Validation documentation
HCK - nutritional supplements (Hepart)

HiperScan GmbH

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Validation documentation of the chemometrics database of the near-infrared spectrometer *Apo-Ident*.
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info@hiperscan.com, www.hiperscan.com

Contents

Introduction

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

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

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

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

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

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

Context of this document

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

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

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 *HCK - nutritional supplements (Hepart)*. 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 demarcation 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. Bezugsquellennachweis für Rezepturbestandteile* [Sources of supply for compounding] [7]).

b) Testing the suitability according to *ApBetrO* [Pharmacies Rules and Regulations] §§ 6, 11, that is to say the availability of a valid manufacturer certificates via identity, purity and contents of the batch.

c) Recording standard 40 spectra of the sample in different positions, as a standard on four instruments. Here, handling and presentation of the samples as later in the pharmacy.

d) Visual checking for anomalies in the spectra. In case of indications of measurement errors, measurement must be repeated. If a signature is missing in the spectrum, the substance may be excluded from the start as not promising (the spectra are nonetheless entered in the database validation as independent *Type B* spectra).

e) Testing identity. For each substance, a certificate of correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the respective following substance page of this validation documentation the *Mahalanobis distance* to this reference sample is specified as well

as the *Mahalanobis distance* to the next non-identical substance. Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

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

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

2. Generating the chemometric models (calibration)

a) Determination of the transformation matrix from the reference spectra using variance maximisation [8, 9]. (*All* reference spectra are always included, even if only a few spectra are added for an update.) All reference spectra receive the same data pre-treatment, which is also later applied to all measurement spectra in the field (in the pharmacies).

b) Checking that the number of principal components used is still sufficient.

c) Calculating the limits for each substance from the spread of the reference spectra. The calculation regulation is identical for each substance in a substance class.

d) 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 *HCK - nutritional supplements (Hepart)* 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, the substance classes with **TCM – Granulated herbal extracts** are separated supplier-specifically. The granulates from the suppliers *HerbaSinica*, *PhytoComm* and *China-Medica* are hardly comparable with each other due to their spectra, because extracts of respectively different drug batches with different carrier materials are granulated. The spectra for all batches from these suppliers are recorded by *HiperScan GmbH* and entered in the respective database. The suppliers organise the respective tests themselves and keep the test certificates. The process implemented with *HerbaSinica* is a particularity: The reference samples are sent to a test laboratory which determines the identity of the sample and sends the container to *HiperScan GmbH* if the result is positive.

A new evaluation option was created for the class *TCM – Granulated herbal extracts (PhytoComm)* with the update 2016-01. As the risks are considerably fewer than those from chemical agents, the

pharmacist can specify a reasonable criterion for the *specificity* in accordance with internal risk estimation. The database for this is created without taking safety distances into account and no criterion is determined in advance for the *specificity*. Instead, the *specificity* for testing the identity with this concrete substance is calculated in the validation for each substance and provided with the measurement result. The pharmacist then judges himself whether this safety is reasonable with regard to the risk of the substance.

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

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

The positive result of the identity test using *Apo-Ident* establishes that the sample spectrum is in accordance with a batch of the specified granulate from this supplier, 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 Pharmacopeia* as a near-infrared spectrometer and proves the validity of the reference database with the existing validation documentation. This means that *Apo-Ident* can be used as an alternative testing method for testing raw materials at pharmacies.

Explanation of terminology

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

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

Substance classes are units of the organisational structure of the *IdentModule*. The substance classes are substance databases which are also broadly independently subscribable. On the one hand, the liquid and semi-solid substances are separated from the solid powders because they are measured against different references and therefore the spectra cannot be compared. On the other hand, for example the Pharmacopoeia substances are kept separated from the manufacturer-specific databases 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 *HerbaSinica* neither needs to be delimited from *Huang Qi* granulate from the company *PhytoComm* nor is matching required. Respectively one single chemometric model is behind a substance class. (Even if several reciprocally secured chemometric models would be permissible.) The terms *substance class*, *chemometric model* and *databases* are mostly used here as synonyms.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

with r_p as the total number of *true positive* classifications and f_n as the total number of *false negative* classifications. The *true positive* rate is a measure for the recognition rate of the validated *Apo-Ident IdentModule*.
In order to ensure that each substance is received with the same weight, the spectra are weighted as described for the true negative rate.

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

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

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

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

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

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

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

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

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

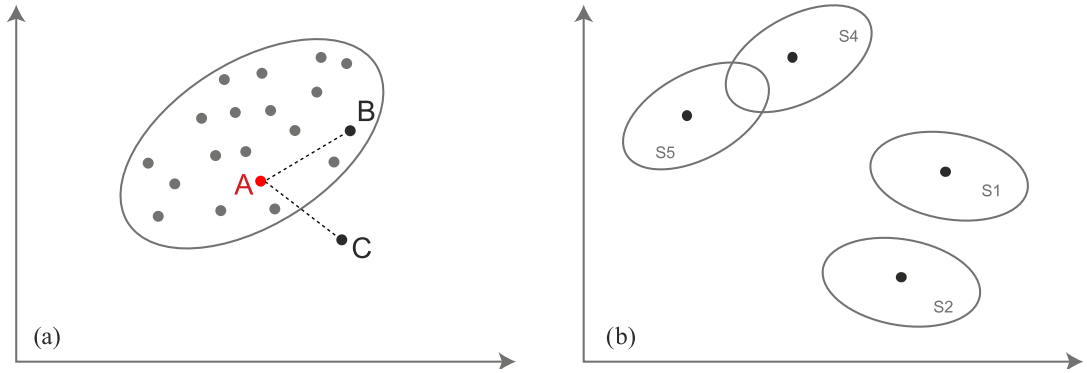

Figure 1: (a) The *Mahalanobis distance* from A to B is less than from A to C. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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

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

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

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 42 629 spectra from 1241 different batches for a total of 94 substances were used to validate the substance class *HCK - nutritional supplements (Hepart)*.

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
HCK - nutritional supplements (Hepart)	79	400	19 154

From category *A* a total of 19 154 spectra from 400 batches for a total of 79 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
HCK - nutritional supplements (Hepart)	91	552	21 896

From category *B* a total of 21 896 spectra from 552 batches for a total of 91 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
HCK - nutritional supplements (Hepart)	60	596	1579

From category *C* a total of 1579 spectra from 596 batches for a total of 60 substances were taken into account for validation.

Validation results

The validation runs checked whether all substances/substance groups in the substance class *HCK - nutritional supplements (Hepart)* 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 *HCK - nutritional supplements (Hepart)* 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	19 154	0	1 283 318
Type B	0	17 758	2609	1 467 684
Type C	0	1325	252	105 793

All substances/substance groups in the substance class *HCK - nutritional supplements (Hepart)* 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 09 %)	100.000 00 % (> 99.938 34 %)
Type B	100.000 00 % (> 99.998 42 %)	81.090 56 % (> 81.030 50 %)
Type C	100.000 00 % (> 99.987 77 %)	79.784 70 % (> 79.512 35 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 1.3-2017-02

Validated substance/substance group	**Amino V complex (H1400)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80745-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Amino V complex (H1400)

Special notes

When selecting the *Amino V complex (H1400)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Amino V complex (H1400)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Amino V complex ...	15001365(MM)	80749	40	from supplier
Hepart	Amino V complex ...	15001366(B1)	80750	40	from supplier
Hepart	Amino V complex ...	16001268	80820	40	from supplier
Hepart	Amino V complex ...	16001229	80821	40	from supplier

Validation samples

A total of 42 629 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 *Amino V complex (H1400)*. These samples are listed above in the *calibration samples* section.

- 18 994 spectra from a total of 395 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 280 spectra of 6 reference samples from the substance/substance group *Amino V complex (H1400)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Amino V complex (H1400)	15001365(F2)	80745	60
Hepart	Amino V complex (H1400)	15001365(B1)	80746	60
Hepart	Amino V complex (H1400)	15001366(MM)	80747	60
Hepart	Amino V complex (H1400)	15001366(F2)	80748	60
Hepart	Amino V complex (H1400)	15001365(MM)	80749†	20
Hepart	Amino V complex (H1400)	15001366(B1)	80750†	20

- 21 616 spectra from a total of 517 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Amino V complex (H1400)*.

†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*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Amino V complex (H1400)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Amino V complex (H1400)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 994
Type B	0	280	0	21 560
Type C	0	0	0	1579

The substance/substance group *Amino V complex (H1400)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9382 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8925 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80749	80749	0.00	19.11
80750	80750	0.00	18.82
80820	80820	0.00	19.25
80821	80821	0.00	19.73

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Aminomix NAC (H1002)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80003-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Aminomix NAC (H1002)

Special notes

When selecting the *Aminomix NAC (H1002)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Aminomix NAC (H1002)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Aminomix NAC (H1…	041401	80312	40	from supplier
Hepart	Aminomix NAC (H1…	041402	80314	60	from supplier
Hepart	Aminomix NAC (H1…	14000258	80407	40	from supplier
Hepart	Aminomix NAC (H1…	14000258	80444	40	from supplier
Hepart	Aminomix NAC (H1…	14000259	80447	40	from supplier
Hepart	Aminomix NAC (H1…	15000295(B1)	80538	40	from supplier

continued on the next page

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Aminomix NAC (H1…	15000297(F2)	80544	40	from supplier
Hepart	Aminomix NAC (H1…	15000320	80545	40	from supplier
Hepart	Aminomix NAC (H1…	15000321	80546	40	from supplier
Hepart	Aminomix NAC (H1…	15000319(F2)	80549	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 420 spectra of 10 reference samples from the substance/substance group *Aminomix NAC (H1002)*. These samples are listed above in the *calibration samples* section.

- 18 734 spectra from a total of 390 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 830 spectra of 20 reference samples from the substance/substance group *Aminomix NAC (H1002)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Aminomix NAC (H1002)	946501	80003	40
Hepart	Aminomix NAC (H1002)	971701	80024	40
Hepart	Aminomix NAC (H1002)	971701	80186	40
Hepart	Aminomix NAC (H1002)	19101	80199	20
Hepart	Aminomix NAC (H1002)	936401	80220	30
Hepart	Aminomix NAC (H1002)	14000259	80408	40
Hepart	Aminomix NAC (H1002)	41401	80457	40
Hepart	Aminomix NAC (H1002)	15000295	80537	60
Hepart	Aminomix NAC (H1002)	15000295(B1)	80538†	20
Hepart	Aminomix NAC (H1002)	15000295(F2)	80539	60
Hepart	Aminomix NAC (H1002)	15000298(F2)	80540	60
Hepart	Aminomix NAC (H1002)	15000298	80541	60
Hepart	Aminomix NAC (H1002)	15000297	80542	60
Hepart	Aminomix NAC (H1002)	15000297(B1)	80543	60
Hepart	Aminomix NAC (H1002)	15000297(F2)	80544†	20
Hepart	Aminomix NAC (H1002)	15000320	80545†	20
Hepart	Aminomix NAC (H1002)	15000321	80546†	20
Hepart	Aminomix NAC (H1002)	15000321(B1)	80547	60
Hepart	Aminomix NAC (H1002)	15000319	80548	60
Hepart	Aminomix NAC (H1002)	15000319(F2)	80549†	20

- 21 066 spectra from a total of 504 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 32 spectra from 9 *Apo-Ident* customers from 15 batches from the substance/substance group *Aminomix NAC (H1002)*.

Supplier	Substance	Batch	Spectra
unisan	Aminomix NAC (H1002)		1
Hepart AG	Aminomix NAC (H1002)	41401	1
Unisan	Aminomix NAC (H1002)	140000259	1
Unisan	Aminomix NAC (H1002)	14000258	2
Unisan	Aminomix NAC (H1002)	14000259	1
Unisan	Aminomix NAC (H1002)	15000295/0	3
unisan	Aminomix NAC (H1002)	15000297	1
Unisan	Aminomix NAC (H1002)	15000298/0	1
Unisan	Aminomix NAC (H1002)	15000320/0	1
Unisan	Aminomix NAC (H1002)	15000320	1
Unisan 02.04.2016	Aminomix NAC (H1002)	15000320/0	1
Euro OTC	Aminomix NAC (H1002)	16001017/0	1
Unisan	Aminomix NAC (H1002)	19101	1
Unisan	Aminomix NAC (H1002)	16001017/0	1
Unisan	Aminomix NAC (H1002)	41401	3
Unisan/Hepart AG	Aminomix NAC (H1002)	41402	1
Hepart AG	Aminomix NAC (H1002)	41402	2
Unisan	Aminomix NAC (H1002)	41402	5
Unisan	Aminomix NAC (H1002)	971701	1
Hepart AG	Aminomix NAC (H1002)	1054019101	2
Hepart AG, CH-8280 Kreu…	Aminomix NAC (H1002)	1054019101	1

- 1547 spectra from 20 *Apo-Ident* customers from a total of 576 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Aminomix NAC (H1002)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Aminomix NAC (H1002)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect.

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

The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	420	0	18 734
Type B	0	735	95	21 066
Type C	0	17	15	1547

The substance/substance group *Aminomix NAC (H1002)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9377 %)	100.0000 % (> 98.5714 %)
Type B	100.0000 % (> 99.8914 %)	88.5542 % (> 88.1928 %)
Type C	100.0000 % (> 99.1635 %)	53.1250 % (> 43.7500 %)

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80312	80312	0.00	24.00
80314	80314	0.00	30.80
80407	80407	0.00	30.36
80444	80444	0.00	26.76
80447	80447	0.00	26.93
80538	80538	0.00	29.97
80544	80544	0.00	26.60
80545	80545	0.00	28.42
80546	80546	0.00	30.30
80549	80549	0.00	28.34

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Antibiosis forte complex (H1115)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80675-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Antibiosis forte complex (H1115)

Special notes

When selecting the *Antibiosis forte complex (H1115)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Antibiosis forte complex (H1115)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antibiosis forte…	15001169	80675	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Antibiosis forte complex (H1115)*. These samples are listed above in the *calibration samples* section.

- 19 114 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 20 spectra of 1 reference samples from the substance/substance group *Antibiosis forte complex (H1115)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Antibiosis forte complex (H1…	15001169	80675†	20

- 21 876 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Antibiosis forte complex (H1115)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *Antibiosis forte complex (H1115)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Antibiosis forte complex (H1115)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	19 114
Type B	0	20	0	21 876
Type C	0	0	0	1579

The substance/substance group *Antibiosis forte complex (H1115)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80675	80675	0.00	73.32

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Antioxidants NAT complex (H1004)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80025-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Antioxidants NAT complex (H1004)

Special notes

When selecting the *Antioxidants NAT complex (H1004)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Antioxidants NAT complex (H1004)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antioxidants NAT…	051901	80311	60	from supplier
Hepart	Antioxidants NAT…	052001	80313	60	from supplier
Hepart	Antioxidants NAT…	052201	80315	60	from supplier
Hepart	Antioxidants NAT…	052101	80317	60	from supplier
Hepart	Antioxidants NAT…	051902	80318	60	from supplier
Hepart	Antioxidants NAT…	067301	80404	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antioxidants NAT…	067201	80405	40	from supplier
Hepart	Antioxidants NAT…	14000044	80419	40	from supplier
Hepart	Antioxidants NAT…	14000965	80469	40	from supplier
Hepart	Antioxidants NAT…	14000964	80473	40	from supplier
Hepart	Antioxidants NAT…	14001849	80504	40	from supplier
Hepart	Antioxidants NAT…	14001850	80505	40	from supplier
Hepart	Antioxidants NAT…	14001851	80506	40	from supplier
Hepart	Antioxidants NAT…	14001846	80507	40	from supplier
Hepart	Antioxidants NAT…	14001848	80508	40	from supplier
Hepart	Antioxidants NAT…	14001847	80509	40	from supplier
Hepart	Antioxidants NAT…	15000875(B1)	80607	40	from supplier
Hepart	Antioxidants NAT…	15000880	80609	40	from supplier
Hepart	Antioxidants NAT…	15000877(B1)	80613	40	from supplier
Hepart	Antioxidants NAT…	15000878(B1)	80616	40	from supplier
Hepart	Antioxidants NAT…	15000874	80618	40	from supplier
Hepart	Antioxidants NAT…	15000874(B1)	80619	40	from supplier
Hepart	Antioxidants NAT…	15000879	80621	40	from supplier
Hepart	Antioxidants NAT…	15000876	80624	40	from supplier
Hepart	Antioxidants NAT…	16000378	80783	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 1100 spectra of 25 reference samples from the substance/substance group *Antioxidants NAT complex (H1004)*. These samples are listed above in the *calibration samples* section.

- 18 054 spectra from a total of 374 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 2299 spectra of 58 reference samples from the substance/substance group *Antioxidants NAT complex (H1004)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Antioxidants NAT complex (H1…	pending	80016	40
Hepart	Antioxidants NAT complex (H1…	2401	80025	40
Hepart	Antioxidants NAT complex (H1…	967901	80179	40
Hepart	Antioxidants NAT complex (H1…	11001	80182	40

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Antioxidants NAT complex (H1…	980001	80188	40
Hepart	Antioxidants NAT complex (H1…	991301	80232	40
Hepart	Antioxidants NAT complex (H1…	19901	80236	40
Hepart	Antioxidants NAT complex (H1…	30901	80258	40
Hepart	Antioxidants NAT complex (H1…	30903	80259	40
Hepart	Antioxidants NAT complex (H1…	30902	80260	40
Hepart	Antioxidants NAT complex (H1…	30904	80261	40
Hepart	Antioxidants NAT complex (H1…	19901	80282	40
Hepart	Antioxidants NAT complex (H1…	14000043	80424	40
Hepart	Antioxidants NAT complex (H1…	14000042	80428	40
Hepart	Antioxidants NAT complex (H1…	14000961	80470	40
Hepart	Antioxidants NAT complex (H1…	14000962	80471	39
Hepart	Antioxidants NAT complex (H1…	14000963	80472	40
Hepart	Antioxidants NAT complex (H1…	14000966	80474	40
Hepart	Antioxidants NAT complex (H1…	14001849	80504†	20
Hepart	Antioxidants NAT complex (H1…	14001850	80505†	20
Hepart	Antioxidants NAT complex (H1…	14001851	80506†	20
Hepart	Antioxidants NAT complex (H1…	14001846	80507†	20
Hepart	Antioxidants NAT complex (H1…	14001848	80508†	20
Hepart	Antioxidants NAT complex (H1…	14001847	80509†	20
Hepart	Antioxidants NAT complex (H1…	15000875	80606	60
Hepart	Antioxidants NAT complex (H1…	15000875(B1)	80607†	20
Hepart	Antioxidants NAT complex (H1…	15000875(F2)	80608	60
Hepart	Antioxidants NAT complex (H1…	15000880	80609†	20
Hepart	Antioxidants NAT complex (H1…	15000880(B1)	80610	60
Hepart	Antioxidants NAT complex (H1…	15000880(F2)	80611	60
Hepart	Antioxidants NAT complex (H1…	15000877	80612	60
Hepart	Antioxidants NAT complex (H1…	15000877(B1)	80613†	20
Hepart	Antioxidants NAT complex (H1…	15000877(F2)	80614	60
Hepart	Antioxidants NAT complex (H1…	15000878	80615	60
Hepart	Antioxidants NAT complex (H1…	15000878(B1)	80616†	20
Hepart	Antioxidants NAT complex (H1…	15000878(F2)	80617	60
Hepart	Antioxidants NAT complex (H1…	15000874	80618†	20
Hepart	Antioxidants NAT complex (H1…	15000874(B1)	80619†	20
Hepart	Antioxidants NAT complex (H1…	15000874(F2)	80620	60
Hepart	Antioxidants NAT complex (H1…	15000879	80621†	20
Hepart	Antioxidants NAT complex (H1…	15000879(B1)	80622	60
Hepart	Antioxidants NAT complex (H1…	15000879(F2)	80623	60
Hepart	Antioxidants NAT complex (H1…	15000876	80624†	20
Hepart	Antioxidants NAT complex (H1…	15000876(B1)	80625	60
Hepart	Antioxidants NAT complex (H1…	15000876(F2)	80626	60
Hepart	Antioxidants NAT complex (H1…	16000380	80784	40
Hepart	Antioxidants NAT complex (H1…	16000376	80785	40
Hepart	Antioxidants NAT complex (H1…	16000377	80786	40
Hepart	Antioxidants NAT complex (H1…	16000965	80834	40
Hepart	Antioxidants NAT complex (H1…	16000966	80835	40
Hepart	Antioxidants NAT complex (H1…	16000967	80836	40
Hepart	Antioxidants NAT complex (H1…	16000968	80837	40
Hepart	Antioxidants NAT complex (H1…	16000969	80838	40
Hepart	Antioxidants NAT complex (H1…	16000970	80839	40
Hepart	Antioxidants NAT complex (H1…	16000971	80840	40
Hepart	Antioxidants NAT complex (H1…	16000972	80841	40
Hepart	Antioxidants NAT complex (H1…	16000973	80842	40
Hepart	Antioxidants NAT complex (H1…	16000974	80843	40

†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*.

- 19 597 spectra from a total of 467 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 78 spectra from 14 *Apo-Ident* customers from 36 batches from the substance/substance group *Antioxidants NAT complex (H1004)*.

Supplier	Substance	Batch	Spectra
Unisan	Antioxidants NAT complex (H1…	1851	1
Unisan	Antioxidants NAT complex (H1…	67201	4
Hepart AG	Antioxidants NAT complex (H1…	67201	1
Hepart AG	Antioxidants NAT complex (H1…	67501	1
Unisan	Antioxidants NAT complex (H1…	14000044	1
UNISAN	Antioxidants NAT complex (H1…	14000042	1
Unisan	Antioxidants NAT complex (H1…	1400042	1
Unisan	Antioxidants NAT complex (H1…	14000961	1
UNISAN	Antioxidants NAT complex (H1…	14000961	1
UNISAN	Antioxidants NAT complex (H1…	14000963	3
Unisan	Antioxidants NAT complex (H1…	14000963	2
Unisan	Antioxidants NAT complex (H1…	14001847/0	2
Unisan	Antioxidants NAT complex (H1…	14001847/1	1
Unisan 02.04.2016	Antioxidants NAT complex (H1…	15000874/0	2
Unisan	Antioxidants NAT complex (H1…	14001851/0	1
unisan	Antioxidants NAT complex (H1…	15000877	1
Unisan	Antioxidants NAT complex (H1…	15000880	1
Unisan	Antioxidants NAT complex (H1…	16000376	1
Unisan	Antioxidants NAT complex (H1…	15000877/0	1
Unisan	Antioxidants NAT complex (H1…	11001	1
Unisan	Antioxidants NAT complex (H1…	19901	3
Unisan	Antioxidants NAT complex (H1…	30901	1
hepart ag	Antioxidants NAT complex (H1…	19901	1
Hepart AG	Antioxidants NAT complex (H1…	30901	1
Unisan	Antioxidants NAT complex (H1…	30903	3
Unisan	Antioxidants NAT complex (H1…	30902	1
Unisan	Antioxidants NAT complex (H1…	30904	1
Unisan	Antioxidants NAT complex (H1…	51901	4
Hedinger	Antioxidants NAT complex (H1…	51901	1
Hepart AG	Antioxidants NAT complex (H1…	51902	1
Unisan	Antioxidants NAT complex (H1…	52001	2
Unisan	Antioxidants NAT complex (H1…	51902	1
Hepart AG	Antioxidants NAT complex (H1…	52101	3
Hepart AG, CH-8280 Kreu…	Antioxidants NAT complex (H1…	52101	1
Unisan	Antioxidants NAT complex (H1…	52101	1
Hepart AG	Antioxidants NAT complex (H1…	52201	2
Unisan	Antioxidants NAT complex (H1…	52201	1
Unisan Gmbh, 78465 Kons…	Antioxidants NAT complex (H1…	52201	1
Unisan Gmbh, 78465 Kons…	Antioxidants NAT complex (H1…	67301	1
Hepart AG	Antioxidants NAT complex (H1…	67301	2
Unisan	Antioxidants NAT complex (H1…	67601	2
Unisan	Antioxidants NAT complex (H1…	67501	1
Unisan	Antioxidants NAT complex (H1…	14001848/0	1
Unisan	Antioxidants NAT complex (H1…	68201	4

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Supplier	Substance	Batch	Spectra
Hepart AG, CH-8280 Kreu…	Antioxidants NAT complex (H1…	1034019901	1
Hepart AG	Antioxidants NAT complex (H1…	1034019901	1
Unisan	Antioxidants NAT complex (H1…	1034019901	1
Hepart AG, CH-8280 Kreu…	Antioxidants NAT complex (H1…	1034030901	1
Hepart AG	Antioxidants NAT complex (H1…	1034030901	1
Hepart AG	Antioxidants NAT complex (H1…	1034030902	1
Unisan	Antioxidants NAT complex (H1…	1034030902	1
Hepart AG	Antioxidants NAT complex (H1…	1034030904	1
Unisan	Antioxidants NAT complex (H1…	1034030904	1
Hepart AG	Antioxidants NAT complex (H1…	1037030904	1

- 1501 spectra from 20 *Apo-Ident* customers from a total of 554 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Antioxidants NAT complex (H1004)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Antioxidants NAT complex (H1004)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	1100	0	18 054
Type B	0	2286	13	19 597
Type C	0	75	3	1501

The substance/substance group *Antioxidants NAT complex (H1004)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9375 %)	100.0000 % (> 99.4545 %)
Type B	100.0000 % (> 99.8913 %)	99.4345 % (> 99.3040 %)
Type C	100.0000 % (> 99.1591 %)	96.1538 % (> 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
80311	80311	0.00	15.35
80313	80313	0.00	15.31
80315	80315	0.00	15.81
80317	80317	0.00	17.04
80318	80318	0.00	15.16
80404	80404	0.00	20.83
80405	80405	0.00	21.49
80419	80419	0.00	23.05
80469	80469	0.00	20.96
80473	80473	0.00	22.01
80504	80504	0.00	23.96
80505	80505	0.00	23.07
80506	80506	0.00	23.26
80507	80507	0.00	21.57
80508	80508	0.00	22.05
80509	80509	0.00	22.69
80607	80607	0.00	18.93
80609	80609	0.00	17.02
80613	80613	0.00	18.72
80616	80616	0.00	17.18
80618	80618	0.00	19.84
80619	80619	0.00	20.28
80621	80621	0.00	17.52
80624	80624	0.00	24.90
80783	80783	0.00	22.39

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Argentum (H1116)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80674-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Argentum (H1116)

Special notes

When selecting the *Argentum (H1116)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Argentum (H1116)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Argentum (H1116)	15001151	80674	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Argentum (H1116)*. These samples are listed above in the *calibration samples* section.

