal [®] base ointment	S061	1
Galderma/Anzag	Kerasal [®] base ointment	S041	4
Gehe	Glycerol trinitrate 5%	214895	1

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Supplier	Substance	Batch	Spectra
Gehe	Ora-Blend [®] SF	2038178	1
Gehe	Ora-Blend [®] SF	3112578	1
GSK Stiefel	Physiogel [®] hypoallerg...	859R	1
GSK/Stiefel	Physiogel [®] hypoallerg...	538T	1
Ichthyol	Milk Cordes [®] O/W Emul...	60613	1
Ichthyol - Gesellschaft	Milk Cordes [®] O/W Emul...	11D037	1
Ichthyol / Noweda	Milk Cordes [®] O/W Emul...	12D008	6
IchthyolGmbH/Anzag	Milk Cordes [®] O/W Emul...	12D003	2
Ichtyol, Noweda	Milk Cordes [®] O/W Emul...	13d007	1
Perrigo	Ora-Blend [®] SF	2088609	1
Pharmapohl	Glycerol trinitrate 5%	18102013A	1
Pharmapol	Glycerol trinitrate 5%	234783	1
Pharmapol	Glycerol trinitrate 5%	228718	12
Pharmapol	Glycerol trinitrate 5%	AKD81	1
Pharmapol	Glycerol trinitrate 5%	221414	4
Pharmapol	Glycerol trinitrate 5%	224310(ex)224658(in)	2
Pharmapol	Glycerol trinitrate 5%	25041301	1
Pharmapol	Glycerol trinitrate 5%	232961	3
Pharmapol Arzneimittel...	Glycerol trinitrate 5%	219108	4
Pharmapol Arzneimittel...	Glycerol trinitrate 5%	232961	6
Pharmapol/Direkt	Glycerol trinitrate 5%	224310	7
Pharmapol/Direkt	Glycerol trinitrate 5%	226578	12
Pharmapol/Zentrum Apo	Glycerol trinitrate 5%	2913A-07002	1
PHOENIX 21.10.2013	Physiogel [®] hypoallerg...	1142N	1
Phoenix/Stiefel	Physiogel [®] hypoallerg...	399P	1
Phönix	Ora-Blend [®] SF	3434856	2
Phönix	Ora-Blend [®] SF	3475164	1
phönix, 09.11.2012	Capsaicin liquid extr...	120503801	2
Spirig Pharma	Kerasal [®] base ointment	N021	1
Spirig/Gehe	Kerasal [®] base ointment	S076	1
Spirig/Noweda	Kerasal [®] base ointment	N032	2
Spirig/Sanacorp	Kerasal [®] base ointment	N011	1
Steidl/Phytolab	Rizol raw material	200812174102290	1
Stiefel	Physiogel [®] hypoallerg...	926Q	1
Stiefel	Physiogel [®] hypoallerg...	270T	1
Stiefel	Physiogel [®] hypoallerg...	537T	1
Stiefel/Noweda	Physiogel [®] hypoallerg...	163R	1
Stiefel/Sanacorp	Physiogel [®] hypoallerg...	10000	1
Taoasis	Tolu res. 50% oil	23772-118646	1
Taoasis	Tolu res. 50% oil	23772-119167	1
Taoasis	Tolu res. 50% oil	546022-114802	2
Taoasis	Tolu res. 50% oil	546022-122636	1
Taoasis	Tolu res. 50% oil	493887-105384	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).

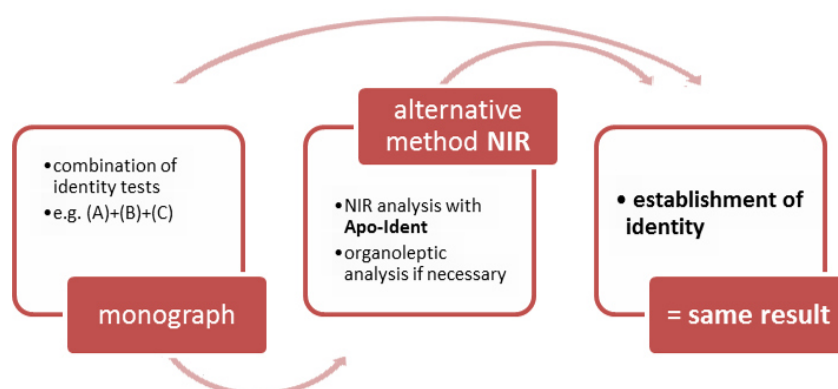


Figure 2: The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

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].

Anhang F: Zusatz zu den Modellen der zweiten Stufe

Wie im allgemeinen Teil der Validierungsdokumentation des *Apo-Ident* im Abschnitt [Ablauf von Modellerstellung und Validierungsläufen](#) unter 2. *Generieren der chemometrischen Modelle (Kalibrierung)* in f) beschrieben, besteht die Möglichkeit für bestimmte Substanzen ein weiteres *chemometrisches Modell* zu erstellen (Zweite-Stufe-Modell) und die Bewertung in mehreren Stufen vorzunehmen.

Substanzen in Stufe-Zwei-Modellen

Im *Apo-Ident Update 2017-05* werden folgende Substanzen in den aufgeführten Stufe-Zwei-Modellen differenziert:

Submodell 1

Betamethason, mikronisiert
Betamethasonvalerat
Budesonid, mikronisiert
Dexamethason
Erythromycin
Hydrocortisonbutyrat
Norethisteronacetat
Prednicarbat, mikronisiert
Prednisolon, mikronisiert
Triamcinolonacetonid

Submodell 2

Beclometasondipropionat, wasserfreies
Betamethasondipropionat, mikronisiert
Clobetasolpropionat
Diphenylcyclopropenon
Gentamicinsulfat
Natriumbenzoat
Natriumcitrat
Oxybutyninhydrochlorid

Submodell 3

Alfatradiol
Chininhydrochlorid
Chininsulfat Dihydrat
Estriol
Pregnenolon
Progesteron, mikronisiert
Spironolacton
Testosteronpropionat

Submodell flüssig

2-Ethylhexyllaurat
Basiscreme DAC
Hydrophile Creme, nichtionisch DAB
Lanette®-Salbe (konserviert)
Squalan
Wollwachsalkoholcreme DAB/SR

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- Oleum citrus aurantium var. amara, *see* [Neroli oil](#)

- Oleum citrus bergamia, *see* [Bergamot oil](#)
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 Oleum coriandri, *see* [Coriander oil](#)
 Oleum cuminum cyminum, *see* [Cumin oil](#)
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 Oleum cymbopogon martinii, *see* [Palmarosa oil, organic](#)
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 Oleum foeniculum vulgare var. dulce, *see* [Fennel oil](#)
 Oleum gaultheria procumbens, *see* [Wintergreen oil](#)
 Oleum helichrysum italicum, *see* [Immortelle oil](#)
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 Oleum myrrha, *see* [Myrrh oil](#)
 Oleum neroli, *see* [Neroli oil](#)
 Oleum niaouli, *see* [Cajeput / Niaouli oil](#)
 Oleum ocimum basilicum, *see* [Basil oil](#)
 Oleum olibanum, *see* [Frankincense oil](#)
 Oleum origani cretici, *see* [Oregano oil](#)
 Oleum ormenis multicaulis, *see* [Matricaria oil, morrocan](#)
 Oleum palmarosae, *see* [Palmarosa oil, organic](#)
 Oleum pelargonium graveolens, *see* [Rose-geranium oil, organic](#)
 Oleum pini pumilionis, *see* [Mountain pine oil](#)
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