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

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

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

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

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

Significance of testing with *Apo-Ident*

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

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

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

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

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

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

Conclusion

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

Explanation of terminology

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

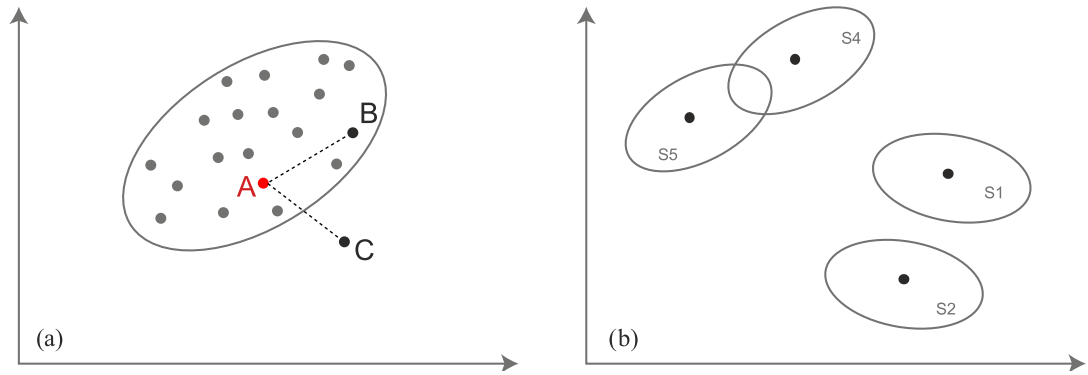

Figure 1: (a) The *Mahalanobis distance* from A to B is less than from A to C. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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

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

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

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 44 432 spectra from 1299 different batches for a total of 101 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)	77	323	14 614

From category *A* a total of 14 614 spectra from 323 batches for a total of 77 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)	101	648	28 205

From category *B* a total of 28 205 spectra from 648 batches for a total of 101 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	614	1613

From category *C* a total of 1613 spectra from 614 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	14 614	0	862 226
Type B	0	19 950	5857	1 665 501
Type C	0	1120	484	95 174

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 % (> 99.998 56 %)	100.000 00 % (> 99.913 84 %)
Type B	100.000 00 % (> 99.998 34 %)	72.161 54 % (> 72.101 80 %)
Type C	100.000 00 % (> 99.983 11 %)	52.796 37 % (> 52.496 77 %)

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

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Amino V complex (H1400)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80745-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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
Hepart	Amino V complex ...	15001365	80862	40	from supplier
Hepart	Amino V complex ...	17000382	80885	40	from supplier

Validation samples

A total of 44 432 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 *Amino V complex (H1400)*. These samples are listed above in the *calibration samples* section.

- 14 374 spectra from a total of 316 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 7 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
Hepart	Amino V complex (H1400)	15001366	80884	40

- 27 885 spectra from a total of 613 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Amino V complex (H1400)*.

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	240	0	14 374
Type B	0	320	0	27 794
Type C	0	0	0	1613

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 % (> 99.9131 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9003 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	21.07
80750	80750	0.00	21.22
80820	80820	0.00	21.77
80821	80821	0.00	22.13
80862	80862	0.00	19.47
80885	80885	0.00	20.48

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Aminomix NAC (H1002)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80003-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

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

continued on the next page

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Aminomix NAC (H1…	15000295(B1)	80538	40	from supplier
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 44 432 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.

- 14 194 spectra from a total of 313 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 27 375 spectra from a total of 601 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 37 spectra from 9 *Apo-Ident* customers from 17 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	4
Unisan	Aminomix NAC (H1002)	14000259	1
Unisan	Aminomix NAC (H1002)	1400258	2
Unisan	Aminomix NAC (H1002)	15000295/0	3
unisan	Aminomix NAC (H1002)	15000297	1
Unisan	Aminomix NAC (H1002)	15000320	1
Unisan	Aminomix NAC (H1002)	15000320/0	1
Unisan	Aminomix NAC (H1002)	15000298/0	1
Euro OTC	Aminomix NAC (H1002)	16001017/0	1
Unisan 02.04.2016	Aminomix NAC (H1002)	15000320/0	1
Unisan	Aminomix NAC (H1002)	16001017/0	1
Hepart	Aminomix NAC (H1002)	16001453/0	1
Unisan	Aminomix NAC (H1002)	19101	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
Hepart AG	Aminomix NAC (H1002)	1054019101	2
Hepart AG, CH-8280 Kreu...	Aminomix NAC (H1002)	1054019101	1
Unisan	Aminomix NAC (H1002)	971701	1

- 1576 spectra from 20 *Apo-Ident* customers from a total of 591 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)*

[†]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*.

and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	14 194
Type B	0	756	74	27 375
Type C	0	25	12	1576

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 % (> 99.9128 %)	100.0000 % (> 98.5714 %)
Type B	100.0000 % (> 99.8993 %)	91.0843 % (> 90.7229 %)
Type C	100.0000 % (> 98.9792 %)	67.5676 % (> 59.4595 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	22.55
80314	80314	0.00	32.08
80407	80407	0.00	31.79
80444	80444	0.00	28.74
80447	80447	0.00	28.95
80538	80538	0.00	31.33
80544	80544	0.00	32.22
80545	80545	0.00	30.72
80546	80546	0.00	32.22
80549	80549	0.00	30.86

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Antibiosis forte complex (H1115)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80675-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Antibiosis forte complex (H1115)*:

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

Validation samples

A total of 44 432 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.

- 14 574 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 185 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 574
Type B	0	20	0	28 185
Type C	0	0	0	1613

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 % (> 99.9166 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	144.33

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Antibiosis mite complex (H1113)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80898-2017-11-17
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Antibiosis mite complex (H1113)

Special notes

When selecting the *Antibiosis mite complex (H1113)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Antibiosis mite complex (H1113)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antibiosis mite ...	16001074	80900	40	from supplier
Hepart	Antibiosis mite ...	16001073	80903	40	from supplier

Validation samples

A total of 44 432 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 *Antibiosis mite complex (H1113)*. These samples are listed above in the *calibration samples* section.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Antibiosis mite complex (H1113)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Antibiosis mite complex (H11…	16001073(B2)	80898	40
Hepart	Antibiosis mite complex (H11…	16001074(B2)	80899	40
Hepart	Antibiosis mite complex (H11…	16001074(B1)	80901	40
Hepart	Antibiosis mite complex (H11…	16001073(B1)	80902	40

- 28 045 spectra from a total of 616 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 mite complex (H1113)*.