- 19 114 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 20 spectra of 1 reference samples from the substance/substance group *Argentum (H1116)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Argentum (H1116)	15001151	80674†	20

- 21 876 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Argentum (H1116)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *Argentum (H1116)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Argentum (H1116)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	19 114
Type B	0	20	0	21 876
Type C	0	0	0	1579

The substance/substance group *Argentum (H1116)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80674	80674	0.00	12.29

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Arginine (L-) (H1036)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80026-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Arginine (L-) (H1036)

Special notes

When selecting the *Arginine (L-) (H1036)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Arginine (L-) (H1036)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Arginine (L-) (H...	0999001	80026	40	from supplier
Hepart	Arginine (L-) (H...	950601	80129	50	from supplier
Hepart	Arginine (L-) (H...	0999001	80157	50	from supplier
Hepart	Arginine (L-) (H...	027802	80256	40	from supplier
Hepart	Arginine (L-) (H...	044301	80280	40	from supplier
Hepart	Arginine (L-) (H...	066501	80373	50	from supplier
Hepart	Arginine (L-) (H...	16000949	80807	40	not required

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 310 spectra of 7 reference samples from the substance/substance group *Arginine (L-) (H1036)*. These samples are listed above in the *calibration samples* section.

- 18 844 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Arginine (L-) (H1036)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Arginine (L-) (H1036)	928302	80212	30
Hepart	Arginine (L-) (H1036)	52401	80330	60
Hepart	Arginine (L-) (H1036)	66501	80373†	10
Hepart	Arginine (L-) (H1036)	14000563	80446	20
Hepart	Arginine (L-) (H1036)	14000564	80448	40
Hepart	Arginine (L-) (H1036)	16000950	80808	40

- 21 696 spectra from a total of 517 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 11 *Apo-Ident* customers from 12 batches from the substance/substance group *Arginine (L-) (H1036)*.

†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
Unisan	Arginine (L-) (H1036)	14000564/0	1
Unisan	Arginine (L-) (H1036)	44301	2
unisan	Arginine (L-) (H1036)	52401	1
Unisan	Arginine (L-) (H1036)	27802	1
Unisan Gmbh, 78465 Kons…	Arginine (L-) (H1036)	52401	2
Unisan	Arginine (L-) (H1036)	52401	1
Hepart AG, Unisan GmbH	Arginine (L-) (H1036)	52401	2
Hepart AG	Arginine (L-) (H1036)	66501	1
Unisan	Arginine (L-) (H1036)	66501	5
UNISAN	Arginine (L-) (H1036)	66501	1
Unisan	Arginine (L-) (H1036)	1320550101	1
Unisan	Arginine (L-) (H1036)	1320025705	1
Unisan	Arginine (L-) (H1036)	1320999001	1
Fagron	Arginine (L-) (H1036)	1324044301	1
Hepart AG	Arginine (L-) (H1036)	1324027802	1
Unisan/Hepart AG	Arginine (L-) (H1036)	1324044301	1
Unisan	Arginine (L-) (H1036)	1324950601	1
Unisan	Arginine (L-) (H1036)	14000563	1

- 1554 spectra from 20 *Apo-Ident* customers from a total of 578 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Arginine (L-) (H1036)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Arginine (L-) (H1036)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	310	0	18 844
Type B	0	200	0	21 696
Type C	0	24	1	1554

The substance/substance group *Arginine (L-) (H1036)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9378 %)	100.0000 % (> 98.0645 %)
Type B	100.0000 % (> 99.8917 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.1655 %)	96.0000 % (> 84.0000 %)

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
80026	80026	0.00	31.81
80129	80129	0.00	32.43
80157	80157	0.00	30.98
80256	80256	0.00	33.61
80280	80280	0.00	34.16
80373	80373	0.00	31.32
80807	80807	0.00	35.05

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Bioflavonoid complex (H1006)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80027-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Bioflavonoid complex (H1006)

Special notes

When selecting the *Bioflavonoid complex (H1006)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Bioflavonoid complex (H1006)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Bioflavonoid com…	0683901	80124	50	from supplier
Hepart	Bioflavonoid com…	694301	80184	40	from supplier
Hepart	Bioflavonoid com…	019001	80252	40	from supplier
Hepart	Bioflavonoid com…	042501	80275	30	from supplier
Hepart	Bioflavonoid com…	028501	80279	40	from supplier
Hepart	Bioflavonoid com…	068101	80342	40	from supplier
Hepart	Bioflavonoid com…	14001675	80492	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 7 reference samples from the substance/substance group *Bioflavonoid complex (H1006)*. These samples are listed above in the *calibration samples* section.

- 18 874 spectra from a total of 392 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Bioflavonoid complex (H1006)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Bioflavonoid complex (H1006)	pending	80017	30
Hepart	Bioflavonoid complex (H1006)	683901	80027	40
Hepart	Bioflavonoid complex (H1006)	948802	80170	40
Hepart	Bioflavonoid complex (H1006)	14001675	80492†	20

- 21 766 spectra from a total of 520 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 24 spectra from 11 *Apo-Ident* customers from 12 batches from the substance/substance group *Bioflavonoid complex (H1006)*.

†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
Hepart AG	Bioflavonoid complex (H1006)	68101	1
Unisan	Bioflavonoid complex (H1006)	68101	3
Unisan	Bioflavonoid complex (H1006)	14001675	2
Hepart AG	Bioflavonoid complex (H1006)	56001	2
Hepart AG	Bioflavonoid complex (H1006)	14001675/1	1
Unisan 2.10.2015	Bioflavonoid complex (H1006)	14001675/1	1
Unisan 02.04.2016	Bioflavonoid complex (H1006)	14001675/2	1
Unisan	Bioflavonoid complex (H1006)	1284019001	1
Hepart AG	Bioflavonoid complex (H1006)	1284019001	1
Unisan	Bioflavonoid complex (H1006)	42501	2
Unisan	Bioflavonoid complex (H1006)	1281683901	1
Hepart AG	Bioflavonoid complex (H1006)	42501	1
Unisan	Bioflavonoid complex (H1006)	19001	1
Unisan	Bioflavonoid complex (H1006)	1284042501	2
Hepart AG	Bioflavonoid complex (H1006)	1284042501	1
Unisan	Bioflavonoid complex (H1006)		1
Hepart AG, CH-8280 Kreu…	Bioflavonoid complex (H1006)	56001	1
Unisan	Bioflavonoid complex (H1006)	1284648802	1

- 1555 spectra from 19 *Apo-Ident* customers from a total of 578 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Bioflavonoid complex (H1006)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Bioflavonoid complex (H1006)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	18 874
Type B	0	125	5	21 766
Type C	0	17	7	1555

The substance/substance group *Bioflavonoid complex (H1006)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.8920 %)	96.1538 % (> 93.8462 %)
Type C	100.0000 % (> 99.1659 %)	70.8333 % (> 58.3333 %)

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80124	80124	0.00	18.80
80184	80184	0.00	18.00
80252	80252	0.00	20.14
80275	80275	0.00	18.24
80279	80279	0.00	19.36
80342	80342	0.00	12.68
80492	80492	0.00	14.89

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Cabbage extract (H1121)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80676-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cabbage extract (H1121)

Special notes

When selecting the *Cabbage extract (H1121)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Cabbage extract (H1121)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Cabbage extract ...	15001355	80676	40	from supplier
Hepart	Cabbage extract ...	16000657	80819	40	not required

Validation samples

A total of 42 629 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 *Cabbage extract (H1121)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 397 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Cabbage extract (H1121)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Cabbage extract (H1121)	15001355	80676†	20
Hepart	Cabbage extract (H1121)	15001474	80677	60

- 21 816 spectra from a total of 521 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Cabbage extract (H1121)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *Cabbage extract (H1121)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cabbage extract (H1121)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	80	0	21 816
Type C	0	0	0	1579

The substance/substance group *Cabbage extract (H1121)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8924 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80676	80676	0.00	20.35
80819	80819	0.00	14.63

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Calcium (H1008) / Rhodiola (H1064)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80322-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Calcium (H1008) / Rhodiola (H1064); Calcium (H1008); Rhodiola (H1064)

Special notes

When selecting the *Calcium (H1008) / Rhodiola (H1064)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Calcium (H1008) / Rhodiola (H1064)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Calcium (H1008)	055201	80322	60	from supplier
Hepart	Calcium (H1008)	055001	80323	60	from supplier
Hepart	Calcium (H1008)	055101	80327	60	from supplier
Hepart	Calcium (H1008)	055601	80329	50	from supplier
Hepart	Rhodiola (H1064)	070501	80390	40	from supplier
Hepart	Calcium (H1008)	14000107	80412	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Calcium (H1008)	14000106	80422	40	from supplier
Hepart	Calcium (H1008)	14001933	80521	40	from supplier
Hepart	Calcium (H1008)	14001934	80522	40	from supplier
Hepart	Calcium (H1008)	14001937	80525	40	from supplier
Hepart	Calcium (H1008)	14001938	80526	40	from supplier
Hepart	Calcium (H1008)	14001939	80527	40	from supplier
Hepart	Rhodiola (H1064)	070501	80632	40	from supplier
Hepart	Rhodiola (H1064)	15001045	80672	40	from supplier
Hepart	Calcium (H1008)	15001669	80707	40	from supplier
Hepart	Calcium (H1008)	15001672(B1)	80709	40	from supplier
Hepart	Calcium (H1008)	15001671	80711	40	from supplier
Hepart	Calcium (H1008)	15001673(MM)	80712	40	from supplier
Hepart	Calcium (H1008)	15001668(B1)	80715	40	from supplier
Hepart	Calcium (H1008)	15001667(MM)	80719	40	from supplier
Hepart	Calcium (H1008)	15001666(MM)	80722	40	from supplier
Hepart	Calcium (H1008)	15001665(B1)	80724	40	from supplier
Hepart	Calcium (H1008)	15001670(B2)	80729	40	from supplier
Hepart	Calcium (H1008)	15001675(B2)	80732	40	from supplier
Hepart	Calcium (H1008)	15001676(MM)	80734	40	from supplier
Hepart	Calcium (H1008)	15001677(B1)	80740	40	from supplier
Hepart	Calcium (H1008)	15001674(B2)	80741	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 1150 spectra of 27 reference samples from the substance/substance group *Calcium (H1008) / Rhodiola (H1064)*. These samples are listed above in the *calibration samples* section.

- 18 004 spectra from a total of 373 batches from further 77 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 2500 spectra of 58 reference samples from the substance/substance group *Calcium (H1008) / Rhodiola (H1064)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Calcium (H1008)	956001	80005	40
Hepart	Calcium (H1008)	pending	80020	40

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Calcium (H1008)	956001	80029	40
Hepart	Calcium (H1008)	8901	80189	40
Hepart	Calcium (H1008)	956001	80190	40
Hepart	Calcium (H1008)	55301	80324	60
Hepart	Calcium (H1008)	55401	80325	60
Hepart	Calcium (H1008)	55501	80326	60
Hepart	Calcium (H1008)	14000110	80406	40
Hepart	Calcium (H1008)	14000111	80414	40
Hepart	Calcium (H1008)	14000108	80415	40
Hepart	Calcium (H1008)	14000109	80417	40
Hepart	Calcium (H1008)	14001933	80521†	20
Hepart	Calcium (H1008)	14001934	80522†	20
Hepart	Calcium (H1008)	14001935	80523	60
Hepart	Calcium (H1008)	14001936	80524	60
Hepart	Calcium (H1008)	14001937	80525†	20
Hepart	Calcium (H1008)	14001938	80526†	20
Hepart	Calcium (H1008)	14001939	80527†	20
Hepart	Rhodiola (H1064)	70501	80632†	20
Hepart	Rhodiola (H1064)	15001045	80672†	20
Hepart	Calcium (H1008)	15001669	80707†	20
Hepart	Calcium (H1008)	15001672(B2)	80708	60
Hepart	Calcium (H1008)	15001672(B1)	80709†	20
Hepart	Calcium (H1008)	15001672(MM)	80710	60
Hepart	Calcium (H1008)	15001671	80711†	20
Hepart	Calcium (H1008)	15001673(MM)	80712†	20
Hepart	Calcium (H1008)	15001673(B2)	80713	60
Hepart	Calcium (H1008)	15001673(B1)	80714	60
Hepart	Calcium (H1008)	15001668(B1)	80715†	20
Hepart	Calcium (H1008)	15001668(MM)	80716	60
Hepart	Calcium (H1008)	15001667(F2)	80717	60
Hepart	Calcium (H1008)	15001667(B1)	80718	60
Hepart	Calcium (H1008)	15001667(MM)	80719†	20
Hepart	Calcium (H1008)	15001666(B1)	80720	60
Hepart	Calcium (H1008)	15001666(F2)	80721	60
Hepart	Calcium (H1008)	15001666(MM)	80722†	20
Hepart	Calcium (H1008)	15001670(B1)	80723	60
Hepart	Calcium (H1008)	15001665(B1)	80724†	20
Hepart	Calcium (H1008)	15001670(MM)	80725	60
Hepart	Calcium (H1008)	15001665(F2)	80726	60
Hepart	Calcium (H1008)	15001665(MM)	80727	60
Hepart	Calcium (H1008)	15001668(F2)	80728	60
Hepart	Calcium (H1008)	15001670(B2)	80729†	20
Hepart	Calcium (H1008)	15001675(MM)	80730	60
Hepart	Calcium (H1008)	15001675(B1)	80731	60
Hepart	Calcium (H1008)	15001675(B2)	80732†	20
Hepart	Calcium (H1008)	15001675/4	80733	60
Hepart	Calcium (H1008)	15001676(MM)	80734†	20
Hepart	Calcium (H1008)	15001676(B2)	80735	60
Hepart	Calcium (H1008)	15001676/4	80736	60
Hepart	Calcium (H1008)	15001676(B1)	80737	60
Hepart	Calcium (H1008)	15001677(MM)	80738	60
Hepart	Calcium (H1008)	15001677/4	80739	60
Hepart	Calcium (H1008)	15001677(B1)	80740†	20
Hepart	Calcium (H1008)	15001674(B2)	80741†	20
Hepart	Calcium (H1008)	15001674(B1)	80742	60
Hepart	Calcium (H1008)	15001674(MM)	80743	60

†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*.

- 19 396 spectra from a total of 467 batches from further 89 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 82 spectra from 15 *Apo-Ident* customers from 31 batches from the substance/substance group *Calcium (H1008) / Rhodiola (H1064)*.

Supplier	Substance	Batch	Spectra
Unisan	Calcium (H1008)	8901	7
Unisan/Hepart AG	Calcium (H1008)	8901	1
Hepart AG	Calcium (H1008)	8901	2
Unisan	Calcium (H1008)	55001	4
Hepart AG	Calcium (H1008)	55001	1
Unisan	Calcium (H1008)	55101	3
unisan	Calcium (H1008)	55001	1
Hepart AG	Calcium (H1008)	55201	1
Unisan	Calcium (H1008)	55201	1
Unisan	Calcium (H1008)	55301	1
Hepart AG	Calcium (H1008)	55301	2
Hepart AG	Calcium (H1008)	55401	4
Unisan	Calcium (H1008)	55401	2
Unisan Gmbh, 78465 Kons...	Calcium (H1008)	55401	1
Hepart AG	Calcium (H1008)	55501	5
Unisan Gmbh, 78465 Kons...	Calcium (H1008)	55501	2
Unisan	Calcium (H1008)	55601	2
Unisan	Calcium (H1008)	55501	1
Hepart AG, CH-8280 Kreu...	Calcium (H1008)	1104008901	4
Fagron	Calcium (H1008)	1104008901	6
Unisan	Calcium (H1008)	1104008901	1
Unisan	Calcium (H1008)	14000106	1
Unisan	Calcium (H1008)	1105008901	1
Unisan	Calcium (H1008)	1104956001	1
Hepart AG	Calcium (H1008)	14001933	1
Unisan	Calcium (H1008)	14001934/0	1
Unisan	Calcium (H1008)	14000110	1
UNISAN	Calcium (H1008)	14000110	1
Unisan	Calcium (H1008)	14000108	1
Unisan	Calcium (H1008)	956001	1
Sanacorp	Calcium (H1008)	Fehlt	1
Unisan	Calcium (H1008)	14001938/0	1
Unisan	Calcium (H1008)	15001667	1
Unisan	Calcium (H1008)	15001666/0	1
Hepart	Calcium (H1008)	15001673	3
hepart	Calcium (H1008)	15001674	3
Unisan	Calcium (H1008)	15001666	1
Hepart	Calcium (H1008)	15001671	1
hepart	Calcium (H1008)	15001675	2
Hepart	Calcium (H1008)	15001676	3
hepart	Calcium (H1008)	15001675/4	1
Hepart	Calcium (H1008)	15001676/4	1

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Supplier	Substance	Batch	Spectra
Hepart	Calcium (H1008)	15001677	1
Hepart AG	Rhodiola (H1064)	70501	1

- 1497 spectra from 19 *Apo-Ident* customers from a total of 559 batches from a further 58 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Calcium (H1008) / Rhodiola (H1064)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Calcium (H1008) / Rhodiola (H1064)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	1150	0	18 004
Type B	0	2500	0	19 396
Type C	0	82	0	1497

The substance/substance group *Calcium (H1008) / Rhodiola (H1064)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9375 %)	100.0000 % (> 99.4783 %)
Type B	100.0000 % (> 99.8913 %)	100.0000 % (> 99.7600 %)
Type C	100.0000 % (> 99.1590 %)	100.0000 % (> 92.6829 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80322	80322	0.00	23.32

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80323	80323	0.00	22.61
80327	80327	0.00	22.02
80329	80329	0.00	16.12
80390	80390	0.00	20.79
80412	80412	0.00	22.22
80422	80422	0.00	22.78
80521	80521	0.00	27.27
80522	80522	0.00	22.92
80525	80525	0.00	18.24
80526	80526	0.00	19.36
80527	80527	0.00	13.97
80632	80632	0.00	23.58
80672	80672	0.00	17.79
80707	80707	0.00	22.50
80709	80709	0.00	24.55
80711	80711	0.00	24.07
80712	80712	0.00	25.40
80715	80715	0.00	22.48
80719	80719	0.00	26.43
80722	80722	0.00	22.54
80724	80724	0.00	25.91
80729	80729	0.00	23.85
80732	80732	0.00	24.78
80734	80734	0.00	25.14
80740	80740	0.00	25.61
80741	80741	0.00	24.29

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Carnitine (L-) (H1038)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80013-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Carnitine (L-) (H1038)

Special notes

When selecting the *Carnitine (L-) (H1038)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Carnitine (L-) (H1038)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Carnitine (L-) (...	938501	80013	40	from supplier
Hepart	Carnitine (L-) (...	965901	80081	30	from supplier
Hepart	Carnitine (L-) (...	965901	80155	50	from supplier
Hepart	Carnitine (L-) (...	965901	80169	40	from supplier
Hepart	Carnitine (L-) (...	938501	80193	40	from supplier
Hepart	Carnitine (L-) (...	026010	80344	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Carnitine (L-) (...	130605300	80371	50	from supplier
Hepart	Carnitine (L-) (...	130605302	80483	40	from supplier
Hepart	Carnitine (L-) (...	15000052	80557	40	from supplier
Hepart	Carnitine (L-) (...	15000054	80559	40	from supplier
Hepart	Carnitine (L-) (...	16000453	80787	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 450 spectra of 11 reference samples from the substance/substance group *Carnitine (L-) (H1038)*. These samples are listed above in the *calibration samples* section.

- 18 704 spectra from a total of 391 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 483 spectra of 13 reference samples from the substance/substance group *Carnitine (L-) (H1038)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Carnitine (L-) (H1038)	pending	80030	40
Hepart	Carnitine (L-) (H1038)	8501	80136	90
Hepart	Carnitine (L-) (H1038)	965901	80169†	3
Hepart	Carnitine (L-) (H1038)	26001	80243	40
Hepart	Carnitine (L-) (H1038)	130605300	80371†	10
Hepart	Carnitine (L-) (H1038)	130605302	80483†	20
Hepart	Carnitine (L-) (H1038)	15000052	80557†	20
Hepart	Carnitine (L-) (H1038)	15000053	80558	60
Hepart	Carnitine (L-) (H1038)	15000054	80559†	20
Hepart	Carnitine (L-) (H1038)	15000055	80560	60
Hepart	Carnitine (L-) (H1038)	16000450	80788	40
Hepart	Carnitine (L-) (H1038)	16000451	80817	40
Hepart	Carnitine (L-) (H1038)	16000454	80818	40

†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*.

- 21 413 spectra from a total of 511 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 51 spectra from 12 *Apo-Ident* customers from 20 batches from the substance/substance group *Carnitine (L-) (H1038)*.

Supplier	Substance	Batch	Spectra
Unisan	Carnitine (L-) (H1038)	130605300/3	2
Unisan	Carnitine (L-) (H1038)	1184965901	1
Unisan	Carnitine (L-) (H1038)	26001	2
Unisan	Carnitine (L-) (H1038)	26020	1
Hepart AG	Carnitine (L-) (H1038)	26010	3
Hepart AG	Carnitine (L-) (H1038)	26001	1
Unisan	Carnitine (L-) (H1038)		1
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	26010	1
Unisan	Carnitine (L-) (H1038)	26010	3
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	26020	2
unisan	Carnitine (L-) (H1038)	26010	1
Unisan	Carnitine (L-) (H1038)	130605300	2
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	1184965901	1
Unisan	Carnitine (L-) (H1038)	965901	1
Unisan	Carnitine (L-) (H1038)	1184026020	3
Unisan	Carnitine (L-) (H1038)	130326002	1
Hepart AG	Carnitine (L-) (H1038)	130605300	1
Hepart AG	Carnitine (L-) (H1038)	1184026001	1
Hepart AG, Unisan GmbH	Carnitine (L-) (H1038)	130605300	3
UNISAN	Carnitine (L-) (H1038)	130605300	3
UNISAN	Carnitine (L-) (H1038)	130605302	1
Unisan	Carnitine (L-) (H1038)	130605302	4
Unisan	Carnitine (L-) (H1038)	130605301	1
Hepart AG	Carnitine (L-) (H1038)	130605301	2
Unisan	Carnitine (L-) (H1038)	15000052	1
Unisan 2.10.2015	Carnitine (L-) (H1038)	15000052/0	2
Unisan	Carnitine (L-) (H1038)	150000540	1
Unisan	Carnitine (L-) (H1038)	15000053	1
Unisan	Carnitine (L-) (H1038)	15000053/0	2
Unisan	Carnitine (L-) (H1038)	15000054/0	1
Hepart AG	Carnitine (L-) (H1038)	480g	1

- 1528 spectra from 20 *Apo-Ident* customers from a total of 571 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Carnitine (L-) (H1038)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this

purpose, all relevant spectra of the various substances were compared with *Carnitine (L-) (H1038)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	450	0	18 704
Type B	0	405	78	21 413
Type C	0	41	10	1528

The substance/substance group *Carnitine (L-) (H1038)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9377 %)	100.0000 % (> 98.6667 %)
Type B	100.0000 % (> 99.8915 %)	83.8509 % (> 83.2298 %)
Type C	100.0000 % (> 99.1607 %)	80.3922 % (> 74.5098 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80013	80013	0.00	35.14
80081	80081	0.00	22.10
80155	80155	0.00	37.98
80169	80169	0.00	38.95
80193	80193	0.00	36.69
80344	80344	0.00	33.73
80371	80371	0.00	42.01
80483	80483	0.00	40.22
80557	80557	0.00	34.00
80559	80559	0.00	35.28
80787	80787	0.00	40.54

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Carnosine (L-) (H1014)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80153-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Carnosine (L-) (H1014)

Special notes

When selecting the *Carnosine (L-) (H1014)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Carnosine (L-) (H1014)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Carnosine (L-) (...	979202	80153	50	from supplier
Hepart	Carnosine (L-) (...	074801	80393	40	from supplier
Hepart	Carnosine (L-) (...	045901	80452	40	from supplier
Hepart	Carnosine (L-) (...	074801	80655	40	from supplier

Validation samples

A total of 42 629 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 *Carnosine (L-) (H1014)*. These samples are listed above in the *calibration samples* section.

- 18 984 spectra from a total of 396 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Carnosine (L-) (H1014)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Carnosine (L-) (H1014)	pending	80048	40
Hepart	Carnosine (L-) (H1014)	74801	80655†	20

- 21 836 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 10 spectra from 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Carnosine (L-) (H1014)*.

Supplier	Substance	Batch	Spectra
Unisan/Hepart AG	Carnosine (L-) (H1014)	45901	1
Hepart AG	Carnosine (L-) (H1014)	45901	1
UNISAN	Carnosine (L-) (H1014)	74801	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
Unisan	Carnosine (L-) (H1014)	45901	1
Hepart AG	Carnosine (L-) (H1014)	1812979202	2
Hepart AG	Carnosine (L-) (H1014)	1812045901	1
Unisan	Carnosine (L-) (H1014)	1812979202	1
Hepart AG, CH-8280 Kreu…	Carnosine (L-) (H1014)	1812045901	1
Purren Apotheke	Carnosine (L-) (H1014)	1813979202	1

- 1569 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Carnosine (L-) (H1014)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Carnosine (L-) (H1014)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 984
Type B	0	34	26	21 836
Type C	0	10	0	1569

The substance/substance group *Carnosine (L-) (H1014)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9382 %)	100.0000 % (> 96.4706 %)
Type B	100.0000 % (> 99.8928 %)	56.6667 % (> 51.6667 %)
Type C	100.0000 % (> 99.1796 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80153	80153	0.00	75.15
80393	80393	0.00	56.42
80452	80452	0.00	74.07
80655	80655	0.00	65.60

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Catechin extract (H1010)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80031-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Catechin extract (H1010)

Special notes

When selecting the *Catechin extract (H1010)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Catechin extract (H1010)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Catechin extract…	0681501	80031	40	from supplier
Hepart	Catechin extract…	638201	80139	50	from supplier
Hepart	Catechin extract…	0681501	80140	50	from supplier
Hepart	Catechin extract…	062901	80338	40	from supplier
Hepart	Catechin extract…	062701	80339	40	from supplier
Hepart	Catechin extract…	062801	80340	40	from supplier
Hepart	Catechin extract…	15000206	80555	40	from supplier
Hepart	Catechin extract…	15000206/4	80849	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 8 reference samples from the substance/substance group *Catechin extract (H1010)*. These samples are listed above in the *calibration samples* section.

- 18 814 spectra from a total of 392 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Catechin extract (H1010)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Catechin extract (H1010)	18601	80240	40
Hepart	Catechin extract (H1010)	15000206	80555†	20

- 21 836 spectra from a total of 521 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 20 spectra from 9 *Apo-Ident* customers from 10 batches from the substance/substance group *Catechin extract (H1010)*.