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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 *Antibiosis mite complex (H1113)* can clearly be 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 mite complex (H1113)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	14 534
Type B	0	153	7	28 045
Type C	0	0	0	1613

The substance/substance group *Antibiosis mite complex (H1113)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8997 %)	95.6250 % (> 93.7500 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80900	80900	0.00	37.73
80903	80903	0.00	39.91

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Argentum (H1116)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80674-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Argentum (H1116)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Argentum (H1116)	15001151	80674	40	from supplier
Hepart	Argentum (H1116)	16001077	80890	40	from supplier

Validation samples

A total of 44 432 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 *Argentum (H1116)*. These samples are listed above in the *calibration samples* section.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 185 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	80	0	14 534
Type B	0	20	0	28 185
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	13.52
80890	80890	0.00	20.12

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Arginine (L-) (H1036)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80026-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Arginine (L-) (H1036)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Arginine (L-) (H...	066501	80373	50	from supplier
Hepart	Arginine (L-) (H...	16000949	80807	40	from supplier
Hepart	Arginine (L-) (H...	16000949	80867	40	from supplier
Hepart	Arginine (L-) (H...	16000950	80876	40	from supplier

Validation samples

A total of 44 432 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 *Arginine (L-) (H1036)*. These samples are listed above in the *calibration samples* section.

- 14 444 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 420 spectra of 11 reference samples from the substance/substance group *Arginine (L-) (H1036)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Arginine (L-) (H1036)	999001	80026	40
Hepart	Arginine (L-) (H1036)	950601	80129	50
Hepart	Arginine (L-) (H1036)	999001	80157	50
Hepart	Arginine (L-) (H1036)	928302	80212	30
Hepart	Arginine (L-) (H1036)	27802	80256	40
Hepart	Arginine (L-) (H1036)	44301	80280	40
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

- 27 785 spectra from a total of 610 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 27 spectra from 11 *Apo-Ident* customers from 13 batches from the substance/substance group *Arginine (L-) (H1036)*.

Supplier	Substance	Batch	Spectra
Unisan	Arginine (L-) (H1036)	14000564/0	1
Unisan	Arginine (L-) (H1036)	27802	1
unisan	Arginine (L-) (H1036)	52401	1
Unisan	Arginine (L-) (H1036)	44301	2
Unisan	Arginine (L-) (H1036)	16000949/0	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	1
Unisan	Arginine (L-) (H1036)	66501	6
Unisan	Arginine (L-) (H1036)	1320025705	1
Unisan	Arginine (L-) (H1036)	1320999001	1
Unisan	Arginine (L-) (H1036)	1320550101	1
Hepart AG	Arginine (L-) (H1036)	1324027802	1
Fagron	Arginine (L-) (H1036)	1324044301	1
Unisan/Hepart AG	Arginine (L-) (H1036)	1324044301	1
Unisan	Arginine (L-) (H1036)	1324950601	1
Unisan	Arginine (L-) (H1036)	14000563	1

- 1586 spectra from 20 *Apo-Ident* customers from a total of 594 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	170	0	14 444
Type B	0	119	301	27 785
Type C	0	12	15	1586

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 % (> 99.9134 %)	100.0000 % (> 96.4706 %)
Type B	100.0000 % (> 99.8994 %)	28.3333 % (> 27.6190 %)
Type C	100.0000 % (> 98.9825 %)	44.4444 % (> 33.3333 %)

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
80373	80373	0.00	53.34
80807	80807	0.00	51.41
80867	80867	0.00	43.80
80876	80876	0.00	46.02

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Cabbage extract (H1121)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80676-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Cabbage extract (H1121)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Cabbage extract ...	15001355	80676	40	from supplier
Hepart	Cabbage extract ...	16000657	80819	40	from supplier

Validation samples

A total of 44 432 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.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 125 spectra from a total of 618 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 534
Type B	0	80	0	28 125
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9003 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	47.68
80819	80819	0.00	15.09

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Carnitine (L-) (H1038)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80013-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Carnitine (L-) (H1038)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Carnitine (L-) (...	026010	80344	40	from supplier
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 44 432 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 *Carnitine (L-) (H1038)*. These samples are listed above in the *calibration samples* section.

- 14 364 spectra from a total of 316 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 643 spectra of 16 reference samples from the substance/substance group *Carnitine (L-) (H1038)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Carnitine (L-) (H1038)	938501	80013	40
Hepart	Carnitine (L-) (H1038)	965901	80081	30
Hepart	Carnitine (L-) (H1038)	8501	80136	90
Hepart	Carnitine (L-) (H1038)	965901	80155	50
Hepart	Carnitine (L-) (H1038)	965901	80169	43
Hepart	Carnitine (L-) (H1038)	938501	80193	40
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

- 27 562 spectra from a total of 607 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples 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.

- 53 spectra from 12 *Apo-Ident* customers from 21 batches from the substance/substance group *Carnitine (L-) (H1038)*.

Supplier	Substance	Batch	Spectra
Unisan	Carnitine (L-) (H1038)	1184965901	1
Unisan	Carnitine (L-) (H1038)	130605300/3	2
Unisan	Carnitine (L-) (H1038)	26020	1
Unisan	Carnitine (L-) (H1038)	26001	2
Hepart AG	Carnitine (L-) (H1038)	26010	3
Hepart AG	Carnitine (L-) (H1038)	26001	1
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	26010	1
Unisan	Carnitine (L-) (H1038)		1
unisan	Carnitine (L-) (H1038)	26010	1
Unisan	Carnitine (L-) (H1038)	26010	3
Hepart AG	Carnitine (L-) (H1038)	1184026001	1
Unisan	Carnitine (L-) (H1038)	1184026020	3
Unisan	Carnitine (L-) (H1038)	965901	1
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	1184965901	1
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	26020	2
Hepart AG	Carnitine (L-) (H1038)	130605300	1
Unisan	Carnitine (L-) (H1038)	130605300	2
Hepart AG, Unisan GmbH	Carnitine (L-) (H1038)	130605300	4
UNISAN	Carnitine (L-) (H1038)	130605300	3
Unisan	Carnitine (L-) (H1038)	130326002	1
Unisan	Carnitine (L-) (H1038)	130605301	1
Hepart AG	Carnitine (L-) (H1038)	130605301	2
Unisan	Carnitine (L-) (H1038)	130605302	4
Unisan 02.04.2016	Carnitine (L-) (H1038)	15000052/0	2
Unisan	Carnitine (L-) (H1038)	15000052	1
UNISAN	Carnitine (L-) (H1038)	130605302	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
Unisan	Carnitine (L-) (H1038)	15000053/3	1
Unisan	Carnitine (L-) (H1038)	150000540	1