Supplier	Substance	Batch	Spectra
Unisan	Catechin extract (H1010)	62901	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
Unisan/Hepart AG	Catechin extract (H1010)	18601	1
Unisan	Catechin extract (H1010)	18601	1
Hepart AG	Catechin extract (H1010)	18601	3
Hepart AG	Catechin extract (H1010)	130208020	1
Unisan	Catechin extract (H1010)	62801	1
Hepart AG, CH-8280 Kreu…	Catechin extract (H1010)	62901	1
Unisan	Catechin extract (H1010)	130208020	2
Hepart AG, CH-8280 Kreu…	Catechin extract (H1010)	18601	1
Unisan	Catechin extract (H1010)	1571025702	2
Unisan	Catechin extract (H1010)	25702	1
Unisan	Catechin extract (H1010)	681501	1
Hepart AG	Catechin extract (H1010)	1574018601	1
Unisan	Catechin extract (H1010)	1571681501	1
Hepart AG, CH-8280 Kreu…	Catechin extract (H1010)	1571025702	1
Unisan	Catechin extract (H1010)	208020	1

- 1559 spectra from 20 *Apo-Ident* customers from a total of 580 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Catechin extract (H1010)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Catechin extract (H1010)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	18 814
Type B	0	20	40	21 836
Type C	0	8	12	1559

The substance/substance group *Catechin extract (H1010)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9378 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.8928 %)	33.3333 % (> 28.3333 %)
Type C	100.0000 % (> 99.1679 %)	40.0000 % (> 25.0000 %)

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
80031	80031	0.00	31.71
80139	80139	0.00	24.92
80140	80140	0.00	33.62
80338	80338	0.00	25.82
80339	80339	0.00	32.19
80340	80340	0.00	23.28
80555	80555	0.00	17.93
80849	80849	0.00	23.18

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Chaga (H1011)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80032-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Chaga (H1011)

Special notes

When selecting the *Chaga (H1011)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Chaga (H1011)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Chaga (H1011)	0675601	80032	40	from supplier
Hepart	Chaga (H1011)	046701	80310	40	from supplier
Hepart	Chaga (H1011)	14000951	80466	40	from supplier
Hepart	Chaga (H1011)	14001688	80493	40	from supplier
Hepart	Chaga (H1011)	16000976	80825	40	from supplier

Validation samples

A total of 42 629 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 *Chaga (H1011)*. These samples are listed above in the *calibration samples* section.

- 18 954 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Chaga (H1011)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Chaga (H1011)	975601	80180	40
Hepart	Chaga (H1011)	14001688	80493†	20
Hepart	Chaga (H1011)	16000235	80763	60

- 21 776 spectra from a total of 520 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Chaga (H1011)*.

Supplier	Substance	Batch	Spectra
Unisan	Chaga (H1011)	64001	2
Purren Apotheke	Chaga (H1011)	1514675601	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
Unisan	Chaga (H1011)	14001688	1
Unisan/Hepart AG	Chaga (H1011)	46701	1
Unisan	Chaga (H1011)	151467601	1

- 1573 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Chaga (H1011)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chaga (H1011)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 954
Type B	0	120	0	21 776
Type C	0	6	0	1573

The substance/substance group *Chaga (H1011)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9381 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8920 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.1953 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80032	80032	0.00	77.21

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80310	80310	0.00	74.66
80466	80466	0.00	74.64
80493	80493	0.00	50.22
80825	80825	0.00	40.34

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Chondroitin sulfate (Sodium-) (H1065)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80093-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Chondroitin sulfate (Sodium-) (H1065)

Special notes

When selecting the *Chondroitin sulfate (Sodium-) (H1065)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Chondroitin sulfate (Sodium-) (H1065)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Chondroitin sulf…	001801	80093	50	from supplier
Hepart	Chondroitin sulf…	964101	80119	50	from supplier
Hepart	Chondroitin sulf…	031801	80269	40	from supplier
Hepart	Chondroitin sulf…	14001985	80532	40	from supplier
Hepart	Chondroitin sulf…	14001991	80533	40	from supplier
Hepart	Chondroitin sulf…	14001985/2	80779	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*. These samples are listed above in the *calibration samples* section.

- 18 894 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 190 spectra of 6 reference samples from the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Chondroitin sulfate (Sodium…	pending	80063	30
Hepart	Chondroitin sulfate (Sodium…	31801	80271	40
Hepart	Chondroitin sulfate (Sodium…	14001985	80532†	20
Hepart	Chondroitin sulfate (Sodium…	14001991	80533†	20
Hepart	Chondroitin sulfate (Sodium…	31801	80584	60
Hepart	Chondroitin sulfate (Sodium…	14001985/2	80779†	20

- 21 706 spectra from a total of 519 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 11 *Apo-Ident* customers from 7 batches from the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*.

†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
Unisan	Chondroitin sulfate (Sodium…	1801	2
Unisan/Hepart AG	Chondroitin sulfate (Sodium…	31801	2
hepart ag	Chondroitin sulfate (Sodium…	31801	1
Unisan	Chondroitin sulfate (Sodium…	31801	5
Hepart AG, CH-8280 Kreu…	Chondroitin sulfate (Sodium…	31801	1
Hepart AG	Chondroitin sulfate (Sodium…	31801	1
Hepart AG	Chondroitin sulfate (Sodium…	1821001801	1
Unisan	Chondroitin sulfate (Sodium…	1820001801	4
Purren Apotheke	Chondroitin sulfate (Sodium…	1821964101	1
Fagron	Chondroitin sulfate (Sodium…	1821031801	1
Hepart AG, CH-8280 Kreu…	Chondroitin sulfate (Sodium…	1820031801	1
Unisan	Chondroitin sulfate (Sodium…	1821964101	1

- 1558 spectra from 20 *Apo-Ident* customers from a total of 583 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chondroitin sulfate (Sodium-) (H1065)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	260	0	18 894
Type B	0	137	53	21 706
Type C	0	17	4	1558

The substance/substance group *Chondroitin sulfate (Sodium-) (H1065)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.8917 %)	72.1053 % (> 70.5263 %)
Type C	100.0000 % (> 99.1673 %)	80.9524 % (> 66.6667 %)

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

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

Identity according to identity test using NIR spectroscopy

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

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80093	80093	0.00	32.79
80119	80119	0.00	24.26
80269	80269	0.00	31.17
80532	80532	0.00	39.11
80533	80533	0.00	30.37
80779	80779	0.00	41.98

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Coenzyme Q10 (H1013)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80015-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Coenzyme Q10 (H1013)

Special notes

When selecting the *Coenzyme Q10 (H1013)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Coenzyme Q10 (H1013)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Coenzyme Q10 (H1…	130521-300	80354	40	from supplier
Hepart	Coenzyme Q10 (H1…	14001546	80484	40	from supplier
Hepart	Coenzyme Q10 (H1…	14001546	80587	40	from supplier
Hepart	Coenzyme Q10 (H1…	16000402/0	80794	40	from supplier
Hepart	Coenzyme Q10 (H1…	16000402/0	80850	40	from supplier
Hepart	Coenzyme Q10 (H1…	16001598/4	80854	40	from supplier

Validation samples

A total of 42 629 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 *Coenzyme Q10 (H1013)*. These samples are listed above in the *calibration samples* section.

- 18 914 spectra from a total of 395 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 310 spectra of 9 reference samples from the substance/substance group *Coenzyme Q10 (H1013)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Coenzyme Q10 (H1013)	943001	80015	40
Hepart	Coenzyme Q10 (H1013)	pending	80021	40
Hepart	Coenzyme Q10 (H1013)	992501	80065	30
Hepart	Coenzyme Q10 (H1013)	992501	80133	50
Hepart	Coenzyme Q10 (H1013)	926101	80209	30
Hepart	Coenzyme Q10 (H1013)	15601	80241	40
Hepart	Coenzyme Q10 (H1013)	14001546	80484†	20
Hepart	Coenzyme Q10 (H1013)	14001546	80587†	20
Hepart	Coenzyme Q10 (H1013)	16000402/4	80795	40

- 21 586 spectra from a total of 517 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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

- 52 spectra from 16 *Apo-Ident* customers from 13 batches from the substance/substance group *Coenzyme Q10 (H1013)*.

Supplier	Substance	Batch	Spectra
Unisan	Coenzyme Q10 (H1013)	15601	12
Hepart AG	Coenzyme Q10 (H1013)	130521-300	5
UNISAN	Coenzyme Q10 (H1013)	130521-300	2
Unisan	Coenzyme Q10 (H1013)	130521-300	6
Unisan	Coenzyme Q10 (H1013)	14001546/1	2
Unisan	Coenzyme Q10 (H1013)	14001546	4
Unisan	Coenzyme Q10 (H1013)	14001446/1	1
Unisan 2.10.2015	Coenzyme Q10 (H1013)	14001546/2	1
hepart	Coenzyme Q10 (H1013)	16000402	1
Unisan	Coenzyme Q10 (H1013)	16000402/0	2
Unisan 02.04.2016	Coenzyme Q10 (H1013)	14001546/3	1
Hedinger	Coenzyme Q10 (H1013)	15601	4
Hepart AG, CH-8280 Kreu…	Coenzyme Q10 (H1013)	15601	1
Unisan	Coenzyme Q10 (H1013)	1194015601	4
Hepart AG, CH-8280 Kreu…	Coenzyme Q10 (H1013)	1194015601	1
Hepart AG	Coenzyme Q10 (H1013)	1194015601	2
Unisan	Coenzyme Q10 (H1013)	119405601	1
Unisan	Coenzyme Q10 (H1013)	H101311	1
Unisan	Coenzyme Q10 (H1013)	992501	1

- 1527 spectra from 20 *Apo-Ident* customers from a total of 577 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Coenzyme Q10 (H1013)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Coenzyme Q10 (H1013)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 914
Type B	0	80	230	21 586
Type C	0	22	30	1527

The substance/substance group *Coenzyme Q10 (H1013)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.8916 %)	25.8065 % (> 24.8387 %)
Type C	100.0000 % (> 99.1606 %)	42.3077 % (> 36.5385 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80354	80354	0.00	28.14
80484	80484	0.00	26.28
80587	80587	0.00	38.91
80794	80794	0.00	22.62
80850	80850	0.00	22.68
80854	80854	0.00	24.13

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Copper (H1032)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80044-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Copper (H1032)

Special notes

When selecting the *Copper (H1032)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Copper (H1032)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Copper (H1032)	933901	80044	40	from supplier
Hepart	Copper (H1032)	007901	80277	40	from supplier
Hepart	Copper (H1032)	046401	80305	40	from supplier
Hepart	Copper (H1032)	130415	80341	40	from supplier
Hepart	Copper (H1032)	15000211	80536	40	from supplier

Validation samples

A total of 42 629 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 *Copper (H1032)*. These samples are listed above in the *calibration samples* section.

- 18 954 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Copper (H1032)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Copper (H1032)	933901	80154	50
Hepart	Copper (H1032)	7901	80200	20
Hepart	Copper (H1032)	46401	80306	40
Hepart	Copper (H1032)	15000211	80536†	20

- 21 766 spectra from a total of 519 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 19 spectra from 7 *Apo-Ident* customers from 9 batches from the substance/substance group *Copper (H1032)*.

Supplier	Substance	Batch	Spectra
Unisan	Copper (H1032)	46401	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
Unisan	Copper (H1032)	7901	1
Hepart AG	Copper (H1032)	46401	1
Unisan	Copper (H1032)	933901	1
Hepart AG	Copper (H1032)	13041501	1
Unisan	Copper (H1032)	13041501	5
Unisan/Hepart AG	Copper (H1032)	13041501	1
Unisan	Copper (H1032)	15000211/0	1
Hepart AG	Copper (H1032)	130415-K1	1
Unisan	Copper (H1032)	1542933901	1
Unisan	Copper (H1032)	1542933901	1
Caelo	Copper (H1032)	933901	1
Hepart AG	Copper (H1032)	1544046401	1
Hepart AG	Copper (H1032)	1544007901	1

- 1560 spectra from 20 *Apo-Ident* customers from a total of 581 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Copper (H1032)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Copper (H1032)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 954
Type B	0	122	8	21 766
Type C	0	14	5	1560

The substance/substance group *Copper (H1032)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9381 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8920 %)	93.8462 % (> 91.5385 %)
Type C	100.0000 % (> 99.1685 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80044	80044	0.00	30.02
80277	80277	0.00	28.03
80305	80305	0.00	13.20
80341	80341	0.00	21.11
80536	80536	0.00	35.65

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Creatine (H1031)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80149-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Creatine (H1031)

Special notes

When selecting the *Creatine (H1031)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Creatine (H1031)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Creatine (H1031)	0965201	80149	40	from supplier
Hepart	Creatine (H1031)	025003	80440	40	from supplier
Hepart	Creatine (H1031)	025004	80441	40	from supplier
Hepart	Creatine (H1031)	15000749	80627	40	from supplier
Hepart	Creatine (H1031)	15000750	80628	40	from supplier

Validation samples

A total of 42 629 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 *Creatine (H1031)*. These samples are listed above in the *calibration samples* section.

- 18 954 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Creatine (H1031)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Creatine (H1031)	pending	80045	40
Hepart	Creatine (H1031)	15000749	80627†	20
Hepart	Creatine (H1031)	15000750	80628†	20

- 21 816 spectra from a total of 521 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 5 batches from the substance/substance group *Creatine (H1031)*.

Supplier	Substance	Batch	Spectra
Unisan Gmbh, 78465 Kons…	Creatine (H1031)	1830025003	1
Unisan	Creatine (H1031)	25003	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
Purren Apotheke	Creatine (H1031)	965201	2
Hepart AG	Creatine (H1031)	1831025005	1
Unisan	Creatine (H1031)	1830025005	1

- 1573 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Creatine (H1031)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Creatine (H1031)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 954
Type B	0	40	40	21 816
Type C	0	6	0	1573

The substance/substance group *Creatine (H1031)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9381 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8924 %)	50.0000 % (> 46.2500 %)
Type C	100.0000 % (> 99.1953 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80149	80149	0.00	47.97

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80440	80440	0.00	47.00
80441	80441	0.00	47.52
80627	80627	0.00	43.67
80628	80628	0.00	47.73

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Curcumin and piperine (H1014)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80034-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Curcumin and piperine (H1014)

Special notes

When selecting the *Curcumin and piperine (H1014)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Curcumin and piperine (H1014)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Curcumin and pip…	0002201	80034	40	from supplier
Hepart	Curcumin and pip…	14001017	80475	40	from supplier
Hepart	Curcumin and pip…	15001589	80705	40	from supplier
Hepart	Curcumin and pip…	16000369	80796	40	from supplier

Validation samples

A total of 42 629 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 *Curcumin and piperine (H1014)*. These samples are listed above in the *calibration samples* section.

- 18 994 spectra from a total of 395 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Curcumin and piperine (H1014)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Curcumin and piperine (H1014)	2201	80166	50
Hepart	Curcumin and piperine (H1014)	929601	80225	30
Hepart	Curcumin and piperine (H1014)	13901	80234	40
Hepart	Curcumin and piperine (H1014)	15001589	80705†	20

- 21 756 spectra from a total of 519 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 8 *Apo-Ident* customers from 5 batches from the substance/substance group *Curcumin and piperine (H1014)*.

†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
Hepart AG	Curcumin and piperine (H1014)	72001	2
Unisan	Curcumin and piperine (H1014)	13901	2
Unisan	Curcumin and piperine (H1014)	72001	4
Hepart AG	Curcumin and piperine (H1014)	13901	3
Unisan	Curcumin and piperine (H1014)	14001017	1
Hepart AG, CH-8280 Kreu…	Curcumin and piperine (H1014)	13901	1
Hepart AG	Curcumin and piperine (H1014)	1534002201	1
Unisan	Curcumin and piperine (H1014)	1534002201	1
Unisan	Curcumin and piperine (H1014)	1534013901	1

- 1563 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Curcumin and piperine (H1014)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Curcumin and piperine (H1014)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 994
Type B	0	23	117	21 756
Type C	0	1	15	1563

The substance/substance group *Curcumin and piperine (H1014)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9382 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8919 %)	16.4286 % (> 14.2857 %)
Type C	100.0000 % (> 99.1708 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80034	80034	0.00	40.91
80475	80475	0.00	37.38
80705	80705	0.00	36.79
80796	80796	0.00	40.01

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Enzyme complex (H1118) / Top Flora multi forte c...**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80664-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Enzyme complex (H1118) / Top Flora multi forte complex (H1119); Enzyme complex (H1118); TopFlora multi forte complex (H1119)

Special notes

When selecting the *Enzyme complex (H1118) / Top Flora multi forte complex (H1119)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Enzyme complex (H1118) / Top Flora multi forte complex (H1119)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	TopFlora multi f...	15001135	80664	40	from supplier
Hepart	Enzyme complex (...	15001134	80665	40	from supplier

Validation samples

A total of 42 629 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 *Enzyme complex (H1118) / Top Flora multi forte complex (H1119)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 397 batches from further 77 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Enzyme complex (H1118) / Top Flora multi forte complex (H1119)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	TopFlora multi forte complex…	15001135	80664†	20
Hepart	Enzyme complex (H1118)	15001134	80665†	20

- 21 856 spectra from a total of 521 batches from further 89 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Enzyme complex (H1118) / Top Flora multi forte complex (H1119)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 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 *Enzyme complex (H1118) / Top Flora multi forte complex (H1119)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Enzyme complex (H1118) / Top Flora multi forte complex (H1119)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	40	0	21 856
Type C	0	0	0	1579

The substance/substance group *Enzyme complex (H1118) / Top Flora multi forte complex (H1119)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8935 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80664	80664	0.00	14.66
80665	80665	0.00	10.15

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Flavour orange (H1405)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80768-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Flavour orange (H1405)

Special notes

When selecting the *Flavour orange (H1405)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Flavour orange (H1405)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Flavour orange (...	16000262	80768	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Flavour orange (H1405)*. These samples are listed above in the *calibration samples* section.

- 19 114 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 20 spectra of 1 reference samples from the substance/substance group *Flavour orange (H1405)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Flavour orange (H1405)	16000262	80768†	20

- 21 876 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Flavour orange (H1405)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *Flavour orange (H1405)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Flavour orange (H1405)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	19 114
Type B	0	20	0	21 876
Type C	0	0	0	1579

The substance/substance group *Flavour orange (H1405)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80768	80768	0.00	21.98

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Garcinia Cambogia (H1017)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80037-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Garcinia Cambogia (H1017)

Special notes

When selecting the *Garcinia Cambogia (H1017)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Garcinia Cambogia (H1017)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Garcinia Cambogi…	956701	80037	40	from supplier
Hepart	Garcinia Cambogi…	956701	80101	90	from supplier
Hepart	Garcinia Cambogi…	7401	80160	90	from supplier
Hepart	Garcinia Cambogi…	056601	80346	40	from supplier
Hepart	Garcinia Cambogi…	056601	80477	40	from supplier
Hepart	Garcinia Cambogi…	14001687	80490	40	from supplier
Hepart	Garcinia Cambogi…	15001048(F2)	80660	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 380 spectra of 7 reference samples from the substance/substance group *Garcinia Cambogia (H1017)*. These samples are listed above in the *calibration samples* section.

- 18 774 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Garcinia Cambogia (H1017)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Garcinia Cambogia (H1017)	14001687	80490†	20
Hepart	Garcinia Cambogia (H1017)	15001048(F2)	80660†	20
Hepart	Garcinia Cambogia (H1017)	15001048	80661	60
Hepart	Garcinia Cambogia (H1017)	15001048(B1)	80662	60

- 21 736 spectra from a total of 519 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 3 batches from the substance/substance group *Garcinia Cambogia (H1017)*.

†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
Unisan	Garcinia Cambogia (H1017)	56601	1
Hepart AG	Garcinia Cambogia (H1017)	7401	2
Hepart AG	Garcinia Cambogia (H1017)	1221007401	1
Unisan	Garcinia Cambogia (H1017)	1221007401	2

- 1573 spectra from 20 *Apo-Ident* customers from a total of 587 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Garcinia Cambogia (H1017)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Garcinia Cambogia (H1017)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	380	0	18 774
Type B	0	157	3	21 736
Type C	0	6	0	1573

The substance/substance group *Garcinia Cambogia (H1017)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9378 %)	100.0000 % (> 98.4211 %)
Type B	100.0000 % (> 99.8918 %)	98.1250 % (> 96.2500 %)
Type C	100.0000 % (> 99.1953 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80037	80037	0.00	29.70

continued on the next page

continued from previous page

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80101	80101	0.00	29.22
80160	80160	0.00	28.86
80346	80346	0.00	21.61
80477	80477	0.00	23.36
80490	80490	0.00	29.33
80660	80660	0.00	21.33

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Ginkgo (H1024)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80391-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Ginkgo (H1024)

Special notes

When selecting the *Ginkgo (H1024)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Ginkgo (H1024)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Ginkgo (H1024)	067901	80391	80	from supplier
Hepart	Ginkgo (H1024)	067901	80476	40	from supplier
Hepart	Ginkgo (H1024)	15001039	80656	40	from supplier
Hepart	Ginkgo (H1024)	15001038(F3)	80657	40	from supplier
Hepart	Ginkgo (H1024)	15001038	80658	40	from supplier

Validation samples

A total of 42 629 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 *Ginkgo (H1024)*. These samples are listed above in the *calibration samples* section.

- 18 914 spectra from a total of 395 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Ginkgo (H1024)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Ginkgo (H1024)	15001039	80656†	20
Hepart	Ginkgo (H1024)	15001038(F3)	80657†	20
Hepart	Ginkgo (H1024)	15001038	80658†	20
Hepart	Ginkgo (H1024)	15001038(F1)	80659	60

- 21 776 spectra from a total of 519 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Ginkgo (H1024)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 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 *Ginkgo (H1024)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ginkgo (H1024)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 914
Type B	0	120	0	21 776
Type C	0	0	0	1579

The substance/substance group *Ginkgo (H1024)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.8920 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80391	80391	0.00	31.13
80476	80476	0.00	23.29
80656	80656	0.00	15.18
80657	80657	0.00	17.39
80658	80658	0.00	29.49

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Ginseng (H1018)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80038-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Ginseng (H1018)

Special notes

When selecting the *Ginseng (H1018)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Ginseng (H1018)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Ginseng (H1018)	018502	80455	40	from supplier
Hepart	Ginseng (H1018)	067801	80456	40	from supplier
Hepart	Ginseng (H1018)	038802	80478	40	from supplier
Hepart	Ginseng (H1018)	14002047	80534	40	from supplier
Hepart	Ginseng (H1018)	15001047	80663	40	from supplier
Hepart	Ginseng (H1018)	15001047	80780	40	from supplier

Validation samples

A total of 42 629 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 *Ginseng (H1018)*. These samples are listed above in the *calibration samples* section.

- 18 914 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 350 spectra of 10 reference samples from the substance/substance group *Ginseng (H1018)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Ginseng (H1018)	701602	80038	40
Hepart	Ginseng (H1018)	701602	80099	50
Hepart	Ginseng (H1018)	630706	80191	40
Hepart	Ginseng (H1018)	38802	80270	40
Hepart	Ginseng (H1018)	18502	80308	40
Hepart	Ginseng (H1018)	67801	80403	40
Hepart	Ginseng (H1018)	67801	80439	40
Hepart	Ginseng (H1018)	14002047	80534†	20
Hepart	Ginseng (H1018)	15001047	80663†	20
Hepart	Ginseng (H1018)	15001047	80780†	20

- 21 546 spectra from a total of 516 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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

- 8 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Ginseng (H1018)*.

Supplier	Substance	Batch	Spectra
Unisan	Ginseng (H1018)	38802	2
Unisan/Hepart AG	Ginseng (H1018)	38802	1
Unisan	Ginseng (H1018)	14002047/1	1
Hepart AG	Ginseng (H1018)	38802	1
Unisan	Ginseng (H1018)	67801	1
UNISAN	Ginseng (H1018)	67801	1
Euro OTC	Ginseng (H1018)	15001047/0	1

- 1571 spectra from 20 *Apo-Ident* customers from a total of 586 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Ginseng (H1018)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ginseng (H1018)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 914
Type B	0	180	170	21 546
Type C	0	8	0	1571

The substance/substance group *Ginseng (H1018)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.8915 %)	51.4286 % (> 50.5714 %)
Type C	100.0000 % (> 99.1855 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80455	80455	0.00	11.53
80456	80456	0.00	23.44
80478	80478	0.00	14.49
80534	80534	0.00	9.83
80663	80663	0.00	21.62
80780	80780	0.00	25.76

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Glucosamine sulfate (H1019)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80094-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Glucosamine sulfate (H1019)

Special notes

When selecting the *Glucosamine sulfate (H1019)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Glucosamine sulfate (H1019)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Glucosamine sulf…	0978401	80094	50	from supplier
Hepart	Glucosamine sulf…	034001	80254	40	from supplier
Hepart	Glucosamine sulf…	025002	80262	40	from supplier
Hepart	Glucosamine sulf…	038001	80319	60	from supplier
Hepart	Glucosamine sulf…	038001	80362	40	from supplier
Hepart	Glucosamine sulf…	075401	80402	40	from supplier
Hepart	Glucosamine sulf…	16000948	80812	40	not required

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 310 spectra of 7 reference samples from the substance/substance group *Glucosamine sulfate (H1019)*. These samples are listed above in the *calibration samples* section.

- 18 844 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 3 reference samples from the substance/substance group *Glucosamine sulfate (H1019)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Glucosamine sulfate (H1019)	pending	80039	40
Hepart	Glucosamine sulfate (H1019)	954901	80131	50
Hepart	Glucosamine sulfate (H1019)	34001	80454	40

- 21 766 spectra from a total of 521 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 13 spectra from 8 *Apo-Ident* customers from 6 batches from the substance/substance group *Glucosamine sulfate (H1019)*.

Supplier	Substance	Batch	Spectra
Hepart AG	Glucosamine sulfate (H1019)	38001	2

continued on the next page

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Supplier	Substance	Batch	Spectra
Unisan/Hepart AG	Glucosamine sulfate (H1019)	38001	1
Unisan	Glucosamine sulfate (H1019)	38001	2
UNISAN	Glucosamine sulfate (H1019)	34001	1
Unisan Gmbh, 78465 Kons…	Glucosamine sulfate (H1019)	38001	1
Unisan	Glucosamine sulfate (H1019)	1822025002	1
Unisan	Glucosamine sulfate (H1019)	1823954901	2
Hepart AG	Glucosamine sulfate (H1019)	1823038001	1
Hepart AG	Glucosamine sulfate (H1019)	1822038001	1
Unisan	Glucosamine sulfate (H1019)	1822038001	1

- 1566 spectra from 20 *Apo-Ident* customers from a total of 584 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Glucosamine sulfate (H1019)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glucosamine sulfate (H1019)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	310	0	18 844
Type B	0	90	40	21 766
Type C	0	3	10	1566

The substance/substance group *Glucosamine sulfate (H1019)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9378 %)	100.0000 % (> 98.0645 %)
Type B	100.0000 % (> 99.8920 %)	69.2308 % (> 66.9231 %)
Type C	100.0000 % (> 99.1742 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80094	80094	0.00	57.60
80254	80254	0.00	58.53
80262	80262	0.00	53.62
80319	80319	0.00	53.08
80362	80362	0.00	52.85
80402	80402	0.00	35.88
80812	80812	0.00	31.99

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Glutamine (L-) (H1043)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80089-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Glutamine (L-) (H1043)

Special notes

When selecting the *Glutamine (L-) (H1043)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Glutamine (L-) (H1043)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Glutamine (L-) (...	994001	80089	50	from supplier
Hepart	Glutamine (L-) (...	955001	80171	40	from supplier
Hepart	Glutamine (L-) (...	061501	80336	40	from supplier
Hepart	Glutamine (L-) (...	15000017	80551	40	from supplier
Hepart	Glutamine (L-) (...	15000018	80552	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 210 spectra of 5 reference samples from the substance/substance group *Glutamine (L-) (H1043)*. These samples are listed above in the *calibration samples* section.

- 18 944 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 350 spectra of 10 reference samples from the substance/substance group *Glutamine (L-) (H1043)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Glutamine (L-) (H1043)	pending	80049	40
Hepart	Glutamine (L-) (H1043)	928301	80218	30
Hepart	Glutamine (L-) (H1043)	26901	80242	40
Hepart	Glutamine (L-) (H1043)	26904	80245	40
Hepart	Glutamine (L-) (H1043)	26903	80246	40
Hepart	Glutamine (L-) (H1043)	15000017	80551†	20
Hepart	Glutamine (L-) (H1043)	15000018	80552†	20
Hepart	Glutamine (L-) (H1043)	16000940	80802	40
Hepart	Glutamine (L-) (H1043)	16000941	80803	40
Hepart	Glutamine (L-) (H1043)	16000942	80804	40

- 21 546 spectra from a total of 514 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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

- 32 spectra from 9 *Apo-Ident* customers from 11 batches from the substance/substance group *Glutamine (L-) (H1043)*.

Supplier	Substance	Batch	Spectra
Unisan/Hepart AG	Glutamine (L-) (H1043)	26901	1
Unisan	Glutamine (L-) (H1043)		1
Unisan	Glutamine (L-) (H1043)	26904	2
Unisan Gmbh, 78465 Kons...	Glutamine (L-) (H1043)	26904	1
Unisan	Glutamine (L-) (H1043)	26903	2
Unisan	Glutamine (L-) (H1043)	61501	9
UNISAN	Glutamine (L-) (H1043)	61501	2
Unisan	Glutamine (L-) (H1043)	15000017	1
Unisan	Glutamine (L-) (H1043)	61501/4	1
UNISAN	Glutamine (L-) (H1043)	15000017/0	1
Unisan	Glutamine (L-) (H1043)	1814026901	8
Unisan	Glutamine (L-) (H1043)	15000017/0	1
Hepart AG	Glutamine (L-) (H1043)	1815026901	1
Unisan	Glutamine (L-) (H1043)	1814026903	1

- 1547 spectra from 20 *Apo-Ident* customers from a total of 580 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Glutamine (L-) (H1043)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glutamine (L-) (H1043)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	210	0	18 944
Type B	0	285	65	21 546
Type C	0	25	7	1547

The substance/substance group *Glutamine (L-) (H1043)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8915 %)	81.4286 % (> 80.5714 %)
Type C	100.0000 % (> 99.1635 %)	78.1250 % (> 68.7500 %)

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80089	80089	0.00	34.67
80171	80171	0.00	30.16
80336	80336	0.00	26.84
80551	80551	0.00	31.40
80552	80552	0.00	32.74

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Glutathione (H1020)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80040-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Glutathione (H1020)

Special notes

When selecting the *Glutathione (H1020)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Glutathione (H1020)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Glutathione (H10…	0955501	80040	40	from supplier
Hepart	Glutathione (H10…	0955501	80125	50	from supplier
Hepart	Glutathione (H10…	019703	80204	20	from supplier
Hepart	Glutathione (H10…	074901	80430	40	from supplier
Hepart	Glutathione (H10…	15000478	80583	40	from supplier
Hepart	Glutathione (H10…	16000938	80813	40	not required

Validation samples

A total of 42 629 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 *Glutathione (H1020)*. These samples are listed above in the *calibration samples* section.

- 18 924 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Glutathione (H1020)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Glutathione (H1020)	19703	80204†	10
Hepart	Glutathione (H1020)	918901	80217	30
Hepart	Glutathione (H1020)	40201	80288	40
Hepart	Glutathione (H1020)	15000478	80583†	20

- 21 796 spectra from a total of 519 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 8 batches from the substance/substance group *Glutathione (H1020)*.

†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
Unisan	Glutathione (H1020)	25703	3
Unisan	Glutathione (H1020)	40201	4
Hepart AG, CH-8280 Kreu…	Glutathione (H1020)	40201	1
Unisan	Glutathione (H1020)	1251019703	2
Unisan	Glutathione (H1020)	74901	3
UNISAN	Glutathione (H1020)	74901	1
Hepart AG, CH-8280 Kreu…	Glutathione (H1020)	1251025703	1
Hepart AG, CH-8280 Kreu…	Glutathione (H1020)	1251019703	1
Unisan	Glutathione (H1020)	1254025703	1
Hepart AG	Glutathione (H1020)	1254025703	1
Hepart AG	Glutathione (H1020)	1254040201	1
Purren Apotheke	Glutathione (H1020)	1254955501	1

- 1559 spectra from 20 *Apo-Ident* customers from a total of 582 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Glutathione (H1020)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glutathione (H1020)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 924
Type B	0	98	2	21 796
Type C	0	20	0	1559

The substance/substance group *Glutathione (H1020)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.3913 %)
Type B	100.0000 % (> 99.8922 %)	98.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.1679 %)	100.0000 % (> 70.0000 %)

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

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

Identity according to identity test using NIR spectroscopy

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

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80040	80040	0.00	15.87
80125	80125	0.00	17.34
80204	80204	0.00	16.94
80430	80430	0.00	16.77
80583	80583	0.00	14.07
80813	80813	0.00	14.20

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Glycine (H1021)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80168-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Glycine (H1021)

Special notes

When selecting the *Glycine (H1021)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Glycine (H1021)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Glycine (H1021)	993401	80197	40	from supplier
Hepart	Glycine (H1021)	061801	80348	40	from supplier
Hepart	Glycine (H1021)	075501	80436	40	from supplier
Hepart	Glycine (H1021)	14001730	80494	40	from supplier
Hepart	Glycine (H1021)	16000239	80764	40	from supplier
Hepart	Glycine (H1021)	16000238	80765	40	from supplier
Hepart	Glycine (H1021)	16000933	80805	40	not required

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 7 reference samples from the substance/substance group *Glycine (H1021)*. These samples are listed above in the *calibration samples* section.

- 18 874 spectra from a total of 392 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 331 spectra of 9 reference samples from the substance/substance group *Glycine (H1021)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Glycine (H1021)	pending	80050	40
Hepart	Glycine (H1021)	965401	80168	51
Hepart	Glycine (H1021)	28101	80253	40
Hepart	Glycine (H1021)	71501	80399	40
Hepart	Glycine (H1021)	14001730	80494†	20
Hepart	Glycine (H1021)	14001731	80495	60
Hepart	Glycine (H1021)	16000239	80764†	20
Hepart	Glycine (H1021)	16000238	80765†	20
Hepart	Glycine (H1021)	16000934	80806	40

- 21 565 spectra from a total of 516 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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

- 12 spectra from 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Glycine (H1021)*.

Supplier	Substance	Batch	Spectra
Unisan	Glycine (H1021)	28101	3
Hepart AG	Glycine (H1021)	28101	3
Unisan/Hepart AG	Glycine (H1021)	28101	1
Hepart AG, CH-8280 Kreu…	Glycine (H1021)	28101	1
Unisan	Glycine (H1021)	14001730	1
Hepart AG	Glycine (H1021)	75501	1
Hepart AG	Glycine (H1021)	1803028101	1
Euro OTC	Glycine (H1021)	16000239/0	1

- 1567 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Glycine (H1021)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glycine (H1021)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	18 874
Type B	0	234	97	21 565
Type C	0	5	7	1567

The substance/substance group *Glycine (H1021)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.8916 %)	70.6949 % (> 69.7885 %)
Type C	100.0000 % (> 99.1757 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80197	80197	0.00	78.26
80348	80348	0.00	89.25
80436	80436	0.00	90.73
80494	80494	0.00	79.42
80764	80764	0.00	91.94
80765	80765	0.00	82.28
80805	80805	0.00	80.18

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**HCK classification**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80008-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

HCK classification; Acacia gum (H1001); Biotin (H1007); Chromium (H1012); Folic acid (H1016); Lycopene (H1058); Melatonin (H1061); Selenium (H1067); Selenium yeast (H1068); Vitamin B12 (H1102); Vitamin D3 (H1105)

Special notes

When selecting the *HCK classification* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

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

Finally, 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 *HCK classification*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin B12 (H11…	944101	80008	40	from supplier
Hepart	Acacia gum (H1001)	639701	80023	40	from supplier
Hepart	Biotin (H1007)	983601	80028	40	from supplier
Hepart	Chromium (H1012)	977201	80033	50	from supplier

continued on the next page

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Folic acid (H1016)	977701	80036	40	from supplier
Hepart	Lycopene (H1058)	999101	80046	40	from supplier
Hepart	Selenium yeast (…	009001	80067	30	from supplier
Hepart	Vitamin B12 (H11…	0966201	80075	30	from supplier
Hepart	Vitamin D3 (H1105)	0959601	80078	30	from supplier
Hepart	Selenium yeast (…	009001	80096	50	from supplier
Hepart	Vitamin D3 (H1105)	0959601	80108	50	from supplier
Hepart	Lycopene (H1058)	927601	80132	40	from supplier
Hepart	Lycopene (H1058)	999101	80144	50	from supplier
Hepart	Folic acid (H1016)	977701	80146	40	from supplier
Hepart	Lycopene (H1058)	004501	80159	50	from supplier
Hepart	Vitamin B12 (H11…	944101	80173	40	from supplier
Hepart	Acacia gum (H1001)	639701	80176	40	from supplier
Hepart	Acacia gum (H1001)	706310	80177	40	from supplier
Hepart	Biotin (H1007)	983601	80187	40	from supplier
Hepart	Selenium yeast (…	997601	80194	40	from supplier
Hepart	Vitamin D3 (H1105)	008101	80201	20	from supplier
Hepart	Lycopene (H1058)	927601	80239	40	from supplier
Hepart	Biotin (H1007)	029603	80247	40	from supplier
Hepart	Acacia gum (H1001)	728201	80266	40	from supplier
Hepart	Vitamin B12 (H11…	026401	80307	40	from supplier
Hepart	Vitamin D3 (H1105)	008101	80309	40	from supplier
Hepart	Folic acid (H1016)	052301	80331	60	from supplier
Hepart	Lycopene (H1058)	053501	80335	40	from supplier
Hepart	Vitamin B12 (H11…	025017	80353	40	from supplier
Hepart	Selenium (H1067)	065601	80361	40	from supplier
Hepart	Selenium (H1067)	065501	80364	40	from supplier
Hepart	Biotin (H1007)	029601	80365	40	from supplier
Hepart	Selenium (H1067)	065701	80366	40	from supplier
Hepart	Melatonin (H1061)	069101	80374	50	from supplier
Hepart	Biotin (H1007)	029601	80385	50	from supplier
Hepart	Folic acid (H1016)	14000639	80442	40	from supplier
Hepart	Folic acid (H1016)	052301	80443	40	from supplier
Hepart	Folic acid (H1016)	14000638	80449	40	from supplier
Hepart	Folic acid (H1016)	14000639	80451	40	from supplier
Hepart	Melatonin (H1061)	069101	80488	40	from supplier
Hepart	Selenium (H1067)	15000157	80530	40	from supplier
Hepart	Selenium (H1067)	15000158	80531	40	from supplier
Hepart	Selenium (H1067)	15000159	80535	40	from supplier
Hepart	Folic acid (H1016)	15000125	80553	40	from supplier
Hepart	Vitamin D3 (H1105)	15000490	80580	40	from supplier
Hepart	Biotin (H1007)	15000735	80586	40	from supplier
Hepart	Vitamin B12 (H11…	15000993	80603	40	from supplier
Hepart	Vitamin B12 (H11…	15000993(B1)	80604	40	from supplier
Hepart	Selenium (H1067)	065501	80706	40	from supplier
Hepart	Chromium (H1012)	16000520/0	80791	40	from supplier
Hepart	Selenium (H1067)	16001349	80822	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 2080 spectra of 51 reference samples from the substance/substance group *HCK classification*. These samples are listed above in the *calibration samples* section.

- 17 074 spectra from a total of 362 batches from further 69 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 995 spectra of 33 reference samples from the substance/substance group *HCK classification*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Selenium (H1067)	933301	80014	40
Hepart	Chromium (H1012)	977201	80033†	5
Hepart	Selenium (H1067)	933301	80066	30
Hepart	Selenium (H1067)	10201	80086	45
Hepart	Selenium (H1067)	10201	80105	50
Hepart	Vitamin B12 (H1102)	966201	80174	40
Hepart	Chromium (H1012)	977201	80181	40
Hepart	Vitamin D3 (H1105)	8101	80201†	5
Hepart	Selenium (H1067)	601901	80211	30
Hepart	Vitamin D3 (H1105)	940201	80215	30
Hepart	Selenium (H1067)	10201	80268	40
Hepart	Selenium (H1067)	10201	80297	40
Hepart	Folic acid (H1016)	56901	80334	40
Hepart	Melatonin (H1061)	69101	80374†	10
Hepart	Biotin (H1007)	29601	80385†	10
Hepart	Melatonin (H1061)	69101	80488†	20
Hepart	Selenium (H1067)	15000157	80530†	20
Hepart	Selenium (H1067)	15000158	80531†	20
Hepart	Selenium (H1067)	15000159	80535†	20
Hepart	Folic acid (H1016)	15000125	80553†	20
Hepart	Vitamin D3 (H1105)	15000490	80580†	20
Hepart	Biotin (H1007)	15000735	80586†	20
Hepart	Vitamin B12 (H1102)	15000993	80603†	20
Hepart	Vitamin B12 (H1102)	15000993(B1)	80604†	20
Hepart	Vitamin B12 (H1102)	15000993(F2)	80605	60
Hepart	Selenium (H1067)	65501	80706†	20
Hepart	Chromium (H1012)	16000520/4	80792	40
Hepart	Chromium (H1012)	16000520/2	80793	40
Hepart	Vitamin D3 (H1105)	16000952	80816	40
Hepart	Selenium (H1067)	16001350	80823	40
Hepart	Selenium (H1067)	16001351	80824	40
Hepart	Folic acid (H1016)	16001098	80833	40
Hepart	Biotin (H1007)	16001396	80855	40

†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*.

- 20 901 spectra from a total of 495 batches from further 84 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 289 spectra from 16 *Apo-Ident* customers from 76 batches from the substance/substance group *HCK classification*.

Supplier	Substance	Batch	Spectra
Hepart AG, CH-8280 Kreu…	Acacia gum (H1001)	1211622002	2
Unisan	Acacia gum (H1001)	1211706310	1
Fagron	Acacia gum (H1001)	1211728201	2
Hepart AG, CH-8280 Kreu…	Acacia gum (H1001)	1211728201	1
Unisan	Acacia gum (H1001)	1211728201	1
Hepart AG	Acacia gum (H1001)	728201	1
Unisan	Acacia gum (H1001)	706310	1
Unisan Gmbh, 78465 Kons…	Acacia gum (H1001)	728201	1
Unisan	Biotin (H1007)	29601	2
Hepart AG	Biotin (H1007)	29601	2
Unisan	Biotin (H1007)	29603	7
Hepart AG	Biotin (H1007)	29603	3
Unisan	Biotin (H1007)	14000862	2
Unisan	Biotin (H1007)	1591983601	1
Unisan	Biotin (H1007)	14000862/2	2
Unisan	Biotin (H1007)	15000735/0	1
Hepart AG, CH-8280 Kreu…	Biotin (H1007)	1592029603	1
Ichthyol Gesellschaft C…	Biotin (H1007)	1591983601	1
Hepart AG	Biotin (H1007)	1592029603	3
Unisan	Biotin (H1007)	15000735	1
Unisan	Biotin (H1007)	1592983601	1
Unisan	Biotin (H1007)	983601	1
Unisan	Biotin (H1007)	H100721	1
UNISAN	Chromium (H1012)	14000429	4
unisan	Chromium (H1012)		1
Unisan	Chromium (H1012)	14000429	2
Hepart AG	Chromium (H1012)	1582977201	4
Unisan	Chromium (H1012)	1581977201	2
Unisan	Chromium (H1012)	1582977201	3
Unisan	Chromium (H1012)	977201	7
Hepart AG, CH-8280 Kreu…	Chromium (H1012)	977201	2
Hepart AG	Chromium (H1012)	977201	5
Unisan	Chromium (H1012)	16000520/0	1
Unisan	Folic acid (H1016)	30201	8
Unisan	Folic acid (H1016)	16000931	1
Unisan/Hepart AG	Folic acid (H1016)	30201	1
Hepart AG	Folic acid (H1016)	52301	3
Unisan	Folic acid (H1016)	52301	7
Unisan Gmbh, 78465 Kons…	Folic acid (H1016)	30201	1
Hepart AG, CH-8280 Kreu…	Folic acid (H1016)	52301	2
Unisan	Folic acid (H1016)	14000638	3
Unisan Gmbh, 78465 Kons…	Folic acid (H1016)	1611030201	1
Unisan	Folic acid (H1016)	14000639/1	1
Hepart AG	Folic acid (H1016)	1613030201	5
Unisan	Folic acid (H1016)	1613030201	3

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Supplier	Substance	Batch	Spectra
Unisan	Folic acid (H1016)	1611030201	1
Bombastus	Folic acid (H1016)	1613052301	1
Unisan	Folic acid (H1016)	1613977701	2
Unisan	Folic acid (H1016)	977701	2
Unisan	Folic acid (H1016)	H101621	1
Unisan	Lycopene (H1058)	47301	2
Unisan/Hepart AG	Lycopene (H1058)	47301	1
Hepart AG	Lycopene (H1058)	47301	1
Unisan	Lycopene (H1058)	53501	6
Hepart AG	Lycopene (H1058)	53501	1
Unisan	Lycopene (H1058)	1195004501	1
Unisan	Lycopene (H1058)	14000803	1
Unisan	Lycopene (H1058)	4501	4
Unisan	Lycopene (H1058)	H105811	1
Unisan	Selenium (H1067)	10201	21
Hepart AG	Selenium (H1067)	10201	9
Hepart AG, CH-8280 Kreu…	Selenium (H1067)	10201	1
Unisan	Selenium (H1067)	65501	1
Unisan	Selenium (H1067)	65601	3
Unisan	Selenium (H1067)	65501/2	1
UNISAN	Selenium (H1067)	65501	1
UNISAN	Selenium (H1067)	65601	3
Unisan	Selenium (H1067)	65601/1	1
Unisan	Selenium (H1067)	65701	5
Unisan	Selenium (H1067)	65601/2	2
Hepart AG	Selenium (H1067)	65701	1
Unisan	Selenium (H1067)	1144010201	2
Hepart AG	Selenium (H1067)	1144010201	3
Hepart AG	Selenium (H1067)	933301	1
Unisan	Selenium (H1067)	1144933301	2
Bombastus	Selenium (H1067)	1144010201	1
Hepart AG, CH-8280 Kreu…	Selenium (H1067)	1144010201	1
Unisan	Selenium (H1067)	15000157	2
Unisan	Selenium yeast (H1068)	25709	1
Unisan	Selenium yeast (H1068)	9001	1
Unisan	Selenium yeast (H1068)	1151009001	3
Unisan	Selenium (H1067)	15000158	1
Unisan	Vitamin B12 (H1102)	75301	6
Unisan	Vitamin B12 (H1102)	75301/2	2
Unisan	Vitamin B12 (H1102)	15000993	1
Unisan	Vitamin B12 (H1102)	25017	6
Hepart AG	Vitamin B12 (H1102)	25017	4
Hydro-Cell-Key	Vitamin B12 (H1102)	25017	1
Unisan	Vitamin B12 (H1102)	26401	2
Unisan	Vitamin B12 (H1102)	1061025017	1
Hepart AG	Vitamin B12 (H1102)	1064025017	1
Hepart AG	Vitamin B12 (H1102)	1064026401	1
Unisan	Vitamin B12 (H1102)	1064025017	3
Hepart AG, CH-8280 Kreu…	Vitamin B12 (H1102)	1064026401	1
Unisan	Vitamin B12 (H1102)	1064026401	2
Unisan	Vitamin B12 (H1102)	3441377	1
Unisan	Vitamin D3 (H1105)	8101	10
Hepart AG	Vitamin D3 (H1105)	8101	1
HCK	Vitamin D3 (H1105)	8101	1
Unisan	Vitamin D3 (H1105)	6108129	1
Hepart AG	Vitamin D3 (H1105)	63701	3
Unisan Gmbh, 78465 Kons…	Vitamin D3 (H1105)	63701	1
UNISAN	Vitamin D3 (H1105)	63601	1
Unisan	Vitamin D3 (H1105)	63701	5
Fagron	Vitamin D3 (H1105)	63701	1

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Supplier	Substance	Batch	Spectra
Hepart AG	Vitamin D3 (H1105)	64801	4
Hepart AG, CH-8280 Kreu…	Vitamin D3 (H1105)	64801	1
Unisan	Vitamin D3 (H1105)	64801	6
Hepart AG	Vitamin D3 (H1105)	1335008101	2
Unisan	Vitamin D3 (H1105)	1335008101	4
Unisan	Vitamin D3 (H1105)	1335008108	1
Hepart AG, Unisan GmbH	Vitamin D3 (H1105)	64801	1
Unisan	Vitamin D3 (H1105)	1335959601	2
Hepart AG, CH-8280 Kreu…	Vitamin D3 (H1105)	1336008101	2
UNISAN	Vitamin D3 (H1105)	14000481	3
Unisan	Vitamin D3 (H1105)	14000481	1
Unisan	Vitamin D3 (H1105)	14000481/2	3
Unisan	Vitamin D3 (H1105)	15000490	2
Unisan	Vitamin D3 (H1105)	15000490/0	3

- 1290 spectra from 20 *Apo-Ident* customers from a total of 515 batches from a further 51 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	2080	0	17 074
Type B	0	989	6	20 383
Type C	0	283	6	1288

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9375 %)	100.0000 % (> 99.7115 %)
Type B	100.0000 % (> 99.8943 %)	99.3970 % (> 99.0955 %)
Type C	100.0000 % (> 99.2746 %)	97.9239 % (> 96.8858 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80008	80008	0.00	14.80
80023	80023	0.00	18.56
80028	80028	0.00	21.91
80033	80033	0.00	14.37
80036	80036	0.00	18.20
80046	80046	0.00	15.43
80067	80067	0.00	16.27
80075	80075	0.00	14.90
80078	80078	0.00	13.82
80096	80096	0.00	22.01
80108	80108	0.00	14.08
80132	80132	0.00	23.88
80144	80144	0.00	18.16
80146	80146	0.00	14.56
80159	80159	0.00	17.09
80173	80173	0.00	14.27
80176	80176	0.00	17.50
80177	80177	0.00	21.20
80187	80187	0.00	24.62
80194	80194	0.00	22.69
80201	80201	0.00	11.34
80239	80239	0.00	20.98
80247	80247	0.00	21.42
80266	80266	0.00	12.18
80307	80307	0.00	10.28
80309	80309	0.00	10.64
80331	80331	0.00	14.26
80335	80335	0.00	22.06
80353	80353	0.00	10.13
80361	80361	0.00	17.30
80364	80364	0.00	19.02
80365	80365	0.00	14.34
80366	80366	0.00	18.14
80374	80374	0.00	19.08
80385	80385	0.00	20.73
80442	80442	0.00	11.28
80443	80443	0.00	14.67
80449	80449	0.00	12.44
80451	80451	0.00	13.22
80488	80488	0.00	18.40
80530	80530	0.00	14.22
80531	80531	0.00	14.49
80535	80535	0.00	19.39
80553	80553	0.00	18.57
80580	80580	0.00	12.90
80586	80586	0.00	14.18
80603	80603	0.00	10.37
80604	80604	0.00	10.67

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80706	80706	0.00	16.39
80791	80791	0.00	16.77
80822	80822	0.00	13.99

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Inositol hexanicotinate (H1022)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80087-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Inositol hexanicotinate (H1022)

Special notes

When selecting the *Inositol hexanicotinate (H1022)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Inositol hexanicotinate (H1022)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Inositol hexanic…	652206	80087	40	from supplier
Hepart	Inositol hexanic…	0979201	80106	50	from supplier
Hepart	Inositol hexanic…	046001	80320	60	from supplier
Hepart	Inositol hexanic…	14000920	80465	40	from supplier
Hepart	Inositol hexanic…	15000013	80554	40	from supplier
Hepart	Inositol hexanic…	16000750	80814	40	not required

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 270 spectra of 6 reference samples from the substance/substance group *Inositol hexanicotinate (H1022)*. These samples are listed above in the *calibration samples* section.

- 18 884 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Inositol hexanicotinate (H1022)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Inositol hexanicotinate (H10…	pending	80042	40
Hepart	Inositol hexanicotinate (H10…	15000013	80554†	20

- 21 836 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 10 spectra from 4 *Apo-Ident* customers from 7 batches from the substance/substance group *Inositol hexanicotinate (H1022)*.

†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
Unisan	Inositol hexanicotinate (H10…	14000920	1
unisan	Inositol hexanicotinate (H10…	15000013	1
Unisan	Inositol hexanicotinate (H10…	46001	1
Unisan	Inositol hexanicotinate (H10…	1810046001	1
Fagron	Inositol hexanicotinate (H10…	1811046001	1
Unisan/Hepart AG	Inositol hexanicotinate (H10…	46001	1
Purren Apotheke	Inositol hexanicotinate (H10…	1811979201	1
Unisan	Inositol hexanicotinate (H10…	1810979201	1
Hepart AG	Inositol hexanicotinate (H10…	1811979201	2

- 1569 spectra from 20 *Apo-Ident* customers from a total of 583 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Inositol hexanicotinate (H1022)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Inositol hexanicotinate (H1022)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	270	0	18 884
Type B	0	20	40	21 836
Type C	0	10	0	1569

The substance/substance group *Inositol hexanicotinate (H1022)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.7778 %)
Type B	100.0000 % (> 99.8928 %)	33.3333 % (> 28.3333 %)
Type C	100.0000 % (> 99.1796 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80087	80087	0.00	49.14
80106	80106	0.00	50.46
80320	80320	0.00	48.21
80465	80465	0.00	50.46
80554	80554	0.00	49.19
80814	80814	0.00	53.15

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Iron (H1015)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80162-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Iron (H1015)

Special notes

When selecting the *Iron (H1015)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Iron (H1015)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Iron (H1015)	0928101	80162	50	from supplier
Hepart	Iron (H1015)	14000285	80510	40	from supplier
Hepart	Iron (H1015)	040901	80511	40	from supplier
Hepart	Iron (H1015)	040901	80568	40	from supplier
Hepart	Iron (H1015)	14000285	80569	40	from supplier
Hepart	Iron (H1015)	15001258	80650	40	from supplier
Hepart	Iron (H1015)	15001259(B1)	80651	40	from supplier
Hepart	Iron (H1015)	15001259	80653	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 330 spectra of 8 reference samples from the substance/substance group *Iron (H1015)*. These samples are listed above in the *calibration samples* section.