- 1560 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 *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	250	0	14 364
Type B	0	507	136	27 562
Type C	0	46	7	1560

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 % (> 99.9131 %)	100.0000 % (> 97.6000 %)
Type B	100.0000 % (> 99.8993 %)	78.8491 % (> 78.3826 %)
Type C	100.0000 % (> 98.9765 %)	86.7925 % (> 81.1321 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80344	80344	0.00	44.65
80371	80371	0.00	47.57
80483	80483	0.00	42.00
80557	80557	0.00	36.30
80559	80559	0.00	37.16
80787	80787	0.00	40.22

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Carnosine (L-) (H1014)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80153-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Carnosine (L-) (H1014)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Carnosine (L-) (H1014)*. These samples are listed above in the *calibration samples* section.

- 14 494 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Carnosine (L-) (H1014)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Carnosine (L-) (H1014)	pending	80048	40
Hepart	Carnosine (L-) (H1014)	979202	80153	50
Hepart	Carnosine (L-) (H1014)	74801	80655†	20

- 28 095 spectra from a total of 618 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Hepart AG	Carnosine (L-) (H1014)	45901	1
Unisan/Hepart AG	Carnosine (L-) (H1014)	45901	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
UNISAN	Carnosine (L-) (H1014)	74801	1
Hepart AG, CH-8280 Kreu…	Carnosine (L-) (H1014)	1812045901	1
Unisan	Carnosine (L-) (H1014)	45901	1
Unisan	Carnosine (L-) (H1014)	1812979202	1
Hepart AG	Carnosine (L-) (H1014)	1812979202	2
Hepart AG	Carnosine (L-) (H1014)	1812045901	1
Purren Apotheke	Carnosine (L-) (H1014)	1813979202	1

- 1603 spectra from 20 *Apo-Ident* customers from a total of 602 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	120	0	14 494
Type B	0	66	44	28 095
Type C	0	6	4	1603

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 % (> 99.9138 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9000 %)	60.0000 % (> 57.2727 %)
Type C	100.0000 % (> 99.0035 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80393	80393	0.00	65.21
80452	80452	0.00	80.52
80655	80655	0.00	73.87

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Catechin extract (H1010)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80031-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Catechin extract (H1010)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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
Hepart	Catechin extract…	17000409/0	80880	40	from supplier

Validation samples

A total of 44 432 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 *Catechin extract (H1010)*. These samples are listed above in the *calibration samples* section.

- 14 374 spectra from a total of 316 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 240 spectra of 6 reference samples from the substance/substance group *Catechin extract (H1010)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Catechin extract (H1010)	681501	80031	40
Hepart	Catechin extract (H1010)	638201	80139	50
Hepart	Catechin extract (H1010)	681501	80140	50
Hepart	Catechin extract (H1010)	18601	80240	40
Hepart	Catechin extract (H1010)	15000206	80555†	20
Hepart	Catechin extract (H1010)	15000206	80872	40

- 27 965 spectra from a total of 616 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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

- 1593 spectra from 20 *Apo-Ident* customers from a total of 597 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	240	0	14 374
Type B	0	66	174	27 965
Type C	0	3	17	1593

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 % (> 99.9131 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.8996 %)	27.5000 % (> 26.2500 %)
Type C	100.0000 % (> 98.9869 %)	15.0000 % (≥ 0.0000 %)

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
80338	80338	0.00	33.90
80339	80339	0.00	36.09
80340	80340	0.00	24.72
80555	80555	0.00	43.23
80849	80849	0.00	40.99
80880	80880	0.00	30.68

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Chaga (H1011)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80032-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Chaga (H1011)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Chaga (H1011)*. These samples are listed above in the *calibration samples* section.

- 14 494 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 200 spectra of 5 reference samples from the substance/substance group *Chaga (H1011)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Chaga (H1011)	675601	80032	40
Hepart	Chaga (H1011)	975601	80180	40
Hepart	Chaga (H1011)	46701	80310	40
Hepart	Chaga (H1011)	14001688	80493†	20
Hepart	Chaga (H1011)	16000235	80763	60

- 28 005 spectra from a total of 615 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

†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	Chaga (H1011)	46701	1
Unisan	Chaga (H1011)	64001	2
Purren Apotheke	Chaga (H1011)	1514675601	1
Unisan	Chaga (H1011)	14001688	1
Unisan	Chaga (H1011)	151467601	1

- 1607 spectra from 20 *Apo-Ident* customers from a total of 602 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	120	0	14 494
Type B	0	200	0	28 005
Type C	0	6	0	1607

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 % (> 99.9138 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8996 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.0256 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80466	80466	0.00	107.04
80493	80493	0.00	81.44
80825	80825	0.00	53.31

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Chondroitin sulfate (Sodium-) (H1065)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80093-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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
Hepart	Chondroitin sulf…	17000211	80871	40	from supplier

Validation samples

A total of 44 432 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 *Chondroitin sulfate (Sodium-) (H1065)*. These samples are listed above in the *calibration samples* section.

- 14 454 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 330 spectra of 9 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…	1801	80093	50
Hepart	Chondroitin sulfate (Sodium…	964101	80119	50
Hepart	Chondroitin sulfate (Sodium…	31801	80269	40
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

- 27 875 spectra from a total of 614 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 21 spectra from 11 *Apo-Ident* customers from 7 batches from the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*.

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
Unisan	Chondroitin sulfate (Sodium…	1820001801	4
Hepart AG	Chondroitin sulfate (Sodium…	1821001801	1
Hepart AG, CH-8280 Kreu…	Chondroitin sulfate (Sodium…	1820031801	1
Unisan	Chondroitin sulfate (Sodium…	1821964101	1
Fagron	Chondroitin sulfate (Sodium…	1821031801	1
Purren Apotheke	Chondroitin sulfate (Sodium…	1821964101	1

- 1592 spectra from 20 *Apo-Ident* customers from a total of 600 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	160	0	14 454
Type B	0	60	270	27 875
Type C	0	0	21	1592

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 % (> 99.9134 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8995 %)	18.1818 % (> 17.2727 %)
Type C	100.0000 % (> 98.9861 %)	0.0000 % (≥ 0.0000 %)

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
80532	80532	0.00	39.75
80533	80533	0.00	30.85
80779	80779	0.00	44.34
80871	80871	0.00	53.68

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Coenzyme Q10 (H1013)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80015-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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
Hepart	Coenzyme Q10 (H1…	16001598	80881	40	from supplier

Validation samples

A total of 44 432 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 *Coenzyme Q10 (H1013)*. These samples are listed above in the *calibration samples* section.

- 14 334 spectra from a total of 317 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *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
Hepart	Coenzyme Q10 (H1013)	16000402	80882	40

- 27 855 spectra from a total of 613 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 53 spectra from 16 *Apo-Ident* customers from 14 batches from the substance/substance group *Coenzyme Q10 (H1013)*.

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

- 1560 spectra from 20 *Apo-Ident* customers from a total of 593 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	280	0	14 334
Type B	0	120	230	27 855
Type C	0	26	27	1560

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 % (> 99.9130 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.8994 %)	34.2857 % (> 33.4286 %)
Type C	100.0000 % (> 98.9765 %)	49.0566 % (> 43.3962 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	29.72
80484	80484	0.00	26.63
80587	80587	0.00	41.95
80794	80794	0.00	26.41
80850	80850	0.00	23.21
80854	80854	0.00	24.08
80881	80881	0.00	42.90

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Creatine (H1031)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80149-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Creatine (H1031)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Creatine (H1031)*. These samples are listed above in the *calibration samples* section.

- 14 454 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Creatine (H1031)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Creatine (H1031)	pending	80045	40
Hepart	Creatine (H1031)	965201	80149	40
Hepart	Creatine (H1031)	15000749	80627†	20
Hepart	Creatine (H1031)	15000750	80628†	20

- 28 085 spectra from a total of 617 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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

- 1607 spectra from 20 *Apo-Ident* customers from a total of 602 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	160	0	14 454
Type B	0	120	0	28 085
Type C	0	6	0	1607

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 % (> 99.9134 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8999 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.0256 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80440	80440	0.00	47.13
80441	80441	0.00	53.94
80627	80627	0.00	43.64
80628	80628	0.00	50.14

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Curcumin and piperine (H1014)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80034-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Curcumin and piperine (H1014)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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
Hepart	Curcumin and pip…	17000258	80883	40	from supplier

Validation samples

A total of 44 432 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.

- 14 454 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Curcumin and piperine (H1014)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Curcumin and piperine (H1014)	2201	80034	40
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

- 28 025 spectra from a total of 615 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Unisan	Curcumin and piperine (H1014)	72001	4
Unisan	Curcumin and piperine (H1014)	14001017	1
Hepart AG	Curcumin and piperine (H1014)	72001	2
Unisan	Curcumin and piperine (H1014)	13901	2
Hepart AG	Curcumin and piperine (H1014)	13901	3
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

- 1597 spectra from 20 *Apo-Ident* customers from a total of 602 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	14 454
Type B	0	37	143	28 025
Type C	0	1	15	1597

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 % (> 99.9134 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8997 %)	20.5556 % (> 18.8889 %)
Type C	100.0000 % (> 98.9910 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80475	80475	0.00	42.02
80705	80705	0.00	40.84
80796	80796	0.00	46.10
80883	80883	0.00	37.94

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Detox complex (H1118)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80892-2017-11-17
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Detox complex (H1118)

Special notes

When selecting the *Detox complex (H1118)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Detox complex (H1118)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Detox complex (H...	16001075(MM)	80894	40	from supplier
Hepart	Detox complex (H...	16001076	80895	40	from supplier

Validation samples

A total of 44 432 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 *Detox complex (H1118)*. These samples are listed above in the *calibration samples* section.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Detox complex (H1118)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Detox complex (H1118)	16001075(Nr.5-7)	80892	40
Hepart	Detox complex (H1118)	16001075(Nr.1-4)	80893	40

- 28 125 spectra from a total of 618 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Detox complex (H1118)*.

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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 *Detox complex (H1118)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Detox complex (H1118)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	14 534
Type B	0	80	0	28 125
Type C	0	0	0	1613

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9003 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80894	80894	0.00	16.07
80895	80895	0.00	14.41

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Enzyme complex (H1118)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80665-2017-11-17
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Enzyme complex (H1118)

Special notes

When selecting the *Enzyme complex (H1118)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Enzyme complex (H1118)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Enzyme complex (...	15001134	80665	40	from supplier

Validation samples

A total of 44 432 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 *Enzyme complex (H1118)*. These samples are listed above in the *calibration samples* section.

- 14 574 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Enzyme complex (H1118)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Enzyme complex (H1118)	15001134	80665†	20

- 28 185 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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 *Enzyme complex (H1118)* can clearly be 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)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	14 574
Type B	0	20	0	28 176
Type C	0	0	0	1613

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9166 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.9040 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80665	80665	0.00	23.42

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Flavour orange (H1405)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80768-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Flavour orange (H1405)*:

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

Validation samples

A total of 44 432 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.

- 14 574 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 185 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 574
Type B	0	20	0	28 185
Type C	0	0	0	1613

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 % (> 99.9166 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	38.27

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Garcinia Cambogia (H1017)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80037-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Garcinia Cambogia (H1017)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Garcinia Cambogia (H1017)*. These samples are listed above in the *calibration samples* section.

- 14 454 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 380 spectra of 7 reference samples from the substance/substance group *Garcinia Cambogia (H1017)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Garcinia Cambogia (H1017)	956701	80037	40
Hepart	Garcinia Cambogia (H1017)	956701	80101	90
Hepart	Garcinia Cambogia (H1017)	7401	80160	90
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

- 27 825 spectra from a total of 614 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 6 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Garcinia Cambogia (H1017)*.