- 18 824 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 550 spectra of 16 reference samples from the substance/substance group *Iron (H1015)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Iron (H1015)	603206	80002	40
Hepart	Iron (H1015)	998701	80035	40
Hepart	Iron (H1015)	998701	80183	40
Hepart	Iron (H1015)	603206	80213	30
Hepart	Iron (H1015)	40901	80276	40
Hepart	Iron (H1015)	14000285	80413	40
Hepart	Iron (H1015)	14000285	80510†	20
Hepart	Iron (H1015)	40901	80511†	20
Hepart	Iron (H1015)	40901	80568†	20
Hepart	Iron (H1015)	14000285	80569†	20
Hepart	Iron (H1015)	15001259(F2)	80649	60
Hepart	Iron (H1015)	15001258	80650†	20
Hepart	Iron (H1015)	15001259(B1)	80651†	20
Hepart	Iron (H1015)	15001258(F2)	80652	60
Hepart	Iron (H1015)	15001259	80653†	20
Hepart	Iron (H1015)	15001258(B1)	80654	60

- 21 346 spectra from a total of 513 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples 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.

- 49 spectra from 15 *Apo-Ident* customers from 13 batches from the substance/substance group *Iron (H1015)*.

Supplier	Substance	Batch	Spectra
Unisan	Iron (H1015)	40901	11
Hepart AG	Iron (H1015)	40901	3
Unisan/Hepart AG	Iron (H1015)	40901	1
Hepart AG, Unisan GmbH	Iron (H1015)	40901	4
Unisan	Iron (H1015)	1114040901	2
Hepart AG	Iron (H1015)	1114040901	2
Unisan	Iron (H1015)	1114998701	5
Unisan	Iron (H1015)	1114603206	1
Hepart AG	Iron (H1015)	1114998701	1
Hepart AG, CH-8280 Kreu…	Iron (H1015)	1114998701	1
UNISAN	Iron (H1015)	14000285	1
Unisan 11.08.2105	Iron (H1015)	14000285/2	1
Unisan 2.10.2015	Iron (H1015)	14000285/3	2
Unisan	Iron (H1015)	14000285/5	1
Unisan	Iron (H1015)	14000285/1	2
Unisan	Iron (H1015)	998701	6
Unisan	Iron (H1015)	15001258/0	1
Unisan	Iron (H1015)	14000285/2	1
Unisan 02.04.2016	Iron (H1015)	15001258/0	1
Unisan	Iron (H1015)	15001258/2	1
Unisan	Iron (H1015)	15001259	1

- 1530 spectra from 20 *Apo-Ident* customers from a total of 577 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Iron (H1015)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Iron (H1015)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	330	0	18 824
Type B	0	550	0	21 346
Type C	0	49	0	1530

The substance/substance group *Iron (H1015)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9378 %)	100.0000 % (> 98.1818 %)
Type B	100.0000 % (> 99.8914 %)	100.0000 % (> 98.9091 %)
Type C	100.0000 % (> 99.1609 %)	100.0000 % (> 87.7551 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80162	80162	0.00	10.90
80510	80510	0.00	16.74
80511	80511	0.00	17.10
80568	80568	0.00	15.68
80569	80569	0.00	17.28
80650	80650	0.00	11.60
80651	80651	0.00	11.39
80653	80653	0.00	11.36

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Isoflavones (H1025)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80041-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Isoflavones (H1025)

Special notes

When selecting the *Isoflavones (H1025)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Isoflavones (H1025)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Isoflavones (H10…	988301	80041	40	from supplier
Hepart	Isoflavones (H10…	0955701	80163	50	from supplier
Hepart	Isoflavones (H10…	988301	80165	50	from supplier
Hepart	Isoflavones (H10…	038801	80272	40	from supplier
Hepart	Isoflavones (H10…	056701	80345	40	from supplier
Hepart	Isoflavones (H10…	15000205	80556	40	from supplier
Hepart	Isoflavones (H10…	15000205/2	80815	40	not required

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 7 reference samples from the substance/substance group *Isoflavones (H1025)*. These samples are listed above in the *calibration samples* section.

- 18 854 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 90 spectra of 3 reference samples from the substance/substance group *Isoflavones (H1025)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Isoflavones (H1025)	591907	80208	30
Hepart	Isoflavones (H1025)	15000205	80556†	20
Hepart	Isoflavones (H1025)	16001644/0	80853	40

- 21 806 spectra from a total of 520 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 17 spectra from 5 *Apo-Ident* customers from 11 batches from the substance/substance group *Isoflavones (H1025)*.

†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
Unisan	Isoflavones (H1025)	25704	1
Unisan/Hepart AG	Isoflavones (H1025)	38801	1
Hepart AG	Isoflavones (H1025)	38801	1
Hepart AG	Isoflavones (H1025)	56701	1
Hepart AG	Isoflavones (H1025)	1314025704	1
Unisan	Isoflavones (H1025)	1310988301	1
Unisan	Isoflavones (H1025)	56701	3
Unisan	Isoflavones (H1025)	15000205/0	3
Hepart AG	Isoflavones (H1025)	1314038801	1
Purren Apotheke	Isoflavones (H1025)	1314955701	1
Unisan 02.04.2016	Isoflavones (H1025)	15000205/1	1
Unisan	Isoflavones (H1025)	15000205	1
Unisan	Isoflavones (H1025)	1310025704	1

- 1562 spectra from 20 *Apo-Ident* customers from a total of 579 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Isoflavones (H1025)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Isoflavones (H1025)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	18 854
Type B	0	60	30	21 806
Type C	0	12	5	1562

The substance/substance group *Isoflavones (H1025)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.8923 %)	66.6667 % (> 63.3333 %)
Type C	100.0000 % (> 99.1699 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80041	80041	0.00	24.07
80163	80163	0.00	14.92
80165	80165	0.00	13.36
80272	80272	0.00	13.97
80345	80345	0.00	13.11
80556	80556	0.00	16.24
80815	80815	0.00	19.55

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Isoleucine (L-) (H1045)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80134-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Isoleucine (L-) (H1045)

Special notes

When selecting the *Isoleucine (L-) (H1045)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Isoleucine (L-) (H1045)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Isoleucine (L-) ...	0968701	80134	50	from supplier
Hepart	Isoleucine (L-) ...	066301	80368	40	from supplier
Hepart	Isoleucine (L-) ...	14001772	80498	40	from supplier
Hepart	Isoleucine (L-) ...	15001641	80678	40	from supplier
Hepart	Isoleucine (L-) ...	15001640	80679	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 210 spectra of 5 reference samples from the substance/substance group *Isoleucine (L-) (H1045)*. These samples are listed above in the *calibration samples* section.

- 18 944 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Isoleucine (L-) (H1045)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Isoleucine (L-) (H1045)	pending	80051	40
Hepart	Isoleucine (L-) (H1045)	942901	80222	30
Hepart	Isoleucine (L-) (H1045)	27701	80249	40
Hepart	Isoleucine (L-) (H1045)	14001772	80498†	20
Hepart	Isoleucine (L-) (H1045)	15001641	80678†	20
Hepart	Isoleucine (L-) (H1045)	15001640	80679†	20

- 21 726 spectra from a total of 518 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 7 *Apo-Ident* customers from 6 batches from the substance/substance group *Isoleucine (L-) (H1045)*.

†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
Unisan	Isoleucine (L-) (H1045)	66301	2
Hepart AG	Isoleucine (L-) (H1045)	66301	1
Unisan	Isoleucine (L-) (H1045)	27701	2
Fritz Schiele	Isoleucine (L-) (H1045)	1805027701	1
Hepart AG, CH-8280 Kreu…	Isoleucine (L-) (H1045)	66301	1
Unisan	Isoleucine (L-) (H1045)	1804027701	2
Hepart AG, CH-8280 Kreu…	Isoleucine (L-) (H1045)	1804968701	1
Hepart AG	Isoleucine (L-) (H1045)	1805027701	2
Unisan	Isoleucine (L-) (H1045)	1805968701	1
Unisan	Isoleucine (L-) (H1045)	1805027701	1

- 1565 spectra from 20 *Apo-Ident* customers from a total of 584 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Isoleucine (L-) (H1045)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Isoleucine (L-) (H1045)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	210	0	18 944
Type B	0	144	26	21 726
Type C	0	11	3	1565

The substance/substance group *Isoleucine (L-) (H1045)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8918 %)	84.7059 % (> 82.9412 %)
Type C	100.0000 % (> 99.1729 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80134	80134	0.00	32.03
80368	80368	0.00	29.81
80498	80498	0.00	35.98
80678	80678	0.00	36.11
80679	80679	0.00	34.26

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Juniper (H1112)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80702-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Juniper (H1112)

Special notes

When selecting the *Juniper (H1112)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 (H1112)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Juniper (H1112)	15001004	80702	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Juniper (H1112)*. These samples are listed above in the *calibration samples* section.

- 19 114 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 20 spectra of 1 reference samples from the substance/substance group *Juniper (H1112)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Juniper (H1112)	15001004	80702†	20

- 21 876 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Juniper (H1112)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *Juniper (H1112)* can clearly be 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 (H1112)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	19 114
Type B	0	20	0	21 876
Type C	0	0	0	1579

The substance/substance group *Juniper (H1112)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80702	80702	0.00	28.01

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**L-5-HTP (H1035)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80111-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

L-5-HTP (H1035)

Special notes

When selecting the *L-5-HTP (H1035)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *L-5-HTP (H1035)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-5-HTP (H1035)	968801	80111	50	from supplier
Hepart	L-5-HTP (H1035)	0999801	80148	40	from supplier
Hepart	L-5-HTP (H1035)	16000441	80797	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 130 spectra of 3 reference samples from the substance/substance group L-*5-HTP (H1035)*. These samples are listed above in the *calibration samples* section.

- 19 024 spectra from a total of 396 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 L-*5-HTP (H1035)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	L-5-HTP (H1035)	pending	80047	40
Hepart	L-5-HTP (H1035)	16000441/0	80851	40

- 21 816 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 8 spectra from 4 *Apo-Ident* customers from 5 batches from the substance/substance group L-*5-HTP (H1035)*.

Supplier	Substance	Batch	Spectra
Unisan	L-5-HTP (H1035)	25006	3
Unisan	L-5-HTP (H1035)	26102	1
Unisan	L-5-HTP (H1035)	1836025006	1
Hepart AG	L-5-HTP (H1035)	1837025006	1
Hepart AG	L-5-HTP (H1035)	1837999801	2

- 1571 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group L-*5-HTP (H1035)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with L-*5-HTP (H1035)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 024
Type B	0	78	2	21 816
Type C	0	8	0	1571

The substance/substance group L-*5-HTP (H1035)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9384 %)	100.0000 % (> 95.3846 %)
Type B	100.0000 % (> 99.8924 %)	97.5000 % (> 93.7500 %)
Type C	100.0000 % (> 99.1855 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80111	80111	0.00	14.10
80148	80148	0.00	21.45
80797	80797	0.00	18.90

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Leucine (L-) (H1046)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80150-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Leucine (L-) (H1046)

Special notes

When selecting the *Leucine (L-) (H1046)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Leucine (L-) (H1046)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Leucine (L-) (H1...	965101	80150	50	from supplier
Hepart	Leucine (L-) (H1...	994101	80203	20	from supplier
Hepart	Leucine (L-) (H1...	965101	80333	60	from supplier
Hepart	Leucine (L-) (H1...	074301	80410	40	from supplier
Hepart	Leucine (L-) (H1...	15000283	80570	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 210 spectra of 5 reference samples from the substance/substance group *Leucine (L-) (H1046)*. These samples are listed above in the *calibration samples* section.

- 18 944 spectra from a total of 395 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 70 spectra of 3 reference samples from the substance/substance group *Leucine (L-) (H1046)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Leucine (L-) (H1046)	pending	80052	40
Hepart	Leucine (L-) (H1046)	994101	80203†	10
Hepart	Leucine (L-) (H1046)	15000283	80570†	20

- 21 826 spectra from a total of 521 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 10 spectra from 7 *Apo-Ident* customers from 5 batches from the substance/substance group *Leucine (L-) (H1046)*.

Supplier	Substance	Batch	Spectra
Unisan	Leucine (L-) (H1046)	25706	1
Unisan/Hepart AG	Leucine (L-) (H1046)	52601	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
Hepart AG, CH-8280 Kreu…	Leucine (L-) (H1046)	52601	2
Unisan	Leucine (L-) (H1046)	1809965101	1
Purren Apotheke	Leucine (L-) (H1046)	1809965101	1
Hepart AG	Leucine (L-) (H1046)	1809994101	2
Unisan	Leucine (L-) (H1046)	52601	1
Unisan	Leucine (L-) (H1046)	994101	1

- 1569 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Leucine (L-) (H1046)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Leucine (L-) (H1046)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	210	0	18 944
Type B	0	38	32	21 826
Type C	0	8	2	1569

The substance/substance group *Leucine (L-) (H1046)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8925 %)	54.2857 % (> 50.0000 %)
Type C	100.0000 % (> 99.1796 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80150	80150	0.00	17.69
80203	80203	0.00	16.78
80333	80333	0.00	19.24
80410	80410	0.00	25.24
80570	80570	0.00	24.04

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Lipoic acid (a-) (H1000)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80022-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Lipoic acid (a-) (H1000)

Special notes

When selecting the *Lipoic acid (a-) (H1000)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Lipoic acid (a-) (H1000)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Lipoic acid (a-)...	054301	80321	59	from supplier
Hepart	Lipoic acid (a-)...	14001420	80482	40	from supplier
Hepart	Lipoic acid (a-)...	14001726	80491	40	from supplier
Hepart	Lipoic acid (a-)...	15001526(B1.2)	80681	40	from supplier
Hepart	Lipoic acid (a-)...	14000497	80682	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 219 spectra of 5 reference samples from the substance/substance group *Lipoic acid (a-) (H1000)*. These samples are listed above in the *calibration samples* section.

- 18 935 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 541 spectra of 14 reference samples from the substance/substance group *Lipoic acid (a-) (H1000)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Lipoic acid (a-) (H1000)	954001	80022	40
Hepart	Lipoic acid (a-) (H1000)	954001	80178	40
Hepart	Lipoic acid (a-) (H1000)	993101	80185	40
Hepart	Lipoic acid (a-) (H1000)	54301	80321†	1
Hepart	Lipoic acid (a-) (H1000)	66601	80369	60
Hepart	Lipoic acid (a-) (H1000)	14000551	80445	40
Hepart	Lipoic acid (a-) (H1000)	14001420	80482†	20
Hepart	Lipoic acid (a-) (H1000)	14001726	80491†	20
Hepart	Lipoic acid (a-) (H1000)	15001526(B1.1)	80680	60
Hepart	Lipoic acid (a-) (H1000)	15001526(B1.2)	80681†	20
Hepart	Lipoic acid (a-) (H1000)	14000497	80682†	20
Hepart	Lipoic acid (a-) (H1000)	14000497(F1)	80683	60
Hepart	Lipoic acid (a-) (H1000)	14000497(F2)	80684	60
Hepart	Lipoic acid (a-) (H1000)	15001526(MM)	80685	60

- 21 355 spectra from a total of 510 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 10 *Apo-Ident* customers from 9 batches from the substance/substance group *Lipoic acid (a-) (H1000)*.

Supplier	Substance	Batch	Spectra
Unisan	Lipoic acid (a-) (H1000)	66601	1
UNISAN	Lipoic acid (a-) (H1000)	14001726	2
Unisan	Lipoic acid (a-) (H1000)	14000497	1
Unisan	Lipoic acid (a-) (H1000)	993101	2
Unisan	Lipoic acid (a-) (H1000)	25701	7
Unisan/Hepart AG	Lipoic acid (a-) (H1000)	25701	1
Hepart AG	Lipoic acid (a-) (H1000)	25701	1
Unisan Gmbh, 78465 Kons...	Lipoic acid (a-) (H1000)	25701	2
Unisan/Hepart AG	Lipoic acid (a-) (H1000)	54301	1
Hepart AG	Lipoic acid (a-) (H1000)	54301	1
unisan	Lipoic acid (a-) (H1000)	66601	1
Unisan	Lipoic acid (a-) (H1000)	1312993101	2
Hepart AG	Lipoic acid (a-) (H1000)	1313025701	2
unisan	Lipoic acid (a-) (H1000)	H100031	1

- 1554 spectra from 20 *Apo-Ident* customers from a total of 581 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Lipoic acid (a-) (H1000)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lipoic acid (a-) (H1000)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	219	0	18 935
Type B	0	404	137	21 355
Type C	0	22	3	1554

The substance/substance group *Lipoic acid (a-) (H1000)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.2603 %)
Type B	100.0000 % (> 99.8914 %)	74.6765 % (> 74.1220 %)
Type C	100.0000 % (> 99.1655 %)	88.0000 % (> 76.0000 %)

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80321	80321	0.00	50.98
80482	80482	0.00	70.77
80491	80491	0.00	52.38
80681	80681	0.00	52.98
80682	80682	0.00	52.58

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Lysine (L-) (H1047)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80151-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Lysine (L-) (H1047)

Special notes

When selecting the *Lysine (L-) (H1047)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Lysine (L-) (H1047)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Lysine (L-) (H10...	065401	80343	40	from supplier
Hepart	Lysine (L-) (H10...	028801	80360	40	from supplier
Hepart	Lysine (L-) (H10...	065401	80453	40	from supplier
Hepart	Lysine (L-) (H10...	028801	80458	40	from supplier
Hepart	Lysine (L-) (H10...	14000944	80468	40	from supplier
Hepart	Lysine (L-) (H10...	15000372	80562	40	from supplier
Hepart	Lysine (L-) (H10...	16001395/0	80847	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 7 reference samples from the substance/substance group *Lysine (L-) (H1047)*. These samples are listed above in the *calibration samples* section.

- 18 874 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 270 spectra of 7 reference samples from the substance/substance group *Lysine (L-) (H1047)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Lysine (L-) (H1047)	pending	80053	40
Hepart	Lysine (L-) (H1047)	17302	80151	50
Hepart	Lysine (L-) (H1047)	955002	80152	50
Hepart	Lysine (L-) (H1047)	941501	80221	30
Hepart	Lysine (L-) (H1047)	28801	80295	40
Hepart	Lysine (L-) (H1047)	15000372	80562†	20
Hepart	Lysine (L-) (H1047)	16001503/0	80848	40

- 21 626 spectra from a total of 517 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 13 spectra from 9 *Apo-Ident* customers from 8 batches from the substance/substance group *Lysine (L-) (H1047)*.

†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
Unisan/Hepart AG	Lysine (L-) (H1047)	65401	1
Hepart AG	Lysine (L-) (H1047)	65401	1
Unisan	Lysine (L-) (H1047)	65401/4	1
Unisan	Lysine (L-) (H1047)	14000944	1
Unisan	Lysine (L-) (H1047)	1800017302	3
Unisan	Lysine (L-) (H1047)	15000372/0	1
Hepart AG	Lysine (L-) (H1047)	1800017302	1
Hepart AG, CH-8280 Kreu…	Lysine (L-) (H1047)	1800955002	1
Unisan	Lysine (L-) (H1047)	1801028801	1
Unisan	Lysine (L-) (H1047)	28801	2

- 1566 spectra from 20 *Apo-Ident* customers from a total of 582 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Lysine (L-) (H1047)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lysine (L-) (H1047)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	18 874
Type B	0	41	229	21 626
Type C	0	4	9	1566

The substance/substance group *Lysine (L-) (H1047)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.8916 %)	15.1852 % (> 14.0741 %)
Type C	100.0000 % (> 99.1742 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80343	80343	0.00	50.34
80360	80360	0.00	49.87
80453	80453	0.00	51.17
80458	80458	0.00	35.64
80468	80468	0.00	56.66
80562	80562	0.00	50.54
80847	80847	0.00	49.36

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Magnesium (H1060)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80061-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Magnesium (H1060)

Special notes

When selecting the *Magnesium (H1060)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Magnesium (H1060)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Magnesium (H1060)	069601	80378	50	from supplier
Hepart	Magnesium (H1060)	14001893	80515	40	from supplier
Hepart	Magnesium (H1060)	16000264	80767	40	from supplier
Hepart	Magnesium (H1060)	16000269	80770	40	from supplier
Hepart	Magnesium (H1060)	16001702	80856	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 210 spectra of 5 reference samples from the substance/substance group *Magnesium (H1060)*. These samples are listed above in the *calibration samples* section.

- 18 944 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 1340 spectra of 30 reference samples from the substance/substance group *Magnesium (H1060)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Magnesium (H1060)	pending	80012	40
Hepart	Magnesium (H1060)	pending	80019	40
Hepart	Magnesium (H1060)	973501	80061	30
Hepart	Magnesium (H1060)	941701	80120	50
Hepart	Magnesium (H1060)	973501	80130	50
Hepart	Magnesium (H1060)	43501	80283	40
Hepart	Magnesium (H1060)	43601	80351	40
Hepart	Magnesium (H1060)	69601	80378†	10
Hepart	Magnesium (H1060)	70001	80423	40
Hepart	Magnesium (H1060)	69801	80427	40
Hepart	Magnesium (H1060)	69901	80429	40
Hepart	Magnesium (H1060)	69701	80437	40
Hepart	Magnesium (H1060)	14001893	80515†	20
Hepart	Magnesium (H1060)	14001895	80516	60
Hepart	Magnesium (H1060)	14001889	80517	60
Hepart	Magnesium (H1060)	14001891	80518	60
Hepart	Magnesium (H1060)	14001894	80519	60
Hepart	Magnesium (H1060)	16000264	80767†	20
Hepart	Magnesium (H1060)	16000270	80769	60
Hepart	Magnesium (H1060)	16000269	80770†	20
Hepart	Magnesium (H1060)	16000267	80771	60
Hepart	Magnesium (H1060)	16000271	80772	60
Hepart	Magnesium (H1060)	16000268	80773	60
Hepart	Magnesium (H1060)	16000265	80774	60
Hepart	Magnesium (H1060)	16000272	80775	60
Hepart	Magnesium (H1060)	16000266	80776	60
Hepart	Magnesium (H1060)	16001703	80857	40
Hepart	Magnesium (H1060)	16001704	80858	40
Hepart	Magnesium (H1060)	16001705	80859	40
Hepart	Magnesium (H1060)	16001706	80860	40

- 20 556 spectra from a total of 495 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 63 spectra from 15 *Apo-Ident* customers from 18 batches from the substance/substance group *Magnesium (H1060)*.

Supplier	Substance	Batch	Spectra
Unisan	Magnesium (H1060)	14001893	1
Unisan	Magnesium (H1060)	14001895	4
Unisan	Magnesium (H1060)	16000265/0	1
unbekannt	Magnesium (H1060)	16000264	1
Unisan	Magnesium (H1060)	43501	2
Hepart AG	Magnesium (H1060)	43501	1
Unisan	Magnesium (H1060)	43601	3
Hepart AG	Magnesium (H1060)	43601	2
Unisan	Magnesium (H1060)	43602	1
Unisan/Hepart AG	Magnesium (H1060)	43601	1
Hepart AG	Magnesium (H1060)	43602	4
Unisan	Magnesium (H1060)	43701	3
Hepart AG, CH-8280 Kreu...	Magnesium (H1060)	43602	1
Hepart AG	Magnesium (H1060)	43701	1
unisan	Magnesium (H1060)	43702	1
Unisan Gmbh, 78465 Kons...	Magnesium (H1060)	43702	1
Unisan	Magnesium (H1060)	69701	3
Unisan	Magnesium (H1060)	43702	1
Unisan	Magnesium (H1060)	69601	1
UNISAN	Magnesium (H1060)	69701	3
Unisan	Magnesium (H1060)	69801	4
Unisan	Magnesium (H1060)	69801/2	1
Hepart AG	Magnesium (H1060)	69901	4
Unisan	Magnesium (H1060)	973501	3
Unisan	Magnesium (H1060)	1134973501	4
Unisan/Hepart AG	Magnesium (H1060)	973501	1
Hepart AG, CH-8280 Kreu...	Magnesium (H1060)	1134043601	1
Hepart AG, CH-8280 Kreu...	Magnesium (H1060)	1134973501	2
Hepart AG	Magnesium (H1060)	1134973501	5
unisan	Magnesium (H1060)	14001895	1
Unisan	Magnesium (H1060)	H106021	1

- 1516 spectra from 20 *Apo-Ident* customers from a total of 572 batches from a further 59 substances. These spectra were recorded 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 *Magnesium (H1060)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Magnesium (H1060)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	210	0	18 944
Type B	0	1073	267	20 556
Type C	0	23	40	1516

The substance/substance group *Magnesium (H1060)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8914 %)	80.0746 % (> 79.8507 %)
Type C	100.0000 % (> 99.1598 %)	36.5079 % (> 31.7460 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80378	80378	0.00	30.83
80515	80515	0.00	33.62
80767	80767	0.00	30.10
80770	80770	0.00	27.36
80856	80856	0.00	24.07

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Methylsulfonylmethane (MSM) (H1062)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80102-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Methylsulfonylmethane (MSM) (H1062)

Special notes

When selecting the *Methylsulfonylmethane (MSM) (H1062)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Methylsulfonylmethane (MSM) (H1062)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Methylsulfonylme…	979401	80102	50	from supplier
Hepart	Methylsulfonylme…	0964001	80115	50	from supplier
Hepart	Methylsulfonylme…	056201	80332	60	from supplier
Hepart	Methylsulfonylme…	14000921	80467	40	from supplier
Hepart	Methylsulfonylme…	15001371	80703	80	from supplier
Hepart	Methylsulfonylme…	16000449/0	80782	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 6 reference samples from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*. These samples are listed above in the *calibration samples* section.

- 18 834 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 70 spectra of 2 reference samples from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Methylsulfonylmethane (MSM) ...	pending	80062	30
Hepart	Methylsulfonylmethane (MSM) ...	15001371	80703†	40

- 21 826 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 6 *Apo-Ident* customers from 9 batches from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*.