Supplier	Substance	Batch	Spectra
Hepart AG	Garcinia Cambogia (H1017)	7401	2
Unisan	Garcinia Cambogia (H1017)	56601	1
Unisan	Garcinia Cambogia (H1017)	1221007401	2
Hepart AG	Garcinia Cambogia (H1017)	1221007401	1

- 1607 spectra from 20 *Apo-Ident* customers from a total of 604 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	160	0	14 454
Type B	0	250	130	27 825
Type C	0	1	5	1607

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 % (> 99.9134 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8994 %)	65.7895 % (> 65.0000 %)
Type C	100.0000 % (> 99.0256 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80346	80346	0.00	43.18
80477	80477	0.00	42.33
80490	80490	0.00	32.47
80660	80660	0.00	24.76

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Ginkgo (H1024)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80391-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 374 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 085 spectra from a total of 616 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

†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*.

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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 *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	14 374
Type B	0	120	0	28 085
Type C	0	0	0	1613

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 % (> 99.9131 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.8999 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	42.49
80476	80476	0.00	32.29
80656	80656	0.00	16.82
80657	80657	0.00	31.18
80658	80658	0.00	38.90

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

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Glucosamine sulfate (H1019)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80094-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Glucosamine sulfate (H1019)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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	from supplier

Validation samples

A total of 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Glucosamine sulfate (H1019)*. These samples are listed above in the *calibration samples* section.

- 14 434 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 300 spectra of 7 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)	978401	80094	50
Hepart	Glucosamine sulfate (H1019)	954901	80131	50
Hepart	Glucosamine sulfate (H1019)	34001	80254	40
Hepart	Glucosamine sulfate (H1019)	25002	80262	40
Hepart	Glucosamine sulfate (H1019)	34001	80454	40
Hepart	Glucosamine sulfate (H1019)	17000073	80877	40

- 27 905 spectra from a total of 615 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Unisan Gmbh, 78465 Kons…	Glucosamine sulfate (H1019)	38001	1
UNISAN	Glucosamine sulfate (H1019)	34001	1
Hepart AG	Glucosamine sulfate (H1019)	38001	2
Unisan/Hepart AG	Glucosamine sulfate (H1019)	38001	1
Unisan	Glucosamine sulfate (H1019)	38001	2
Hepart AG	Glucosamine sulfate (H1019)	1822038001	1
Unisan	Glucosamine sulfate (H1019)	1822025002	1
Unisan	Glucosamine sulfate (H1019)	1822038001	1
Hepart AG	Glucosamine sulfate (H1019)	1823038001	1
Unisan	Glucosamine sulfate (H1019)	1823954901	2

- 1600 spectra from 20 *Apo-Ident* customers from a total of 601 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	180	0	14 434
Type B	0	93	207	27 905
Type C	0	7	6	1600

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 % (> 99.9133 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8995 %)	31.0000 % (> 30.0000 %)
Type C	100.0000 % (> 98.9958 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80319	80319	0.00	102.70
80362	80362	0.00	100.53
80402	80402	0.00	86.94
80812	80812	0.00	78.22

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Glutamine (L-) (H1043)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80089-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Glutamine (L-) (H1043)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Glutamine (L-) (...	061501	80336	40	from supplier
Hepart	Glutamine (L-) (...	15000017	80551	40	from supplier
Hepart	Glutamine (L-) (...	15000018	80552	40	from supplier
Hepart	Glutamine (L-) (...	16000940	80802	40	from supplier

Validation samples

A total of 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Glutamine (L-) (H1043)*. These samples are listed above in the *calibration samples* section.

- 14 454 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 400 spectra of 11 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)	994001	80089	50
Hepart	Glutamine (L-) (H1043)	955001	80171	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)	16000941	80803	40
Hepart	Glutamine (L-) (H1043)	16000942	80804	40

- 27 805 spectra from a total of 610 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information

†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*.

provided by the customer regarding manufacturer and batch number.

- 35 spectra from 9 *Apo-Ident* customers from 12 batches from the substance/substance group *Glutamine (L-) (H1043)*.

Supplier	Substance	Batch	Spectra
Unisan	Glutamine (L-) (H1043)	16000940/0	2
Unisan	Glutamine (L-) (H1043)		1
Unisan	Glutamine (L-) (H1043)	26903	2
Unisan	Glutamine (L-) (H1043)	26904	2
Unisan/Hepart AG	Glutamine (L-) (H1043)	26901	1
Unisan Gmbh, 78465 Kons...	Glutamine (L-) (H1043)	26904	1
Unisan	Glutamine (L-) (H1043)	61501	10
UNISAN	Glutamine (L-) (H1043)	61501	2
Unisan	Glutamine (L-) (H1043)	61501/4	1
Unisan	Glutamine (L-) (H1043)	15000017	1
Unisan	Glutamine (L-) (H1043)	15000017/0	1
UNISAN	Glutamine (L-) (H1043)	15000017/0	1
Unisan	Glutamine (L-) (H1043)	1814026901	8
Unisan	Glutamine (L-) (H1043)	1814026903	1
Hepart AG	Glutamine (L-) (H1043)	1815026901	1

- 1578 spectra from 20 *Apo-Ident* customers from a total of 596 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	160	0	14 454
Type B	0	348	52	27 805
Type C	0	29	6	1578

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 % (> 99.9134 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8994 %)	87.0000 % (> 86.2500 %)
Type C	100.0000 % (> 98.9797 %)	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
80336	80336	0.00	42.01
80551	80551	0.00	38.20
80552	80552	0.00	41.35
80802	80802	0.00	41.38

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Glycine (H1021)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80168-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Glycine (H1021)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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	from supplier

Validation samples

A total of 44 432 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 *Glycine (H1021)*. These samples are listed above in the *calibration samples* section.

- 14 374 spectra from a total of 316 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 371 spectra of 10 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)	993401	80197	40
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

- 27 834 spectra from a total of 612 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Hepart AG	Glycine (H1021)	28101	3
Unisan/Hepart AG	Glycine (H1021)	28101	1
Unisan	Glycine (H1021)	28101	3
Hepart AG, CH-8280 Kreu…	Glycine (H1021)	28101	1
Hepart AG	Glycine (H1021)	75501	1
Euro OTC	Glycine (H1021)	16000239/0	1
Hepart AG	Glycine (H1021)	1803028101	1
Unisan	Glycine (H1021)	14001730	1

- 1601 spectra from 20 *Apo-Ident* customers from a total of 602 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	240	0	14 374
Type B	0	255	116	27 834
Type C	0	10	2	1601

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 % (> 99.9131 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.8994 %)	68.7332 % (> 67.9245 %)
Type C	100.0000 % (> 98.9979 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80348	80348	0.00	103.22
80436	80436	0.00	111.84
80494	80494	0.00	111.71
80764	80764	0.00	108.71
80765	80765	0.00	120.38
80805	80805	0.00	113.17

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**HCK classification I**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80067-2017-11-17
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

HCK classification I; Acacia gum (H1001); Biotin (H1007); Chromium (H1012); Folic acid (H1016); Ginseng (H1018); Lycopene (H1058); Selenium (H1067); Selenium yeast (H1068); Vitamin B12 (H1102); Vitamin D3 (H1105)

Special notes

When selecting the *HCK classification I* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

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

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Selenium yeast (...	009001	80067	30	from supplier
Hepart	Acacia gum (H1001)	728201	80266	40	from supplier
Hepart	Folic acid (H1016)	052301	80331	60	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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	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	Ginseng (H1018)	018502	80455	40	from supplier
Hepart	Ginseng (H1018)	067801	80456	40	from supplier
Hepart	Ginseng (H1018)	038802	80478	40	from supplier
Hepart	Selenium (H1067)	15000157	80530	40	from supplier
Hepart	Selenium (H1067)	15000158	80531	40	from supplier
Hepart	Ginseng (H1018)	14002047	80534	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	Ginseng (H1018)	15001047	80663	40	from supplier
Hepart	Selenium (H1067)	065501	80706	40	from supplier
Hepart	Ginseng (H1018)	15001047	80780	40	from supplier
Hepart	Chromium (H1012)	16000520/0	80791	40	from supplier
Hepart	Chromium (H1012)	16000520/4	80792	40	from supplier
Hepart	Vitamin D3 (H1105)	16000952	80816	40	from supplier
Hepart	Selenium (H1067)	16001349	80822	40	from supplier
Hepart	Biotin (H1007)	16001396	80855	40	from supplier
Hepart	Vitamin D3 (H1105)	16001212	80863	40	from supplier

Validation samples

A total of 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 1420 spectra of 35 reference samples from the substance/substance group *HCK classification I*. These samples are listed above in the *calibration samples* section.

- 13 194 spectra from a total of 292 batches from further 67 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 2205 spectra of 61 reference samples from the substance/substance group *HCK classification I*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin B12 (H1102)	944101	80008	40
Hepart	Selenium (H1067)	933301	80014	40
Hepart	Acacia gum (H1001)	639701	80023	40
Hepart	Biotin (H1007)	983601	80028	40
Hepart	Chromium (H1012)	977201	80033	55
Hepart	Folic acid (H1016)	977701	80036	40
Hepart	Ginseng (H1018)	701602	80038	40
Hepart	Lycopene (H1058)	999101	80046	40
Hepart	Selenium (H1067)	933301	80066	30
Hepart	Vitamin B12 (H1102)	966201	80075	30
Hepart	Vitamin D3 (H1105)	959601	80078	30
Hepart	Selenium (H1067)	10201	80086	45
Hepart	Selenium yeast (H1068)	9001	80096	50
Hepart	Ginseng (H1018)	701602	80099	50
Hepart	Selenium (H1067)	10201	80105	50
Hepart	Vitamin D3 (H1105)	959601	80108	50
Hepart	Lycopene (H1058)	927601	80132	40
Hepart	Lycopene (H1058)	999101	80144	50
Hepart	Folic acid (H1016)	977701	80146	40
Hepart	Lycopene (H1058)	4501	80159	50
Hepart	Vitamin B12 (H1102)	944101	80173	40
Hepart	Vitamin B12 (H1102)	966201	80174	40
Hepart	Acacia gum (H1001)	639701	80176	40
Hepart	Acacia gum (H1001)	706310	80177	40
Hepart	Chromium (H1012)	977201	80181	40
Hepart	Biotin (H1007)	983601	80187	40
Hepart	Ginseng (H1018)	630706	80191	40
Hepart	Selenium yeast (H1068)	997601	80194	40
Hepart	Vitamin D3 (H1105)	8101	80201	25
Hepart	Selenium (H1067)	601901	80211	30
Hepart	Vitamin D3 (H1105)	940201	80215	30
Hepart	Lycopene (H1058)	927601	80239	40
Hepart	Biotin (H1007)	29603	80247	40
Hepart	Selenium (H1067)	10201	80268	40
Hepart	Ginseng (H1018)	38802	80270	40
Hepart	Selenium (H1067)	10201	80297	40
Hepart	Vitamin B12 (H1102)	26401	80307	40
Hepart	Ginseng (H1018)	18502	80308	40
Hepart	Vitamin D3 (H1105)	8101	80309	40
Hepart	Folic acid (H1016)	56901	80334	40
Hepart	Biotin (H1007)	29601	80385†	10
Hepart	Ginseng (H1018)	67801	80403	40
Hepart	Ginseng (H1018)	67801	80439	40
Hepart	Selenium (H1067)	15000157	80530†	20
Hepart	Selenium (H1067)	15000158	80531†	20
Hepart	Ginseng (H1018)	14002047	80534†	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

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin B12 (H1102)	15000993(F2)	80605	60
Hepart	Ginseng (H1018)	15001047	80663†	20
Hepart	Selenium (H1067)	65501	80706†	20
Hepart	Ginseng (H1018)	15001047	80780†	20
Hepart	Chromium (H1012)	16000520/2	80793	40
Hepart	Selenium (H1067)	16001350	80823	40
Hepart	Selenium (H1067)	16001351	80824	40
Hepart	Folic acid (H1016)	16001098	80833	40
Hepart	Ginseng (H1018)	17000285	80873	40

- 26 000 spectra from a total of 575 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 301 spectra from 16 *Apo-Ident* customers from 82 batches from the substance/substance group *HCK classification I*.