†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
Unisan	Methylsulfonylmethane (MSM) …	56201	2
Unisan	Methylsulfonylmethane (MSM) …	25013	2
Unisan	Methylsulfonylmethane (MSM) …	15001371	1
HCK	Methylsulfonylmethane (MSM) …	1400921/1	1
Unisan	Methylsulfonylmethane (MSM) …	979401	1
Unisan	Methylsulfonylmethane (MSM) …	26101	1
Unisan	Methylsulfonylmethane (MSM) …	1818025013	1
Unisan/Hepart AG	Methylsulfonylmethane (MSM) …	1819025013	1
Hepart AG	Methylsulfonylmethane (MSM) …	1819026101	1

- 1568 spectra from 20 *Apo-Ident* customers from a total of 581 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Methylsulfonylmethane (MSM) (H1062)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methylsulfonylmethane (MSM) (H1062)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	18 834
Type B	0	43	27	21 826
Type C	0	9	2	1568

The substance/substance group *Methylsulfonylmethane (MSM) (H1062)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9378 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.8925 %)	61.4286 % (> 57.1429 %)
Type C	100.0000 % (> 99.1775 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80102	80102	0.00	64.19
80115	80115	0.00	76.12
80332	80332	0.00	69.28
80467	80467	0.00	76.59
80703	80703	0.00	73.71
80782	80782	0.00	68.90

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**OPC Grape seed (H1066)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80064-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

OPC Grape seed (H1066)

Special notes

When selecting the *OPC Grape seed (H1066)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *OPC Grape seed (H1066)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	OPC Grape seed (...	130208-77	80337	40	from supplier
Hepart	OPC Grape seed (...	068301	80352	40	from supplier
Hepart	OPC Grape seed (...	070401	80380	50	from supplier
Hepart	OPC Grape seed (...	070401	80398	40	from supplier

Validation samples

A total of 42 629 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 *OPC Grape seed (H1066)*. These samples are listed above in the *calibration samples* section.

- 18 984 spectra from a total of 396 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 220 spectra of 6 reference samples from the substance/substance group *OPC Grape seed (H1066)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	OPC Grape seed (H1066)	672201	80064	30
Hepart	OPC Grape seed (H1066)	672201	80118	50
Hepart	OPC Grape seed (H1066)	16201	80128	50
Hepart	OPC Grape seed (H1066)	643901	80196	40
Hepart	OPC Grape seed (H1066)	18401	80233	40
Hepart	OPC Grape seed (H1066)	70401	80380†	10

- 21 676 spectra from a total of 518 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 18 spectra from 10 *Apo-Ident* customers from 7 batches from the substance/substance group *OPC Grape seed (H1066)*.

†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
Unisan	OPC Grape seed (H1066)		1
Hepart AG	OPC Grape seed (H1066)	70401	2
Unisan	OPC Grape seed (H1066)	70401	2
Hepart AG	OPC Grape seed (H1066)	18401	1
Unisan	OPC Grape seed (H1066)	68301	4
UNISAN	OPC Grape seed (H1066)	70401	1
Hepart	OPC Grape seed (H1066)	15000215	1
Unisan	OPC Grape seed (H1066)	18401	2
Hepart AG, CH-8280 Kreu…	OPC Grape seed (H1066)	130208	1
Hepart AG	OPC Grape seed (H1066)	1504018401	2
Unisan	OPC Grape seed (H1066)	1504018401	1

- 1561 spectra from 20 *Apo-Ident* customers from a total of 584 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *OPC Grape seed (H1066)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *OPC Grape seed (H1066)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 984
Type B	0	10	210	21 676
Type C	0	13	5	1561

The substance/substance group *OPC Grape seed (H1066)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9382 %)	100.0000 % (> 96.4706 %)
Type B	100.0000 % (> 99.8917 %)	4.5455 % (> 3.1818 %)
Type C	100.0000 % (> 99.1692 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80337	80337	0.00	27.95
80352	80352	0.00	15.33
80380	80380	0.00	14.68
80398	80398	0.00	12.82

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Ornithine (L-) (H1048)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80175-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Ornithine (L-) (H1048)

Special notes

When selecting the *Ornithine (L-) (H1048)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Ornithine (L-) (H1048)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Ornithine (L-) (...	979301	80175	40	from supplier
Hepart	Ornithine (L-) (...	646703	80195	40	from supplier
Hepart	Ornithine (L-) (...	001202	80206	20	from supplier
Hepart	Ornithine (L-) (...	15000004	80629	40	from supplier
Hepart	Ornithine (L-) (...	15001364	80667	40	from supplier
Hepart	Ornithine (L-) (...	15001364(F1)	80669	40	from supplier
Hepart	Ornithine (L-) (...	16000935	80811	40	not required

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 7 reference samples from the substance/substance group *Ornithine (L-) (H1048)*. These samples are listed above in the *calibration samples* section.

- 18 894 spectra from a total of 392 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Ornithine (L-) (H1048)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Ornithine (L-) (H1048)	pending	80054	40
Hepart	Ornithine (L-) (H1048)	1202	80206†	10
Hepart	Ornithine (L-) (H1048)	15000004	80629†	20
Hepart	Ornithine (L-) (H1048)	15001364	80667†	20
Hepart	Ornithine (L-) (H1048)	15001364(F2)	80668	60
Hepart	Ornithine (L-) (H1048)	15001364(F1)	80669†	20

- 21 726 spectra from a total of 518 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 11 spectra from 7 *Apo-Ident* customers from 5 batches from the substance/substance group *Ornithine (L-) (H1048)*.

†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
Unisan	Ornithine (L-) (H1048)	27001	5
Purren Apotheke	Ornithine (L-) (H1048)	1817979301	1
Unisan	Ornithine (L-) (H1048)	1816979301	2
Unisan	Ornithine (L-) (H1048)	979301	2
Hepart AG	Ornithine (L-) (H1048)	1817025008	1

- 1568 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Ornithine (L-) (H1048)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ornithine (L-) (H1048)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	18 894
Type B	0	158	12	21 726
Type C	0	8	3	1568

The substance/substance group *Ornithine (L-) (H1048)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.8918 %)	92.9412 % (> 91.1765 %)
Type C	100.0000 % (> 99.1775 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80175	80175	0.00	68.97
80195	80195	0.00	81.29
80206	80206	0.00	70.24
80629	80629	0.00	72.48
80667	80667	0.00	72.25
80669	80669	0.00	75.38
80811	80811	0.00	64.15

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Orthovimin Neutral Complex (H1403)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80744-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Orthovimin Neutral Complex (H1403)

Special notes

When selecting the *Orthovimin Neutral Complex (H1403)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Orthovimin Neutral Complex (H1403)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Orthovimin Neutr…	15001850	80744	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Orthovimin Neutral Complex (H1403)*. These samples are listed above in the *calibration samples* section.

- 19 114 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 20 spectra of 1 reference samples from the substance/substance group *Orthovimin Neutral Complex (H1403)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Orthovimin Neutral Complex (…	15001850	80744†	20

- 21 876 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Orthovimin Neutral Complex (H1403)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *Orthovimin Neutral Complex (H1403)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Orthovimin Neutral Complex (H1403)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	19 114
Type B	0	20	0	21 851
Type C	0	0	0	1579

The substance/substance group *Orthovimin Neutral Complex (H1403)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8961 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80744	80744	0.00	17.84

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**PET basis (H1503)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80566-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

PET basis (H1503)

Special notes

When selecting the *PET basis (H1503)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *PET basis (H1503)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET basis (H1503)	15000402	80566	40	from supplier
Hepart	PET basis (H1503)	15000402	80636	40	from supplier

Validation samples

A total of 42 629 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 *PET basis (H1503)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *PET basis (H1503)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	PET basis (H1503)	15000402	80566†	20
Hepart	PET basis (H1503)	15000402	80636†	20

- 21 856 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *PET basis (H1503)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *PET basis (H1503)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET basis (H1503)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	40	0	21 816
Type C	0	0	0	1579

The substance/substance group *PET basis (H1503)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80566	80566	0.00	22.18
80636	80636	0.00	18.18

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**PET coenzyme Q10 (H0022)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80561-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

PET coenzyme Q10 (H0022)

Special notes

When selecting the *PET coenzyme Q10 (H0022)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *PET coenzyme Q10 (H0022)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET coenzyme Q10…	15000401	80561	40	from supplier
Hepart	PET coenzyme Q10…	15000401	80635	40	from supplier

Validation samples

A total of 42 629 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 *PET coenzyme Q10 (H0022)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 399 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *PET coenzyme Q10 (H0022)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	PET coenzyme Q10 (H0022)	15000401	80561†	20
Hepart	PET coenzyme Q10 (H0022)	15000401	80635†	20

- 21 856 spectra from a total of 523 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *PET coenzyme Q10 (H0022)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded 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 *PET coenzyme Q10 (H0022)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET coenzyme Q10 (H0022)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	40	0	21 856
Type C	0	0	0	1579

The substance/substance group *PET coenzyme Q10 (H0022)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8935 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80561	80561	0.00	18.35
80635	80635	0.00	19.27

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**PET immune system (H1502)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80564-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

PET immune system (H1502)

Special notes

When selecting the *PET immune system (H1502)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *PET immune system (H1502)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET immune syste…	15000405	80564	40	from supplier
Hepart	PET immune syste…	15000405	80634	40	from supplier

Validation samples

A total of 42 629 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 *PET immune system (H1502)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *PET immune system (H1502)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	PET immune system (H1502)	15000405	80564†	20
Hepart	PET immune system (H1502)	15000405	80634†	20

- 21 856 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *PET immune system (H1502)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded 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 *PET immune system (H1502)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET immune system (H1502)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	40	0	21 816
Type C	0	0	0	1579

The substance/substance group *PET immune system (H1502)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80564	80564	0.00	29.25
80634	80634	0.00	27.56

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**PET joints (H1501)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80567-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

PET joints (H1501)

Special notes

When selecting the *PET joints (H1501)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *PET joints (H1501)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET joints (H1501)	15000404	80567	40	from supplier
Hepart	PET joints (H1501)	15000404	80630	40	from supplier

Validation samples

A total of 42 629 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 *PET joints (H1501)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *PET joints (H1501)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	PET joints (H1501)	15000404	80567†	20
Hepart	PET joints (H1501)	15000404	80630†	20

- 21 856 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *PET joints (H1501)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *PET joints (H1501)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET joints (H1501)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	40	0	21 816
Type C	0	0	0	1579

The substance/substance group *PET joints (H1501)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80567	80567	0.00	15.93
80630	80630	0.00	17.27

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**PET skin and hair (H1504)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80565-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

PET skin and hair (H1504)

Special notes

When selecting the *PET skin and hair (H1504)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *PET skin and hair (H1504)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET skin and hai…	15000403	80565	40	from supplier
Hepart	PET skin and hai…	15000403	80633	40	from supplier

Validation samples

A total of 42 629 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 *PET skin and hair (H1504)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *PET skin and hair (H1504)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	PET skin and hair (H1504)	15000403	80565†	20
Hepart	PET skin and hair (H1504)	15000403	80633†	20

- 21 856 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *PET skin and hair (H1504)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded 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 *PET skin and hair (H1504)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET skin and hair (H1504)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	40	0	21 816
Type C	0	0	0	1579

The substance/substance group *PET skin and hair (H1504)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80565	80565	0.00	39.39
80633	80633	0.00	43.48

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**PET well-aging (H1500)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80563-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

PET well-aging (H1500)

Special notes

When selecting the *PET well-aging (H1500)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *PET well-aging (H1500)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET well-aging (...	15000401	80563	40	from supplier
Hepart	PET well-aging (...	15000406	80631	40	from supplier

Validation samples

A total of 42 629 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 *PET well-aging (H1500)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *PET well-aging (H1500)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	PET well-aging (H1500)	15000401	80563†	20
Hepart	PET well-aging (H1500)	15000406	80631†	20

- 21 856 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *PET well-aging (H1500)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *PET well-aging (H1500)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET well-aging (H1500)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	40	0	21 856
Type C	0	0	0	1579

The substance/substance group *PET well-aging (H1500)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8935 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80563	80563	0.00	13.19
80631	80631	0.00	12.57

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Phenylalanine (L-) (H1049)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80090-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Phenylalanine (L-) (H1049)

Special notes

When selecting the *Phenylalanine (L-) (H1049)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Phenylalanine (L-) (H1049)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Phenylalanine (L...	964401	80090	50	from supplier
Hepart	Phenylalanine (L...	001201	80198	60	from supplier
Hepart	Phenylalanine (L...	019707	80202	20	from supplier
Hepart	Phenylalanine (L...	074401	80400	40	from supplier
Hepart	Phenylalanine (L...	16001096	80852	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 210 spectra of 5 reference samples from the substance/substance group *Phenylalanine (L-) (H1049)*. These samples are listed above in the *calibration samples* section.

- 18 944 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 45 spectra of 3 reference samples from the substance/substance group *Phenylalanine (L-) (H1049)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Phenylalanine (L-) (H1049)	pending	80055	30
Hepart	Phenylalanine (L-) (H1049)	964401	80090†	5
Hepart	Phenylalanine (L-) (H1049)	19707	80202†	10

- 21 851 spectra from a total of 521 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 11 spectra from 7 *Apo-Ident* customers from 4 batches from the substance/substance group *Phenylalanine (L-) (H1049)*.

Supplier	Substance	Batch	Spectra
Unisan	Phenylalanine (L-) (H1049)	25009	7

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
Unisan	Phenylalanine (L-) (H1049)	74401/0	1
Unisan/Hepart AG	Phenylalanine (L-) (H1049)	1828025009	1
Unisan	Phenylalanine (L-) (H1049)	1828019707	1
Hepart AG	Phenylalanine (L-) (H1049)	1828025009	1

- 1568 spectra from 20 *Apo-Ident* customers from a total of 586 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Phenylalanine (L-) (H1049)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Phenylalanine (L-) (H1049)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	210	0	18 944
Type B	0	43	2	21 851
Type C	0	11	0	1568

The substance/substance group *Phenylalanine (L-) (H1049)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8932 %)	95.5556 % (> 88.8889 %)
Type C	100.0000 % (> 99.1775 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80090	80090	0.00	21.95
80198	80198	0.00	20.63
80202	80202	0.00	24.17
80400	80400	0.00	41.21
80852	80852	0.00	41.51

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Potassium (H1030)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80043-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Potassium (H1030)

Special notes

When selecting the *Potassium (H1030)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Potassium (H1030)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Potassium (H1030)	0944201	80043	40	from supplier
Hepart	Potassium (H1030)	039302	80372	50	from supplier
Hepart	Potassium (H1030)	15000597	80571	40	from supplier
Hepart	Potassium (H1030)	15000598(B1)	80574	40	from supplier
Hepart	Potassium (H1030)	15000599	80576	40	from supplier
Hepart	Potassium (H1030)	15000600	80578	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 250 spectra of 6 reference samples from the substance/substance group *Potassium (H1030)*. These samples are listed above in the *calibration samples* section.

- 18 904 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 639 spectra of 16 reference samples from the substance/substance group *Potassium (H1030)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Potassium (H1030)	944201	80156	50
Hepart	Potassium (H1030)	931901	80224	30
Hepart	Potassium (H1030)	28901	80264	39
Hepart	Potassium (H1030)	28901	80267	40
Hepart	Potassium (H1030)	130328001	80347	40
Hepart	Potassium (H1030)	39302	80372†	10
Hepart	Potassium (H1030)	69201	80376	50
Hepart	Potassium (H1030)	15000597	80571†	20
Hepart	Potassium (H1030)	15000597(B1)	80572	60
Hepart	Potassium (H1030)	15000598	80573	60
Hepart	Potassium (H1030)	15000598(B1)	80574†	20
Hepart	Potassium (H1030)	15000598(F2)	80575	60
Hepart	Potassium (H1030)	15000599	80576†	20
Hepart	Potassium (H1030)	15000599(F2)	80577	60
Hepart	Potassium (H1030)	15000600	80578†	20
Hepart	Potassium (H1030)	15000600(B1)	80579	60

- 21 257 spectra from a total of 508 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples 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.

- 39 spectra from 11 *Apo-Ident* customers from 14 batches from the substance/substance group *Potassium (H1030)*.

Supplier	Substance	Batch	Spectra
Unisan	Potassium (H1030)	288903	1
Unisan	Potassium (H1030)	39301	8
Unisan	Potassium (H1030)	28903	2
Fagron	Potassium (H1030)	39301	1
Hepart AG	Potassium (H1030)	39302	1
Hepart AG	Potassium (H1030)	39301	1
Unisan	Potassium (H1030)	39302	1
Unisan	Potassium (H1030)	69201	4
Unisan/Hepart AG	Potassium (H1030)	39302	1
UNISAN	Potassium (H1030)	69201	1
Unisan	Potassium (H1030)	69301	3
Unisan	Potassium (H1030)	69401/0	1
Unisan	Potassium (H1030)	69401	1
Unisan	Potassium (H1030)	944201	4
Unisan	Potassium (H1030)	1124028903	1
Hepart AG	Potassium (H1030)	1124028903	1
Unisan	Potassium (H1030)	130328001	3
Hepart AG	Potassium (H1030)	1124944201	1
Unisan	Potassium (H1030)	1124944201	1
Unisan	Potassium (H1030)	15000599	1
Unisan	Potassium (H1030)	15000597/0	1

- 1540 spectra from 20 *Apo-Ident* customers from a total of 576 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Potassium (H1030)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Potassium (H1030)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	250	0	18 904
Type B	0	597	42	21 257
Type C	0	33	6	1540

The substance/substance group *Potassium (H1030)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.6000 %)
Type B	100.0000 % (> 99.8914 %)	93.4272 % (> 92.9577 %)
Type C	100.0000 % (> 99.1621 %)	84.6154 % (> 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
80043	80043	0.00	41.93
80372	80372	0.00	29.62
80571	80571	0.00	40.56
80574	80574	0.00	41.97
80576	80576	0.00	40.54
80578	80578	0.00	41.39

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Proline (-L) (H1051)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80114-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Proline (-L) (H1051)

Special notes

When selecting the *Proline (-L) (H1051)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Proline (-L) (H1051)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Proline (-L) (H1…	596805	80114	50	from supplier
Hepart	Proline (-L) (H1…	0695301	80126	50	from supplier
Hepart	Proline (-L) (H1…	707801	80147	40	from supplier
Hepart	Proline (-L) (H1…	025707	80298	40	from supplier
Hepart	Proline (-L) (H1…	066401	80370	50	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 230 spectra of 5 reference samples from the substance/substance group *Proline (-L) (H1051)*. These samples are listed above in the *calibration samples* section.

- 18 924 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Proline (-L) (H1051)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Proline (-L) (H1051)	pending	80056	30
Hepart	Proline (-L) (H1051)	66401	80370†	10

- 21 856 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 7 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Proline (-L) (H1051)*.

Supplier	Substance	Batch	Spectra
Hepart AG	Proline (-L) (H1051)	25707	2
Hepart AG	Proline (-L) (H1051)	707801	2
Unisan	Proline (-L) (H1051)	66401	2
Unisan	Proline (-L) (H1051)	1834707801	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*.

- 1572 spectra from 20 *Apo-Ident* customers from a total of 586 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Proline (-L) (H1051)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Proline (-L) (H1051)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 924
Type B	0	40	0	21 856
Type C	0	5	2	1572

The substance/substance group *Proline (-L) (H1051)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.3913 %)
Type B	100.0000 % (> 99.8935 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1897 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80114	80114	0.00	78.72
80126	80126	0.00	69.44
80147	80147	0.00	42.49
80298	80298	0.00	30.17
80370	80370	0.00	19.09

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Silymarin (H1071)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80068-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Silymarin (H1071)

Special notes

When selecting the *Silymarin (H1071)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Silymarin (H1071)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Silymarin (H1071)	950401	80068	30	from supplier
Hepart	Silymarin (H1071)	950401	80138	50	from supplier
Hepart	Silymarin (H1071)	029901	80265	40	from supplier
Hepart	Silymarin (H1071)	15001046	80671	40	from supplier

Validation samples

A total of 42 629 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 *Silymarin (H1071)*. These samples are listed above in the *calibration samples* section.

- 18 994 spectra from a total of 396 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 110 spectra of 3 reference samples from the substance/substance group *Silymarin (H1071)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Silymarin (H1071)	915601	80210	30
Hepart	Silymarin (H1071)	67701	80375	60
Hepart	Silymarin (H1071)	15001046	80671†	20

- 21 786 spectra from a total of 520 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 11 *Apo-Ident* customers from 10 batches from the substance/substance group *Silymarin (H1071)*.

Supplier	Substance	Batch	Spectra
Hepart AG, CH-8280 Kreu…	Silymarin (H1071)	29901	2
Unisan/Hepart AG	Silymarin (H1071)	29901	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
unisan	Silymarin (H1071)	67701	2
Unisan	Silymarin (H1071)	67701/7	1
Unisan	Silymarin (H1071)	29901	3
Unisan	Silymarin (H1071)	46101	1
Unisan	Silymarin (H1071)	46101/0	1
Hepart AG	Silymarin (H1071)	67701	1
Unisan	Silymarin (H1071)	1241950401	2
UNISAN	Silymarin (H1071)	67701	1
Hepart AG	Silymarin (H1071)	1244029901	1
Hepart AG, CH-8280 Kreu…	Silymarin (H1071)	1241950401	1
Hepart AG, CH-8280 Kreu…	Silymarin (H1071)	1241046101	1
hepart ag	Silymarin (H1071)	1244950401	1
Unisan	Silymarin (H1071)	950401	2

- 1558 spectra from 20 *Apo-Ident* customers from a total of 580 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Silymarin (H1071)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Silymarin (H1071)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 994
Type B	0	50	60	21 786
Type C	0	14	7	1558

The substance/substance group *Silymarin (H1071)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9382 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8921 %)	45.4545 % (> 42.7273 %)
Type C	100.0000 % (> 99.1673 %)	66.6667 % (> 52.3810 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80068	80068	0.00	29.43
80138	80138	0.00	27.65
80265	80265	0.00	26.25
80671	80671	0.00	24.13

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Stomach complex (H1120)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80666-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Stomach complex (H1120)

Special notes

When selecting the *Stomach complex (H1120)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Stomach complex (H1120)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Stomach complex ...	15001350	80666	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Stomach complex (H1120)*. These samples are listed above in the *calibration samples* section.

- 19 114 spectra from a total of 398 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 20 spectra of 1 reference samples from the substance/substance group *Stomach complex (H1120)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Stomach complex (H1120)	15001350	80666†	20

- 21 876 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Stomach complex (H1120)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *Stomach complex (H1120)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Stomach complex (H1120)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	19 114
Type B	0	20	0	21 876
Type C	0	0	0	1579

The substance/substance group *Stomach complex (H1120)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9407 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8957 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80666	80666	0.00	29.35

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Taurine (H1084)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80071-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Taurine (H1084)

Special notes

When selecting the *Taurine (H1084)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Taurine (H1084)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Taurine (H1084)	960201	80071	30	from supplier
Hepart	Taurine (H1084)	960201	80088	50	from supplier
Hepart	Taurine (H1084)	017301	80142	50	from supplier
Hepart	Taurine (H1084)	14001767	80497	40	from supplier
Hepart	Taurine (H1084)	16000946	80809	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 210 spectra of 5 reference samples from the substance/substance group *Taurine (H1084)*. These samples are listed above in the *calibration samples* section.

- 18 944 spectra from a total of 395 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Taurine (H1084)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Taurine (H1084)	600402	80216	30
Hepart	Taurine (H1084)	28001	80250	40
Hepart	Taurine (H1084)	14001767	80497†	20
Hepart	Taurine (H1084)	16000947	80810	40

- 21 766 spectra from a total of 519 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 6 batches from the substance/substance group *Taurine (H1084)*.

Supplier	Substance	Batch	Spectra
Hepart AG, CH-8280 Kreu…	Taurine (H1084)	25710	3

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

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Supplier	Substance	Batch	Spectra
Unisan	Taurine (H1084)	25710	1
Hepart AG	Taurine (H1084)	28001	2
Unisan	Taurine (H1084)	28001	8
Unisan/Hepart AG	Taurine (H1084)	28001	1
Unisan	Taurine (H1084)	1294960201	2
Unisan	Taurine (H1084)	1294028001	1
unisan	Taurine (H1084)	14001767	1
Unisan	Taurine (H1084)	14001767/0	1
Hepart AG	Taurine (H1084)	1294028001	1

- 1558 spectra from 20 *Apo-Ident* customers from a total of 584 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Taurine (H1084)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Taurine (H1084)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	210	0	18 944
Type B	0	130	0	21 766
Type C	0	19	2	1558

The substance/substance group *Taurine (H1084)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8920 %)	100.0000 % (> 95.3846 %)
Type C	100.0000 % (> 99.1673 %)	90.4762 % (> 76.1905 %)

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
80071	80071	0.00	64.26
80088	80088	0.00	62.83
80142	80142	0.00	62.31
80497	80497	0.00	61.68
80809	80809	0.00	62.06

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Threonine (L-) (H1052)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80107-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Threonine (L-) (H1052)

Special notes

When selecting the *Threonine (L-) (H1052)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Threonine (L-) (H1052)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Threonine (L-) (...	638802	80107	50	from supplier
Hepart	Threonine (L-) (...	014901	80122	50	from supplier
Hepart	Threonine (L-) (...	14001718	80496	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Threonine (L-) (H1052)*. These samples are listed above in the *calibration samples* section.

- 19 014 spectra from a total of 396 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 50 spectra of 2 reference samples from the substance/substance group *Threonine (L-) (H1052)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Threonine (L-) (H1052)	pending	80057	30
Hepart	Threonine (L-) (H1052)	14001718	80496†	20

- 21 846 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 5 batches from the substance/substance group *Threonine (L-) (H1052)*.

Supplier	Substance	Batch	Spectra
Hedinger	Threonine (L-) (H1052)	25708	3
Unisan	Threonine (L-) (H1052)	25708	2
unisan	Threonine (L-) (H1052)	25708	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
Unisan	Threonine (L-) (H1052)	14001718	1
UNISAN	Threonine (L-) (H1052)	25708	1
Unisan	Threonine (L-) (H1052)	1832014901	1
Unisan	Threonine (L-) (H1052)	14001718/1	1
Purren Apotheke	Threonine (L-) (H1052)	1833014901	1
Hepart AG	Threonine (L-) (H1052)	1832014901	1

- 1567 spectra from 20 *Apo-Ident* customers from a total of 585 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Threonine (L-) (H1052)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Threonine (L-) (H1052)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	19 014
Type B	0	20	30	21 846
Type C	0	10	2	1567

The substance/substance group *Threonine (L-) (H1052)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9384 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.8930 %)	40.0000 % (> 34.0000 %)
Type C	100.0000 % (> 99.1757 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80107	80107	0.00	55.11
80122	80122	0.00	52.65
80496	80496	0.00	44.84

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Trace elements BAG (H1078)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80205-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Trace elements BAG (H1078)

Special notes

When selecting the *Trace elements BAG (H1078)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Trace elements BAG (H1078)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Trace elements B...	16000795	80799	40	not required
Hepart	Trace elements B...	16000796	80800	40	not required

Validation samples

A total of 42 629 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 *Trace elements BAG (H1078)*. These samples are listed above in the *calibration samples* section.

- 19 074 spectra from a total of 397 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Trace elements BAG (H1078)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Trace elements BAG (H1078)	16000797	80801	40

- 21 856 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Trace elements BAG (H1078)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Trace elements BAG (H1078)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Trace elements BAG (H1078)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 074
Type B	0	40	0	21 856
Type C	0	0	0	1579

The substance/substance group *Trace elements BAG (H1078)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9391 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8935 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80799	80799	0.00	15.40
80800	80800	0.00	14.76

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Trace elements JK (H1080)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80069-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Trace elements JK (H1080)

Special notes

When selecting the *Trace elements JK (H1080)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Trace elements JK (H1080)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Trace elements J…	0956901	80069	30	from supplier
Hepart	Trace elements J…	011701	80235	40	from supplier
Hepart	Trace elements J…	072701	80387	40	from supplier
Hepart	Trace elements J…	072901	80388	40	from supplier
Hepart	Trace elements J…	072801	80389	40	from supplier
Hepart	Trace elements J…	072901	80701	40	from supplier
Hepart	Trace elements J…	15000526	80766	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 270 spectra of 7 reference samples from the substance/substance group *Trace elements JK (H1080)*. These samples are listed above in the *calibration samples* section.

- 18 884 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Trace elements JK (H1080)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Trace elements JK (H1080)	956901	80137	50
Hepart	Trace elements JK (H1080)	919701	80223	30
Hepart	Trace elements JK (H1080)	15000525	80673	60
Hepart	Trace elements JK (H1080)	72901	80701†	20
Hepart	Trace elements JK (H1080)	15000526	80766†	20

- 21 716 spectra from a total of 518 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 35 spectra from 12 *Apo-Ident* customers from 9 batches from the substance/substance group *Trace elements JK (H1080)*.

†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
Unisan	Trace elements JK (H1080)	11701	9
UNISAN	Trace elements JK (H1080)	72701	1
Hepart AG	Trace elements JK (H1080)	72701	1
Unisan	Trace elements JK (H1080)	15000526	1
Unisan	Trace elements JK (H1080)	15000525/0	1
Euro OTC	Trace elements JK (H1080)	15000526/0	1
Hepart AG	Trace elements JK (H1080)	11701	8
Unisan/Hepart AG	Trace elements JK (H1080)	11701	3
Unisan	Trace elements JK (H1080)	72701	1
Unisan	Trace elements JK (H1080)	1026011701	2
Hepart AG	Trace elements JK (H1080)	1026011701	2
Unisan Gmbh, 78465 Kons…	Trace elements JK (H1080)	1026011701	1
Unisan GmbH, 78465 Kons…	Trace elements JK (H1080)	1026956901	1
Unisan	Trace elements JK (H1080)	1028956901	1
Unisan	Trace elements JK (H1080)	1026919701	1
Unisan	Trace elements JK (H1080)	1026956901	1

- 1544 spectra from 20 *Apo-Ident* customers from a total of 581 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Trace elements JK (H1080)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Trace elements JK (H1080)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	270	0	18 884
Type B	0	100	80	21 716
Type C	0	29	6	1544

The substance/substance group *Trace elements JK (H1080)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.7778 %)
Type B	100.0000 % (> 99.8918 %)	55.5556 % (> 53.8889 %)
Type C	100.0000 % (> 99.1628 %)	82.8571 % (> 74.2857 %)

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80069	80069	0.00	30.10
80235	80235	0.00	22.76
80387	80387	0.00	25.77
80388	80388	0.00	25.57
80389	80389	0.00	27.52
80701	80701	0.00	21.40
80766	80766	0.00	20.02

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Trace elements SE (H1082)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80070-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Trace elements SE (H1082)

Special notes

When selecting the *Trace elements SE (H1082)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Trace elements SE (H1082)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Trace elements S...	0937201	80070	30	from supplier
Hepart	Trace elements S...	0937201	80092	50	from supplier
Hepart	Trace elements S...	012401	80141	50	from supplier
Hepart	Trace elements S...	929202	80172	40	from supplier
Hepart	Trace elements S...	031301	80263	40	from supplier
Hepart	Trace elements S...	042301	80278	50	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Trace elements S…	042301	80290	50	from supplier
Hepart	Trace elements S…	14000722	80459	40	from supplier
Hepart	Trace elements S…	14000720	80460	40	from supplier
Hepart	Trace elements S…	14000721	80461	40	from supplier
Hepart	Trace elements S…	14000721	80464	40	from supplier
Hepart	Trace elements S…	15000555	80588	40	from supplier
Hepart	Trace elements S…	15000556(B1)	80592	40	from supplier
Hepart	Trace elements S…	15000557	80594	40	from supplier
Hepart	Trace elements S…	15000558	80597	40	from supplier
Hepart	Trace elements S…	15000553(B1)	80601	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 670 spectra of 16 reference samples from the substance/substance group *Trace elements SE (H1082)*. These samples are listed above in the *calibration samples* section.

- 18 484 spectra from a total of 386 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 830 spectra of 20 reference samples from the substance/substance group *Trace elements SE (H1082)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Trace elements SE (H1082)	pending	80007	40
Hepart	Trace elements SE (H1082)	42301	80278†	5
Hepart	Trace elements SE (H1082)	42301	80290†	5
Hepart	Trace elements SE (H1082)	14000722	80462	40
Hepart	Trace elements SE (H1082)	14000720	80463	40
Hepart	Trace elements SE (H1082)	15000555	80588†	20
Hepart	Trace elements SE (H1082)	15000555(B1)	80589	60
Hepart	Trace elements SE (H1082)	15000555(F2)	80590	60
Hepart	Trace elements SE (H1082)	15000556	80591	60
Hepart	Trace elements SE (H1082)	15000556(B1)	80592†	20
Hepart	Trace elements SE (H1082)	15000556(F2)	80593	60
Hepart	Trace elements SE (H1082)	15000557	80594†	20
Hepart	Trace elements SE (H1082)	15000557(B1)	80595	60

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Trace elements SE (H1082)	15000557(F2)	80596	60
Hepart	Trace elements SE (H1082)	15000558	80597†	20
Hepart	Trace elements SE (H1082)	15000558(B1)	80598	60
Hepart	Trace elements SE (H1082)	15000558(F2)	80599	60
Hepart	Trace elements SE (H1082)	15000553	80600	60
Hepart	Trace elements SE (H1082)	15000553(B1)	80601†	20
Hepart	Trace elements SE (H1082)	15000553(F2)	80602	60

- 21 066 spectra from a total of 505 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 32 spectra from 12 *Apo-Ident* customers from 12 batches from the substance/substance group *Trace elements SE (H1082)*.

Supplier	Substance	Batch	Spectra
Unisan	Trace elements SE (H1082)	42301	2
Unisan	Trace elements SE (H1082)	31301	5
Hepart AG	Trace elements SE (H1082)	14000720	2
Hepart AG	Trace elements SE (H1082)	120435-14	1
Unisan	Trace elements SE (H1082)	14000721/0	1
Unisan	Trace elements SE (H1082)	14000721	1
Unisan	Trace elements SE (H1082)	14000722	1
Unisan	Trace elements SE (H1082)	14000720	1
Unisan	Trace elements SE (H1082)	15000553	1
Hepart AG	Trace elements SE (H1082)	31301	2
Hepart AG, CH-8280 Kreu…	Trace elements SE (H1082)	31301	1
Hepart AG	Trace elements SE (H1082)	42301	3
Unisan	Trace elements SE (H1082)	1024012401	2
Unisan	Trace elements SE (H1082)	1024929202	1
Hepart AG, CH-8280 Kreu…	Trace elements SE (H1082)	937201	1
Unisan	Trace elements SE (H1082)	1024042301	1
Hepart AG	Trace elements SE (H1082)	937201	4
Unisan	Trace elements SE (H1082)	937201	2

- 1547 spectra from 20 *Apo-Ident* customers from a total of 578 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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 *Trace elements SE (H1082)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Trace elements SE (H1082)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	670	0	18 484
Type B	0	800	30	21 066
Type C	0	28	4	1547

The substance/substance group *Trace elements SE (H1082)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9376 %)	100.0000 % (> 99.1045 %)
Type B	100.0000 % (> 99.8914 %)	96.3855 % (> 96.0241 %)
Type C	100.0000 % (> 99.1635 %)	87.5000 % (> 78.1250 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80070	80070	0.00	33.24
80092	80092	0.00	24.67
80141	80141	0.00	27.07
80172	80172	0.00	25.56
80263	80263	0.00	23.37
80278	80278	0.00	28.49
80290	80290	0.00	27.51
80459	80459	0.00	29.29
80460	80460	0.00	30.12
80461	80461	0.00	30.47
80464	80464	0.00	30.99
80588	80588	0.00	41.68
80592	80592	0.00	32.95
80594	80594	0.00	37.42
80597	80597	0.00	47.19
80601	80601	0.00	40.73

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Tryptophan (L-) (H1053)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80127-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Tryptophan (L-) (H1053)

Special notes

When selecting the *Tryptophan (L-) (H1053)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Tryptophan (L-) (H1053)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Tryptophan (L-) ...	0950001	80127	50	from supplier
Hepart	Tryptophan (L-) ...	0978501	80135	50	from supplier
Hepart	Tryptophan (L-) ...	074501	80401	40	from supplier
Hepart	Tryptophan (L-) ...	15000441	80581	40	from supplier
Hepart	Tryptophan (L-) ...	15000443	80582	40	from supplier
Hepart	Tryptophan (L-) ...	16001394	80845	40	from supplier
Hepart	Tryptophan (L-) ...	16001404	80846	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 7 reference samples from the substance/substance group *Tryptophan (L-) (H1053)*. These samples are listed above in the *calibration samples* section.

- 18 854 spectra from a total of 392 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 110 spectra of 4 reference samples from the substance/substance group *Tryptophan (L-) (H1053)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Tryptophan (L-) (H1053)	pending	80058	30
Hepart	Tryptophan (L-) (H1053)	27901	80251	40
Hepart	Tryptophan (L-) (H1053)	15000441	80581†	20
Hepart	Tryptophan (L-) (H1053)	15000443	80582†	20

- 21 786 spectra from a total of 520 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 9 *Apo-Ident* customers from 14 batches from the substance/substance group *Tryptophan (L-) (H1053)*.

†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
unisan	Tryptophan (L-) (H1053)		1
Unisan	Tryptophan (L-) (H1053)	74501	2
Unisan	Tryptophan (L-) (H1053)	74501/4	1
Caelo	Tryptophan (L-) (H1053)	15000443/0	1
Unisan	Tryptophan (L-) (H1053)	25011	1
Unisan	Tryptophan (L-) (H1053)	150000441	1
Hepart AG	Tryptophan (L-) (H1053)	27901	4
Unisan	Tryptophan (L-) (H1053)	27901	2
Hepart AG, CH-8280 Kreu...	Tryptophan (L-) (H1053)	27901	1
Unisan/Hepart AG	Tryptophan (L-) (H1053)	27901	1
Unisan	Tryptophan (L-) (H1053)	27902	2
Hepart AG	Tryptophan (L-) (H1053)	1824025011	1
Unisan	Tryptophan (L-) (H1053)	1824025011	1
Hepart AG	Tryptophan (L-) (H1053)	1824027901	2
Unisan	Tryptophan (L-) (H1053)	1824950001	2
Hepart AG	Tryptophan (L-) (H1053)	27902	1
Purren Apotheke	Tryptophan (L-) (H1053)	1825950001	1
Purren Apotheke	Tryptophan (L-) (H1053)	978501	1
Unisan	Tryptophan (L-) (H1053)	950001	1

- 1552 spectra from 20 *Apo-Ident* customers from a total of 577 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Tryptophan (L-) (H1053)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tryptophan (L-) (H1053)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	18 854
Type B	0	64	46	21 786
Type C	0	22	5	1552

The substance/substance group *Tryptophan (L-) (H1053)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.8921 %)	58.1818 % (> 55.4545 %)
Type C	100.0000 % (> 99.1648 %)	81.4815 % (> 70.3704 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80127	80127	0.00	59.97
80135	80135	0.00	58.89
80401	80401	0.00	28.97
80581	80581	0.00	33.15
80582	80582	0.00	36.26
80845	80845	0.00	40.43
80846	80846	0.00	42.43

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Tyrosine (L-) (H1054)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80121-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Tyrosine (L-) (H1054)

Special notes

When selecting the *Tyrosine (L-) (H1054)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Tyrosine (L-) (H1054)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Tyrosine (L-) (H...	979102	80121	50	from supplier
Hepart	Tyrosine (L-) (H...	074601	80386	80	from supplier
Hepart	Tyrosine (L-) (H...	15001380	80704	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 170 spectra of 3 reference samples from the substance/substance group *Tyrosine (L-) (H1054)*. These samples are listed above in the *calibration samples* section.

- 18 984 spectra from a total of 396 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 150 spectra of 5 reference samples from the substance/substance group *Tyrosine (L-) (H1054)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Tyrosine (L-) (H1054)	pending	80059	30
Hepart	Tyrosine (L-) (H1054)	29502	80244	40
Hepart	Tyrosine (L-) (H1054)	29502	80248	40
Hepart	Tyrosine (L-) (H1054)	74601	80386†	20
Hepart	Tyrosine (L-) (H1054)	15001380	80704†	20

- 21 746 spectra from a total of 520 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 18 spectra from 7 *Apo-Ident* customers from 7 batches from the substance/substance group *Tyrosine (L-) (H1054)*.

†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
Unisan	Tyrosine (L-) (H1054)	29502	5
Unisan	Tyrosine (L-) (H1054)	29501	4
Hepart AG	Tyrosine (L-) (H1054)	29502	1
Hepart AG	Tyrosine (L-) (H1054)	74601	1
UNISAN	Tyrosine (L-) (H1054)	74601	1
Unisan	Tyrosine (L-) (H1054)	74601/3	1
Unisan	Tyrosine (L-) (H1054)	1826029501	2
Unisan	Tyrosine (L-) (H1054)	979102	2
Hepart AG	Tyrosine (L-) (H1054)	1827029501	1

- 1561 spectra from 20 *Apo-Ident* customers from a total of 583 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Tyrosine (L-) (H1054)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tyrosine (L-) (H1054)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 984
Type B	0	147	3	21 746
Type C	0	17	1	1561

The substance/substance group *Tyrosine (L-) (H1054)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9382 %)	100.0000 % (> 96.4706 %)
Type B	100.0000 % (> 99.8919 %)	98.0000 % (> 96.0000 %)
Type C	100.0000 % (> 99.1692 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80121	80121	0.00	70.13
80386	80386	0.00	76.16
80704	80704	0.00	79.70

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Valine (L-) (H1056)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80145-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Valine (L-) (H1056)

Special notes

When selecting the *Valine (L-) (H1056)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Valine (L-) (H1056)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Valine (L-) (H10...	961101	80145	50	from supplier
Hepart	Valine (L-) (H10...	025012	80291	40	from supplier
Hepart	Valine (L-) (H10...	14001947	80520	40	from supplier
Hepart	Valine (L-) (H10...	15001436	80670	40	from supplier
Hepart	Valine (L-) (H10...	16001380/0	80844	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 210 spectra of 5 reference samples from the substance/substance group *Valine (L-) (H1056)*. These samples are listed above in the *calibration samples* section.

- 18 944 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Valine (L-) (H1056)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Valine (L-) (H1056)	pending	80060	30
Hepart	Valine (L-) (H1056)	916201	80226	30
Hepart	Valine (L-) (H1056)	936701	80228	40
Hepart	Valine (L-) (H1056)	14001947	80520†	20
Hepart	Valine (L-) (H1056)	15001436	80670†	20

- 21 756 spectra from a total of 519 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 6 batches from the substance/substance group *Valine (L-) (H1056)*.

†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
Unisan	Valine (L-) (H1056)	25012	2
Unisan	Valine (L-) (H1056)	15001436	1
Unisan	Valine (L-) (H1056)	1806025012	2
Purren Apotheke	Valine (L-) (H1056)	1807936701	1
Hepart AG	Valine (L-) (H1056)	1807025012	1
Unisan	Valine (L-) (H1056)	1807961101	1

- 1571 spectra from 20 *Apo-Ident* customers from a total of 584 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Valine (L-) (H1056)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Valine (L-) (H1056)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	210	0	18 944
Type B	0	97	43	21 756
Type C	0	6	2	1571

The substance/substance group *Valine (L-) (H1056)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8919 %)	69.2857 % (> 67.1429 %)
Type C	100.0000 % (> 99.1855 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80145	80145	0.00	65.73
80291	80291	0.00	62.69
80520	80520	0.00	64.13
80670	80670	0.00	68.10
80844	80844	0.00	57.95

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Vitamin B1 (H1101)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80072-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Vitamin B1 (H1101)

Special notes

When selecting the *Vitamin B1 (H1101)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Vitamin B1 (H1101)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin B1 (H1101)	977301	80072	30	from supplier
Hepart	Vitamin B1 (H1101)	977301	80116	50	from supplier
Hepart	Vitamin B1 (H1101)	053301	80316	60	from supplier
Hepart	Vitamin B1 (H1101)	075001	80392	40	from supplier
Hepart	Vitamin B1 (H1101)	075001	80479	40	from supplier
Hepart	Vitamin B1 (H1101)	14001112	80480	40	from supplier
Hepart	Vitamin B1 (H1101)	14001113	80481	40	from supplier
Hepart	Vitamin B1 (H1101)	075001	80529	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 8 reference samples from the substance/substance group *Vitamin B1 (H1101)*. These samples are listed above in the *calibration samples* section.

- 18 814 spectra from a total of 394 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Vitamin B1 (H1101)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin B1 (H1101)	30501	80255	40
Hepart	Vitamin B1 (H1101)	75001	80529†	20

- 21 836 spectra from a total of 521 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 11 *Apo-Ident* customers from 10 batches from the substance/substance group *Vitamin B1 (H1101)*.

Supplier	Substance	Batch	Spectra
Unisan/Hepart AG	Vitamin B1 (H1101)	53301	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
Unisan	Vitamin B1 (H1101)	30202	4
Hepart AG	Vitamin B1 (H1101)	53301	2
Unisan	Vitamin B1 (H1101)	53301	1
Hepart AG, CH-8280 Kreu…	Vitamin B1 (H1101)	53301	1
UNISAN	Vitamin B1 (H1101)	75001	1
Unisan	Vitamin B1 (H1101)	14001112/0	1
Unisan	Vitamin B1 (H1101)	15001620/0	1
Hepart AG	Vitamin B1 (H1101)	1621030202	1
Hepart AG, Unisan GmbH	Vitamin B1 (H1101)	15001622/0	1
Unisan	Vitamin B1 (H1101)	15001622/0	1
Hepart AG	Vitamin B1 (H1101)	1622030202	2
Unisan	Vitamin B1 (H1101)	1622977301	1
Unisan	Vitamin B1 (H1101)	977301	2
Unisan	Vitamin B1 (H1101)	1621030202	1

- 1558 spectra from 20 *Apo-Ident* customers from a total of 580 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Vitamin B1 (H1101)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin B1 (H1101)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	340	0	18 814
Type B	0	20	40	21 836
Type C	0	21	0	1558

The substance/substance group *Vitamin B1 (H1101)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9378 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.8928 %)	33.3333 % (> 28.3333 %)
Type C	100.0000 % (> 99.1673 %)	100.0000 % (> 71.4286 %)

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80072	80072	0.00	12.80
80116	80116	0.00	13.40
80316	80316	0.00	20.92
80392	80392	0.00	34.39
80479	80479	0.00	34.10
80480	80480	0.00	12.22
80481	80481	0.00	12.71
80529	80529	0.00	32.58

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Vitamin B6 (H1103)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80074-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Vitamin B6 (H1103)

Special notes

When selecting the *Vitamin B6 (H1103)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Vitamin B6 (H1103)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin B6 (H1103)	960401	80074	30	from supplier
Hepart	Vitamin B6 (H1103)	960401	80110	50	from supplier
Hepart	Vitamin B6 (H1103)	938001	80192	40	from supplier
Hepart	Vitamin B6 (H1103)	15000279	80550	40	from supplier
Hepart	Vitamin B6 (H1103)	15000279	80781	40	from supplier
Hepart	Vitamin B6 (H1103)	14001576	80798	40	from supplier

Validation samples

A total of 42 629 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 *Vitamin B6 (H1103)*. These samples are listed above in the *calibration samples* section.

- 18 914 spectra from a total of 395 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Vitamin B6 (H1103)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin B6 (H1103)	15000279	80550†	20
Hepart	Vitamin B6 (H1103)	15000279	80781†	20

- 21 856 spectra from a total of 522 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 12 batches from the substance/substance group *Vitamin B6 (H1103)*.

Supplier	Substance	Batch	Spectra
Unisan	Vitamin B6 (H1103)	25711	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
Unisan	Vitamin B6 (H1103)	20101	1
Hepart AG, CH-8280 Kreu…	Vitamin B6 (H1103)	25711	1
Hepart AG, Unisan GmbH	Vitamin B6 (H1103)	15000279/0	1
Hepart AG	Vitamin B6 (H1103)	25711	1
Unisan	Vitamin B6 (H1103)	14001576/2	1
Unisan	Vitamin B6 (H1103)	1554025711	1
Hepart AG	Vitamin B6 (H1103)	1552025711	1
Euro OTC	Vitamin B6 (H1103)	15000279/1	1
Unisan	Vitamin B6 (H1103)	14001576	1
Unisan	Vitamin B6 (H1103)	15000279/2	1
Hepart AG, CH-8280 Kreu…	Vitamin B6 (H1103)	1552025711	1
Unisan	Vitamin B6 (H1103)	1552020101	1
Hepart AG	Vitamin B6 (H1103)	1554020101	1
Purren Apotheke	Vitamin B6 (H1103)	1554938001	1

- 1558 spectra from 20 *Apo-Ident* customers from a total of 578 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Vitamin B6 (H1103)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin B6 (H1103)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	18 914
Type B	0	40	0	21 856
Type C	0	20	1	1558

The substance/substance group *Vitamin B6 (H1103)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9380 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.8935 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.1673 %)	95.2381 % (> 80.9524 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80074	80074	0.00	50.93
80110	80110	0.00	53.33
80192	80192	0.00	46.14
80550	80550	0.00	60.34
80781	80781	0.00	61.49
80798	80798	0.00	57.31

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Vitamin C (H1104)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80009-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Vitamin C (H1104)

Special notes

When selecting the *Vitamin C (H1104)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Vitamin C (H1104)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin C (H1104)	946901	80009	40	from supplier
Hepart	Vitamin C (H1104)	946901	80112	50	from supplier
Hepart	Vitamin C (H1104)	013201	80161	50	from supplier
Hepart	Vitamin C (H1104)	044501	80296	40	from supplier
Hepart	Vitamin C (H1104)	025020	80304	40	from supplier
Hepart	Vitamin C (H1104)	044502	80363	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin C (H1104)	074201	80394	40	from supplier
Hepart	Vitamin C (H1104)	074001	80395	40	from supplier
Hepart	Vitamin C (H1104)	073901	80396	40	from supplier
Hepart	Vitamin C (H1104)	074101	80397	40	from supplier
Hepart	Vitamin C (H1104)	074201	80418	40	from supplier
Hepart	Vitamin C (H1104)	044602	80438	40	from supplier
Hepart	Vitamin C (H1104)	14001780	80499	40	from supplier
Hepart	Vitamin C (H1104)	14001788	80500	40	from supplier
Hepart	Vitamin C (H1104)	14001794	80501	40	from supplier
Hepart	Vitamin C (H1104)	14001797	80502	40	from supplier
Hepart	Vitamin C (H1104)	16000200	80751	40	from supplier
Hepart	Vitamin C (H1104)	16000198	80753	40	from supplier
Hepart	Vitamin C (H1104)	16000229	80756	40	from supplier
Hepart	Vitamin C (H1104)	16000230	80760	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 820 spectra of 20 reference samples from the substance/substance group *Vitamin C (H1104)*. These samples are listed above in the *calibration samples* section.

- 18 334 spectra from a total of 381 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 639 spectra of 17 reference samples from the substance/substance group *Vitamin C (H1104)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin C (H1104)	960901	80076	29
Hepart	Vitamin C (H1104)	960901	80123	50
Hepart	Vitamin C (H1104)	13202	80229	40
Hepart	Vitamin C (H1104)	14001780	80499†	20
Hepart	Vitamin C (H1104)	14001788	80500†	20
Hepart	Vitamin C (H1104)	14001794	80501†	20
Hepart	Vitamin C (H1104)	14001797	80502†	20
Hepart	Vitamin C (H1104)	16000200	80751†	20
Hepart	Vitamin C (H1104)	16000197	80752	60
Hepart	Vitamin C (H1104)	16000198	80753†	20

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin C (H1104)	16000199	80754	60
Hepart	Vitamin C (H1104)	16000201	80755	60
Hepart	Vitamin C (H1104)	16000229	80756†	20
Hepart	Vitamin C (H1104)	16000203	80757	60
Hepart	Vitamin C (H1104)	16000202	80758	60
Hepart	Vitamin C (H1104)	16000231	80759	60
Hepart	Vitamin C (H1104)	16000230	80760†	20

- 21 257 spectra from a total of 507 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 66 spectra from 12 *Apo-Ident* customers from 25 batches from the substance/substance group *Vitamin C (H1104)*.