Supplier	Substance	Batch	Spectra
Hepart AG, CH-8280 Kreu…	Acacia gum (H1001)	1211622002	2
Unisan	Acacia gum (H1001)	1211706310	2
Hepart AG	Acacia gum (H1001)	1211728201	2
Unisan	Acacia gum (H1001)	1211728201	1
Hepart AG, CH-8280 Kreu…	Acacia gum (H1001)	1211728201	1
Unisan	Acacia gum (H1001)	706310	1
Hepart AG	Acacia gum (H1001)	728201	1
Unisan Gmbh, 78465 Kons…	Acacia gum (H1001)	728201	1
Hepart AG	Biotin (H1007)	29601	2
Unisan	Biotin (H1007)	29601	2
Unisan	Biotin (H1007)	29603	7
Hepart AG	Biotin (H1007)	29603	3
Unisan	Biotin (H1007)	14000862	2
Unisan	Biotin (H1007)	14000862/2	2
Unisan	Biotin (H1007)	15000735	1
Ichthyol Gesellschaft C…	Biotin (H1007)	1591983601	1
Unisan	Biotin (H1007)	15000735/0	1
Unisan	Biotin (H1007)	1591983601	1
Hepart AG, CH-8280 Kreu…	Biotin (H1007)	1592029603	1
Hepart AG	Biotin (H1007)	1592029603	3
Unisan	Biotin (H1007)	1592983601	1
Unisan	Biotin (H1007)	H100721	1
Unisan	Biotin (H1007)	983601	1
unisan	Chromium (H1012)		1
Unisan	Chromium (H1012)	14000429	6
Unisan	Chromium (H1012)	1581977201	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	Chromium (H1012)	1582977201	3
Hepart AG	Chromium (H1012)	1582977201	4
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)	16000931	1
Unisan	Folic acid (H1016)	30201	8
Unisan/Hepart AG	Folic acid (H1016)	30201	1
Unisan Gmbh, 78465 Kons…	Folic acid (H1016)	30201	1
Hepart AG	Folic acid (H1016)	52301	3
Hepart AG, CH-8280 Kreu…	Folic acid (H1016)	52301	2
Unisan	Folic acid (H1016)	52301	7
Unisan	Folic acid (H1016)	14000638	3
Unisan	Folic acid (H1016)	14000639/1	1
Unisan	Folic acid (H1016)	1611030201	1
Unisan Gmbh, 78465 Kons…	Folic acid (H1016)	1611030201	1
Hepart AG	Folic acid (H1016)	1613030201	5
Unisan	Folic acid (H1016)	1613030201	3
Unisan	Folic acid (H1016)	1613977701	2
Bombastus	Folic acid (H1016)	1613052301	1
Unisan	Folic acid (H1016)	977701	2
Unisan	Folic acid (H1016)	H101621	1
Unisan/Hepart AG	Ginseng (H1018)	38802	1
Unisan	Ginseng (H1018)	38802	2
Hepart AG	Ginseng (H1018)	38802	1
Unisan	Ginseng (H1018)	67801	1
Unisan	Ginseng (H1018)	14002047/1	1
Euro OTC	Ginseng (H1018)	15001047/0	1
UNISAN	Ginseng (H1018)	67801	1
Hepart AG	Lycopene (H1058)	47301	1
Unisan/Hepart AG	Lycopene (H1058)	47301	1
Unisan	Lycopene (H1058)	47301	2
Hepart AG	Lycopene (H1058)	53501	1
Unisan	Lycopene (H1058)	53501	6
Unisan	Lycopene (H1058)	14000803	1
Unisan	Lycopene (H1058)	1195004501	1
Unisan	Lycopene (H1058)	4501	4
Unisan	Lycopene (H1058)	H105811	1
Unisan/Hepart AG	Selenium (H1067)	10201	3
Unisan	Selenium (H1067)	10201	18
Hedinger	Selenium (H1067)	10201	10
Hepart AG, CH-8280 Kreu…	Selenium (H1067)	10201	1
UNISAN	Selenium (H1067)	65501	1
Unisan	Selenium (H1067)	65501	1
Unisan	Selenium (H1067)	65601	3
UNISAN	Selenium (H1067)	65601	3
Unisan	Selenium (H1067)	65501/2	1
Unisan	Selenium (H1067)	65701	5
Unisan	Selenium (H1067)	65601/2	2
Hepart AG	Selenium (H1067)	65701	1
Unisan	Selenium (H1067)	65601/1	1
Hepart AG	Selenium (H1067)	933301	1
Hepart AG	Selenium (H1067)	1144010201	3
Unisan	Selenium (H1067)	1144010201	2
Bombastus	Selenium (H1067)	1144010201	1
Hepart AG, CH-8280 Kreu…	Selenium (H1067)	1144010201	1
Unisan	Selenium (H1067)	1144933301	2
Unisan	Selenium (H1067)	15000157	2
Unisan	Selenium (H1067)	15000158	1

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Supplier	Substance	Batch	Spectra
Hepart	Selenium (H1067)	15000158/1	1
Unisan	Selenium yeast (H1068)	9001	1
Unisan	Selenium yeast (H1068)	1151009001	3
Unisan	Selenium yeast (H1068)	25709	1
Unisan	Vitamin B12 (H1102)	75301	6
Unisan	Vitamin B12 (H1102)	75301/2	2
Unisan	Vitamin B12 (H1102)	15000993/3	1
Unisan	Vitamin B12 (H1102)	15000993	1
Hepart AG	Vitamin B12 (H1102)	25017	4
Unisan	Vitamin B12 (H1102)	25017	6
Hydro-Cell-Key	Vitamin B12 (H1102)	25017	1
Unisan	Vitamin B12 (H1102)	1061025017	1
Unisan	Vitamin B12 (H1102)	26401	2
Hepart AG	Vitamin B12 (H1102)	1064025017	1
Unisan	Vitamin B12 (H1102)	1064025017	3
Unisan	Vitamin B12 (H1102)	1064026401	2
Hepart AG	Vitamin B12 (H1102)	1064026401	1
Hepart AG, CH-8280 Kreu…	Vitamin B12 (H1102)	1064026401	1
Unisan	Vitamin B12 (H1102)	3441377	1
Unisan	Vitamin D3 (H1105)	8101	10
Hepart AG	Vitamin D3 (H1105)	8101	1
Unisan	Vitamin D3 (H1105)	6108129	1
HCK	Vitamin D3 (H1105)	8101	1
UNISAN	Vitamin D3 (H1105)	63601	1
Unisan	Vitamin D3 (H1105)	63701	5
Unisan Gmbh, 78465 Kons…	Vitamin D3 (H1105)	63701	1
Hepart AG	Vitamin D3 (H1105)	63701	3
Fagron	Vitamin D3 (H1105)	63701	1
Hepart AG	Vitamin D3 (H1105)	64801	4
Unisan	Vitamin D3 (H1105)	64801	6
Hepart AG, CH-8280 Kreu…	Vitamin D3 (H1105)	64801	1
Unisan	Vitamin D3 (H1105)	1335008101	4
Hepart AG, Unisan GmbH	Vitamin D3 (H1105)	64801	1
Hepart AG	Vitamin D3 (H1105)	1335008101	2
Unisan	Vitamin D3 (H1105)	1335008108	1
Unisan	Vitamin D3 (H1105)	1335959601	2
Hepart AG, CH-8280 Kreu…	Vitamin D3 (H1105)	1336008101	2
Unisan	Vitamin D3 (H1105)	14000481	1
UNISAN	Vitamin D3 (H1105)	14000481	3
Unisan	Vitamin D3 (H1105)	14000481/2	3
Unisan	Vitamin D3 (H1105)	15000490	2
Unisan	Vitamin D3 (H1105)	15000490/0	3