Supplier	Substance	Batch	Spectra
unbekannt	Vitamin C (H1104)	16000200	1
unbekannt	Vitamin C (H1104)	16000199	1
unbekannt	Vitamin C (H1104)	16000198	1
unbekannt	Vitamin C (H1104)	16000197	1
Unisan	Vitamin C (H1104)	14001797	1
unisan	Vitamin C (H1104)	14001794	1
Unisan	Vitamin C (H1104)	16000198	1
unbekannt	Vitamin C (H1104)	16000201	1
unbekannt	Vitamin C (H1104)	16000203	1
unbekannt	Vitamin C (H1104)	16000229	1
unbekannt	Vitamin C (H1104)	16000202	1
unbekannt	Vitamin C (H1104)	16000231	1
Unisan	Vitamin C (H1104)	25020	2
unbekannt	Vitamin C (H1104)	16000230	1
Unisan	Vitamin C (H1104)	44501	7
Unisan Gmbh, 78465 Kons…	Vitamin C (H1104)	25020	1
Hepart AG	Vitamin C (H1104)	44501	3
Unisan/Hepart AG	Vitamin C (H1104)	44501	1
Unisan	Vitamin C (H1104)	44502	4
Hepart AG	Vitamin C (H1104)	44502	3
Unisan	Vitamin C (H1104)	44601	1
Hepart AG	Vitamin C (H1104)	44601	2
Unisan	Vitamin C (H1104)	44602	2
Fagron	Vitamin C (H1104)	44502	1
Hepart AG	Vitamin C (H1104)	73901	3
Falcento	Vitamin C (H1104)	44602	1
Unisan	Vitamin C (H1104)	73901	3
UNISAN	Vitamin C (H1104)	74001	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
Unisan	Vitamin C (H1104)	74001	2
Unisan	Vitamin C (H1104)	1084025020	1
Hepart AG	Vitamin C (H1104)	1084025020	3
Unisan	Vitamin C (H1104)	1085025020	5
Hepart AG	Vitamin C (H1104)	74201	2
Hepart AG, CH-8280 Kreu…	Vitamin C (H1104)	1084025019	1
Hepart AG	Vitamin C (H1104)	1085025020	2
Unisan	Vitamin C (H1104)	14001780/0	1
Unisan	Vitamin C (H1104)	14001788	1

- 1513 spectra from 20 *Apo-Ident* customers from a total of 566 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Vitamin C (H1104)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin C (H1104)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	820	0	18 334
Type B	0	610	29	21 257
Type C	0	65	1	1513

The substance/substance group *Vitamin C (H1104)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9376 %)	100.0000 % (> 99.2683 %)
Type B	100.0000 % (> 99.8914 %)	95.4617 % (> 94.9922 %)
Type C	100.0000 % (> 99.1597 %)	98.4848 % (> 93.9394 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80009	80009	0.00	36.60
80112	80112	0.00	34.61
80161	80161	0.00	38.69
80296	80296	0.00	33.72
80304	80304	0.00	46.59
80363	80363	0.00	47.97
80394	80394	0.00	28.43
80395	80395	0.00	26.44
80396	80396	0.00	32.30
80397	80397	0.00	26.43
80418	80418	0.00	33.90
80438	80438	0.00	48.18
80499	80499	0.00	28.16
80500	80500	0.00	29.26
80501	80501	0.00	30.18
80502	80502	0.00	40.51
80751	80751	0.00	41.53
80753	80753	0.00	47.49
80756	80756	0.00	39.78
80760	80760	0.00	40.69

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Vitamin complex (H1100)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80073-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Vitamin complex (H1100)

Special notes

When selecting the *Vitamin complex (H1100)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Vitamin complex (H1100)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin complex ...	049201	80349	40	from supplier
Hepart	Vitamin complex ...	077201	80411	40	from supplier
Hepart	Vitamin complex ...	077001	80431	40	from supplier
Hepart	Vitamin complex ...	077101	80432	40	from supplier
Hepart	Vitamin complex ...	14001590	80485	40	from supplier
Hepart	Vitamin complex ...	14001589	80486	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin complex …	14001591	80487	40	from supplier
Hepart	Vitamin complex …	15001276(B1)	80637	40	from supplier
Hepart	Vitamin complex …	15001277(F2)	80638	40	from supplier
Hepart	Vitamin complex …	15001274(B1)	80640	40	from supplier
Hepart	Vitamin complex …	15001275(F2)	80642	40	from supplier
Hepart	Vitamin complex …	15001277	80643	40	from supplier
Hepart	Vitamin complex …	15001276(F2)	80646	40	from supplier
Hepart	Vitamin complex …	15001274	80647	40	from supplier
Hepart	Vitamin complex …	15001275	80648	40	from supplier
Hepart	Vitamin complex …	16000957	80827	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 640 spectra of 16 reference samples from the substance/substance group *Vitamin complex (H1100)*. These samples are listed above in the *calibration samples* section.

- 18 514 spectra from a total of 383 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 1005 spectra of 29 reference samples from the substance/substance group *Vitamin complex (H1100)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin complex (H1100)	pending	80004	40
Hepart	Vitamin complex (H1100)	9901	80073	30
Hepart	Vitamin complex (H1100)	9901	80091	40
Hepart	Vitamin complex (H1100)	966901	80109	40
Hepart	Vitamin complex (H1100)	923902	80214	35
Hepart	Vitamin complex (H1100)	23401	80231	40
Hepart	Vitamin complex (H1100)	966901	80237	40
Hepart	Vitamin complex (H1100)	25301	80292	40
Hepart	Vitamin complex (H1100)	25101	80293	40
Hepart	Vitamin complex (H1100)	14001590	80485†	20
Hepart	Vitamin complex (H1100)	14001589	80486†	20
Hepart	Vitamin complex (H1100)	14001591	80487†	20
Hepart	Vitamin complex (H1100)	15001276(B1)	80637†	20

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin complex (H1100)	15001277(F2)	80638†	20
Hepart	Vitamin complex (H1100)	15001275(B1)	80639	60
Hepart	Vitamin complex (H1100)	15001274(B1)	80640†	20
Hepart	Vitamin complex (H1100)	15001277(B1)	80641	60
Hepart	Vitamin complex (H1100)	15001275(F2)	80642†	20
Hepart	Vitamin complex (H1100)	15001277	80643†	20
Hepart	Vitamin complex (H1100)	15001274(F2)	80644	60
Hepart	Vitamin complex (H1100)	15001276	80645	60
Hepart	Vitamin complex (H1100)	15001276(F2)	80646†	20
Hepart	Vitamin complex (H1100)	15001274	80647†	20
Hepart	Vitamin complex (H1100)	15001275	80648†	20
Hepart	Vitamin complex (H1100)	16000958	80828	40
Hepart	Vitamin complex (H1100)	16000959	80829	40
Hepart	Vitamin complex (H1100)	16000960	80830	40
Hepart	Vitamin complex (H1100)	16000961	80831	40
Hepart	Vitamin complex (H1100)	16000962	80832	40

- 20 891 spectra from a total of 497 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 68 spectra from 13 *Apo-Ident* customers from 26 batches from the substance/substance group *Vitamin complex (H1100)*.

Supplier	Substance	Batch	Spectra
Unisan/Hepart AG	Vitamin complex (H1100)	48301	1
Unisan	Vitamin complex (H1100)	74101	1
Hepart AG	Vitamin complex (H1100)	77201	3
Unisan	Vitamin complex (H1100)	77001	1
Unisan	Vitamin complex (H1100)	77201	3
Unisan	Vitamin complex (H1100)	14001589	1
Unisan	Vitamin complex (H1100)	1400159/0	1
Unisan	Vitamin complex (H1100)	14001590/0	1
Unisan	Vitamin complex (H1100)	14001590/1	1
Unisan	Vitamin complex (H1100)	25101	1
Unisan	Vitamin complex (H1100)	15001276/0	1
Unisan	Vitamin complex (H1100)	25201	1
Unisan	Vitamin complex (H1100)	15001275/0	1
Hepart AG	Vitamin complex (H1100)	49201	4
Unisan	Vitamin complex (H1100)	15001277/0	1
Unisan	Vitamin complex (H1100)	49201	2
Unisan/Hepart AG	Vitamin complex (H1100)	49201	1
Hepart AG	Vitamin complex (H1100)	49202	5
Unisan	Vitamin complex (H1100)	49202	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
Unisan	Vitamin complex (H1100)	49301	8
Hepart AG	Vitamin complex (H1100)	49301	7
Fagron	Vitamin complex (H1100)	49301	5
Unisan	Vitamin complex (H1100)	49302	2
Unisan	Vitamin complex (H1100)	1014009901	1
unisan	Vitamin complex (H1100)	49302	1
Hepart AG, CH-8280 Kreu…	Vitamin complex (H1100)	1014025101	1
Hepart AG	Vitamin complex (H1100)	1014025101	1
Unisan	Vitamin complex (H1100)	1014025301	1
Unisan	Vitamin complex (H1100)	1014025401	1
Hepart AG	Vitamin complex (H1100)	1014025301	1
hepart ag	Vitamin complex (H1100)	1015954801	2
Unisan	Vitamin complex (H1100)	H110031	2
Unisan	Vitamin complex (H1100)	904006	1
hepart ag	Vitamin complex (H1100)	10159548011	1
Unisan	Vitamin complex (H1100)	4966901	1

- 1511 spectra from 20 *Apo-Ident* customers from a total of 564 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Vitamin complex (H1100)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin complex (H1100)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	640	0	18 514
Type B	0	949	56	20 891
Type C	0	60	8	1511

The substance/substance group *Vitamin complex (H1100)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9376 %)	100.0000 % (> 99.0625 %)
Type B	100.0000 % (> 99.8914 %)	94.4279 % (> 94.1294 %)
Type C	100.0000 % (> 99.1596 %)	88.2353 % (> 83.8235 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80349	80349	0.00	33.56
80411	80411	0.00	41.96
80431	80431	0.00	41.49
80432	80432	0.00	41.68
80485	80485	0.00	40.92
80486	80486	0.00	43.34
80487	80487	0.00	42.28
80637	80637	0.00	42.21
80638	80638	0.00	43.11
80640	80640	0.00	43.62
80642	80642	0.00	42.56
80643	80643	0.00	42.08
80646	80646	0.00	42.22
80647	80647	0.00	43.63
80648	80648	0.00	42.28
80827	80827	0.00	42.74

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Vitamin E NAT (H1107)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80010-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Vitamin E NAT (H1107)

Special notes

When selecting the *Vitamin E NAT (H1107)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Vitamin E NAT (H1107)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin E NAT (H...	071601	80421	40	from supplier
Hepart	Vitamin E NAT (H...	071701	80426	35	from supplier
Hepart	Vitamin E NAT (H...	14001815	80512	40	from supplier
Hepart	Vitamin E NAT (H...	14001821	80513	40	from supplier
Hepart	Vitamin E NAT (H...	14001822	80514	40	from supplier
Hepart	Vitamin E NAT (H...	15001558	80688	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin E NAT (H…	15001559(F2)	80690	40	from supplier
Hepart	Vitamin E NAT (H…	15001561	80693	40	from supplier
Hepart	Vitamin E NAT (H…	15001560(B1)	80694	40	from supplier
Hepart	Vitamin E NAT (H…	15001557	80697	40	from supplier
Hepart	Vitamin E NAT (H…	16001246	80826	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 435 spectra of 11 reference samples from the substance/substance group *Vitamin E NAT (H1107)*. These samples are listed above in the *calibration samples* section.

- 18 719 spectra from a total of 388 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 1320 spectra of 30 reference samples from the substance/substance group *Vitamin E NAT (H1107)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin E NAT (H1107)	945901	80010	40
Hepart	Vitamin E NAT (H1107)	961301	80077	30
Hepart	Vitamin E NAT (H1107)	961301	80098	50
Hepart	Vitamin E NAT (H1107)	17901	80117	50
Hepart	Vitamin E NAT (H1107)	919301	80219	30
Hepart	Vitamin E NAT (H1107)	17701	80230	40
Hepart	Vitamin E NAT (H1107)	961301	80238	40
Hepart	Vitamin E NAT (H1107)	65001	80350	40
Hepart	Vitamin E NAT (H1107)	71501	80381	60
Hepart	Vitamin E NAT (H1107)	71501	80382	60
Hepart	Vitamin E NAT (H1107)	71501	80383	60
Hepart	Vitamin E NAT (H1107)	71501	80384	60
Hepart	Vitamin E NAT (H1107)	14001815	80512†	20
Hepart	Vitamin E NAT (H1107)	14001821	80513†	20
Hepart	Vitamin E NAT (H1107)	14001822	80514†	20
Hepart	Vitamin E NAT (H1107)	15001557(B1)	80686	60
Hepart	Vitamin E NAT (H1107)	15001558(F2)	80687	60
Hepart	Vitamin E NAT (H1107)	15001558	80688†	20

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin E NAT (H1107)	15001561(B1)	80689	60
Hepart	Vitamin E NAT (H1107)	15001559(F2)	80690†	20
Hepart	Vitamin E NAT (H1107)	15001559	80691	60
Hepart	Vitamin E NAT (H1107)	15001561(F2)	80692	60
Hepart	Vitamin E NAT (H1107)	15001561	80693†	20
Hepart	Vitamin E NAT (H1107)	15001560(B1)	80694†	20
Hepart	Vitamin E NAT (H1107)	15001560(F2)	80695	60
Hepart	Vitamin E NAT (H1107)	15001557(F2)	80696	60
Hepart	Vitamin E NAT (H1107)	15001557	80697†	20
Hepart	Vitamin E NAT (H1107)	15001559(B1)	80698	60
Hepart	Vitamin E NAT (H1107)	15001558(B1)	80699	60
Hepart	Vitamin E NAT (H1107)	15001560	80700	60

- 20 576 spectra from a total of 498 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 45 spectra from 13 *Apo-Ident* customers from 18 batches from the substance/substance group *Vitamin E NAT (H1107)*.

Supplier	Substance	Batch	Spectra
UNISAN	Vitamin E NAT (H1107)	71701	1
Unisan	Vitamin E NAT (H1107)	71501	4
Unisan	Vitamin E NAT (H1107)	65001	3
Unisan	Vitamin E NAT (H1107)	71701	2
Unisan	Vitamin E NAT (H1107)	14001821	1
Unisan 2.10.2015	Vitamin E NAT (H1107)	14001821/0	1
Unisan	Vitamin E NAT (H1107)	14001821/0	1
HCK	Vitamin E NAT (H1107)	14001822/0	1
Unisan 02.04.2016	Vitamin E NAT (H1107)	15001558/0	1
Unisan	Vitamin E NAT (H1107)	15001558	1
Unisan	Vitamin E NAT (H1107)	15001659/0	1
Unisan	Vitamin E NAT (H1107)	17901	1
Purren Apotheke	Vitamin E NAT (H1107)	945901	1
	Vitamin E NAT (H1107)	25022	2
Unisan	Vitamin E NAT (H1107)	25022	8
Unisan	Vitamin E NAT (H1107)	25021	1
Hepart AG, CH-8280 Kreu…	Vitamin E NAT (H1107)	65001	1
Hepart AG	Vitamin E NAT (H1107)	25022	2
Hepart AG	Vitamin E NAT (H1107)	65101	3
Hepart AG, Unisan GmbH	Vitamin E NAT (H1107)	65001	2
Unisan	Vitamin E NAT (H1107)	1094025021	2
Hepart AG, CH-8280 Kreu…	Vitamin E NAT (H1107)	1094017701	1
Hepart AG	Vitamin E NAT (H1107)	1094025022	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
Unisan	Vitamin E NAT (H1107)	1094017701	1
Hepart AG	Vitamin E NAT (H1107)	1094025021	1
Unisan	Vitamin E NAT (H1107)	1095961301	1

- 1534 spectra from 20 *Apo-Ident* customers from a total of 572 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Vitamin E NAT (H1107)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin E NAT (H1107)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	435	0	18 719
Type B	0	1302	18	20 576
Type C	0	44	1	1534

The substance/substance group *Vitamin E NAT (H1107)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9377 %)	100.0000 % (> 98.6207 %)
Type B	100.0000 % (> 99.8914 %)	98.6364 % (> 98.4091 %)
Type C	100.0000 % (> 99.1613 %)	97.7778 % (> 91.1111 %)

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80421	80421	0.00	19.07

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80426	80426	0.00	19.13
80512	80512	0.00	21.97
80513	80513	0.00	20.12
80514	80514	0.00	20.44
80688	80688	0.00	23.84
80690	80690	0.00	23.38
80693	80693	0.00	24.73
80694	80694	0.00	23.49
80697	80697	0.00	23.89
80826	80826	0.00	19.38

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Vitamin K2-Ca-Mn-Si complex (osteo complex) (H11…**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80585-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)

Special notes

When selecting the *Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin K2-Ca-Mn…	15000836	80585	40	from supplier
Hepart	Vitamin K2-Ca-Mn…	15000836	80762	40	from supplier
Hepart	Vitamin K2-Ca-Mn…	16000403	80778	40	from supplier

Validation samples

A total of 42 629 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 *Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)*. These samples are listed above in the *calibration samples* section.

- 19 034 spectra from a total of 397 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 3 reference samples from the substance/substance group *Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin K2-Ca-Mn-Si complex …	15000836	80585†	20
Hepart	Vitamin K2-Ca-Mn-Si complex …	15000836	80762†	20
Hepart	Vitamin K2-Ca-Mn-Si complex …	16000403	80778†	20

- 21 836 spectra from a total of 521 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)*.

- 1579 spectra from 20 *Apo-Ident* customers from a total of 590 batches from a further 60 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 *Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 034
Type B	0	60	0	21 836
Type C	0	0	0	1579

The substance/substance group *Vitamin K2-Ca-Mn-Si complex (osteo complex) (H1109)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9385 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8928 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 99.1561 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80585	80585	0.00	15.48
80762	80762	0.00	25.05
80778	80778	0.00	32.72

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

VALIDATION REPORT

IdentModul 1.3-2017-02

Validated substance/substance group	**Zinc (H1110)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	12/04/2017
Report number	80011-2017-04-12
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Zinc (H1110)

Special notes

When selecting the *Zinc (H1110)* 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* 2.2.40 Ph. Eur. *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

Finally, 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 *Zinc (H1110)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Zinc (H1110)	949701	80011	40	from supplier
Hepart	Zinc (H1110)	0991001	80100	50	from supplier
Hepart	Zinc (H1110)	0949701	80143	50	from supplier
Hepart	Zinc (H1110)	14001803	80503	40	from supplier
Hepart	Zinc (H1110)	16000196	80761	40	from supplier
Hepart	Zinc (H1110)	16000518	80789	40	from supplier

Validation samples

A total of 42 629 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Zinc (H1110)*. These samples are listed above in the *calibration samples* section.

- 18 894 spectra from a total of 393 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 320 spectra of 9 reference samples from the substance/substance group *Zinc (H1110)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Zinc (H1110)	pending	80018	40
Hepart	Zinc (H1110)	949701	80079	30
Hepart	Zinc (H1110)	593403	80227	30
Hepart	Zinc (H1110)	41501	80287	40
Hepart	Zinc (H1110)	991001	80294	40
Hepart	Zinc (H1110)	14001753	80489	60
Hepart	Zinc (H1110)	14001803	80503†	20
Hepart	Zinc (H1110)	16000196	80761†	20
Hepart	Zinc (H1110)	16000519	80790	40

- 21 576 spectra from a total of 515 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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

- 54 spectra from 14 *Apo-Ident* customers from 12 batches from the substance/substance group *Zinc (H1110)*.

Supplier	Substance	Batch	Spectra
Unisan	Zinc (H1110)	410501	1
Hepart AG	Zinc (H1110)	41501	7
Unisan	Zinc (H1110)	41501	7
Unisan	Zinc (H1110)	44502	1
Unisan	Zinc (H1110)	991001	15
Unisan	Zinc (H1110)	1164949701	1
Hepart AG	Zinc (H1110)	1164991001	4
Unisan	Zinc (H1110)	1164991001	3
Unisan	Zinc (H1110)	99101	2
Hepart AG, CH-8280 Kreu…	Zinc (H1110)	1164991001	1
Unisan	Zinc (H1110)	14001753/0	1
Unisan	Zinc (H1110)	14001803/1	1
Unisan	Zinc (H1110)	14001803	3
Unisan	Zinc (H1110)	14001753	1
Hepart AG	Zinc (H1110)	991001	3
Unisan Gmbh, 78465 Kons…	Zinc (H1110)	991001	1
Unisan	Zinc (H1110)	16000196	1
unbekannt	Zinc (H1110)	16000196	1

- 1525 spectra from 20 *Apo-Ident* customers from a total of 579 batches from a further 59 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Zinc (H1110)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zinc (H1110)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	18 894
Type B	0	290	30	21 458
Type C	0	54	0	1525

The substance/substance group *Zinc (H1110)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9379 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.8926 %)	90.6250 % (> 89.6875 %)
Type C	100.0000 % (> 99.1605 %)	100.0000 % (> 88.8889 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80011	80011	0.00	12.10
80100	80100	0.00	14.29
80143	80143	0.00	13.29
80503	80503	0.00	12.53
80761	80761	0.00	7.47
80789	80789	0.00	11.16

Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

Appendix A: Additional calibration samples (*Type A*)

Not required.

Appendix B: Additional validation samples (*Type B*)

It is necessary that spectra also enter the validation which cannot be identified with this model. In this manner, it is verified that the model also rejects unknown substances. The spectra for these samples were recorded by *HiperScan GmbH*. They are allocated to the *Type B*. They also include the calibration spectra for other models.

The samples originate from 37 batches. From these 1529 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
Hepart	Amino H drink	683401	30	from supplier
Hepart	Guar (H1023)	703603	50	from supplier
Hepart	Guar (H1023)	130506-GG1	40	from supplier
Hepart	Guar (H1023)	130513-GG2	40	from supplier
Hepart	Guar (H1023)	048501	40	from supplier
Hepart	Guar (H1023)	048402	40	from supplier
Hepart	Guar (H1023)	048401	40	from supplier
Hepart	Guar (H1023)	048001	40	from supplier
Hepart	Guar (H1023)	048502	40	from supplier
Hepart	Guar (H1023)	699304	50	from supplier
Hepart	Guar (H1023)	073701	40	from supplier
Hepart	Guar (H1023)	970001	30	from supplier
Hepart	Guar (H1023)	701401	50	from supplier
Hepart	Guar (H1023)	130514-GG4	40	from supplier
Hepart	Guar (H1023)	130514-GG5	48	from supplier
Hepart	Guar (H1023)	130514-GG3	40	from supplier
Hepart	Omega-3-fish oil...	30011403	30	from supplier
Hepart	Orthovimin B	748901	60	from supplier
Hepart	Orthovimin B	130619100	40	from supplier
Hepart	Orthovimin B	735701	40	from supplier
Hepart	Orthovimin B	0692701	30	from supplier
Hepart	Orthovimin B	735701	31	from supplier
Hepart	Orthovimin B w. ...	700208	50	from supplier
Hepart	Orthovimin B w. ...	699308	50	from supplier
Hepart	Orthovimin B w. ...	706303	50	from supplier
Hepart	Probiotic capcon	12-01	40	from supplier
Hepart	Provisan amino V...	070201	60	from supplier
Hepart	Provisan amino V...	070301	40	from supplier
Hepart	Q10 capsules	0609140101	30	from supplier
Hepart	Salusdog basis	034401	40	from supplier
Hepart	Salusdog for joi...	910003.0000	40	from supplier
Hepart	Salusdog immune ...	035301	40	from supplier
Hepart	Salusdog skin + ...	035401	40	from supplier
Hepart	Vegetable proteins	041001	40	from supplier
Hepart	Vitamin K2-Ca-Mn...	069001	50	from supplier
Hepart	Vitamins BAG (H1...	14000037	40	from supplier
Hepart	Vitamins BAG (H1...	952201	30	from supplier

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 1 batches. From these, 2 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
Unisan	Vitamin K2-Ca-Mn comp...	69001	2

Appendix D: Requirements of validation

In order to ensure adherence to the safe scientific status, the individual methods for manufacturing and testing must be validated under certain circumstances (compare § 34 para. 1 no. 3, § 35 para. 1 no. 4 and para. 4 sentence 1 no. 2 b, para. 6 sentence 3 *ApoBetrO* [Pharmacies Rules and Regulations]). The *ApoBetrO* [Pharmacies Rules and Regulations] incorporates a legal definition in § 1 a para. 16 (quotation translated):

> *"Validation is the provision of documented proof which with a high degree of safety documents that, via a specific process or standard work process, a medicinal product is manufactured and tested, which is in accordance with previously determined quality features."*

Validation documentation can be used to prove that methods or devices which are not described in the Pharmacopoeia within the meaning of § 6 para. 1 sentence 3 *ApBetrO* [Pharmacies Rules and Regulations] achieve the same results as those in the Pharmacopoeia. On the other hand, with the requirements of the demanded validation it must be observed whether the respective testing method is already incorporated in the Pharmacopoeia.

NIR spectroscopy as a general testing method need not be validated in accordance with the express ruling in the *Ph. Eur. Section 1.1* [3], as it is already described in *Section 2.2.40* of the *Ph. Eur.* as an area of application for the identification of raw materials.

However, a special validation requirement exists for the reference database. This requirement is met with the existing document. Further requirements or rules as to how this proof must be furnished do not exist. It is required that the processes guarantee the same results as the methods and devices in the Pharmacopoeia [17].

Carrying out identity tests with *Apo-Ident* is therefore also possible if the NIR spectroscopy process is not required in the Pharmacopoeia monograph of the substance for identity testing. All NIR analyses with *Apo-Ident* prove several, often all molecule groups and are therefore comparable with a series of individual, targeted chemical proofs [4]. Therefore, the identity proof with *Apo-Ident* replaces the monograph test series (with two or more test combinations).

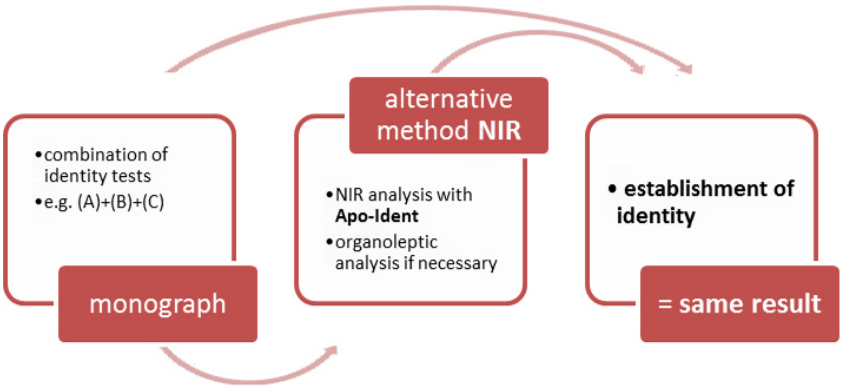

Figure 2: The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

With this validation documentation, proof is furnished that identical results are achieved with *Apo-Ident* and Pharmacopoeia methods, i.e. confirmation of the identity of the raw material [2].

Appendix E: Conformity of *Apo-Ident* with the *European pharmacopeia*

According to *Ph. Eur. Section 2.2.40*, NIR spectroscopy is basically suitable for: "Identification of agents, excipients, dosage forms, intermediate manufacturing products, chemical raw materials and packaging materials" ([3], quotation translated).

The fact that *Apo-Ident* meets the further criteria of the European Pharmacopoeia under the headings in *Section 2.2.40*

- Apparatus
- Measurement methods
- Sample preparation and presentation
- Testing the functionality of the instrument
- Identification and characterisation (qualitative analysis)
- Quantitative analysis
- Ongoing model evaluation
- Transfer of databases
- Data storage

can be proven based on the *HiperScan GmbH* documentation of "Meeting *2.2.40 Ph. Eur.* by *Apo-Ident*" [4].

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Index