- 1312 spectra from 20 *Apo-Ident* customers from a total of 526 batches from a further 50 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance 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 I* can clearly be 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 I* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The

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

	False positive	True positive	False negative	True negative
Type A	0	1420	0	13 194
Type B	0	1724	481	25 303
Type C	0	272	29	1310

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9125 %)	100.0000 % (> 99.5775 %)
Type B	100.0000 % (> 99.9022 %)	78.1859 % (> 78.0499 %)
Type C	100.0000 % (> 99.1375 %)	90.3654 % (> 89.3688 %)

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80067	80067	0.00	27.21
80266	80266	0.00	30.94
80331	80331	0.00	32.61
80335	80335	0.00	26.83
80353	80353	0.00	26.24
80361	80361	0.00	47.66
80364	80364	0.00	50.90
80365	80365	0.00	36.62
80366	80366	0.00	49.42
80385	80385	0.00	38.65
80442	80442	0.00	28.70
80443	80443	0.00	31.70
80449	80449	0.00	30.03
80451	80451	0.00	30.56
80455	80455	0.00	23.92
80456	80456	0.00	25.05
80478	80478	0.00	44.09
80530	80530	0.00	34.41
80531	80531	0.00	35.31
80534	80534	0.00	10.75
80535	80535	0.00	30.86
80553	80553	0.00	31.33

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80580	80580	0.00	34.89
80586	80586	0.00	30.48
80603	80603	0.00	28.26
80604	80604	0.00	27.71
80663	80663	0.00	20.93
80706	80706	0.00	38.21
80780	80780	0.00	21.00
80791	80791	0.00	37.89
80792	80792	0.00	34.39
80816	80816	0.00	39.31
80822	80822	0.00	30.37
80855	80855	0.00	29.12
80863	80863	0.00	35.15

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**HCK classification II**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80311-2017-11-17
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

HCK classification II; Antioxidants NAT complex (H1004); Bioflavonoid complex (H1006); Calcium (H1008); Glutathione (H1020); Isoflavones (H1025); OPC Grape seed (H1066); Rhodiola (H1064); Vitamin B1 (H1101)

Special notes

When selecting the *HCK classification II* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

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

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

Calibration samples

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

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

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin B1 (H1101)	053301	80316	60	from supplier
Hepart	Antioxidants NAT…	052101	80317	60	from supplier
Hepart	Antioxidants NAT…	051902	80318	60	from supplier
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	OPC Grape seed (…	130208-77	80337	40	from supplier
Hepart	Bioflavonoid com…	068101	80342	40	from supplier
Hepart	Isoflavones (H10…	056701	80345	40	from supplier
Hepart	OPC Grape seed (…	068301	80352	40	from supplier
Hepart	OPC Grape seed (…	070401	80380	50	from supplier
Hepart	Rhodiola (H1064)	070501	80390	40	from supplier
Hepart	Vitamin B1 (H1101)	075001	80392	40	from supplier
Hepart	OPC Grape seed (…	070401	80398	40	from supplier
Hepart	Antioxidants NAT…	067301	80404	40	from supplier
Hepart	Antioxidants NAT…	067201	80405	40	from supplier
Hepart	Calcium (H1008)	14000107	80412	40	from supplier
Hepart	Antioxidants NAT…	14000044	80419	40	from supplier
Hepart	Calcium (H1008)	14000106	80422	40	from supplier
Hepart	Glutathione (H10…	074901	80430	40	from supplier
Hepart	Antioxidants NAT…	14000965	80469	40	from supplier
Hepart	Antioxidants NAT…	14000964	80473	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	Bioflavonoid com…	14001675	80492	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	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	Vitamin B1 (H1101)	075001	80529	40	from supplier
Hepart	Isoflavones (H10…	15000205	80556	40	from supplier
Hepart	Glutathione (H10…	15000478	80583	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	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

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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
Hepart	Antioxidants NAT…	16000378	80783	40	from supplier
Hepart	Glutathione (H10…	16000938	80813	40	from supplier
Hepart	Isoflavones (H10…	15000205/2	80815	40	from supplier
Hepart	Isoflavones (H10…	16001644/0	80853	40	from supplier
Hepart	OPC Grape seed (…	16001439	80864	40	from supplier
Hepart	Bioflavonoid com…	17000256	80878	40	from supplier

Validation samples

A total of 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 3120 spectra of 73 reference samples from the substance/substance group *HCK classification II*. These samples are listed above in the *calibration samples* section.

- 11 494 spectra from a total of 253 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 †.

- 6049 spectra of 150 reference samples from the substance/substance group *HCK classification II*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Calcium (H1008)	956001	80005	40
Hepart	Antioxidants NAT complex (H1…	pending	80016	40
Hepart	Bioflavonoid complex (H1006)	pending	80017	30
Hepart	Calcium (H1008)	pending	80020	40
Hepart	Antioxidants NAT complex (H1…	2401	80025	40
Hepart	Bioflavonoid complex (H1006)	683901	80027	40
Hepart	Calcium (H1008)	956001	80029	40
Hepart	Glutathione (H1020)	955501	80040	40
Hepart	Isoflavones (H1025)	988301	80041	40
Hepart	OPC Grape seed (H1066)	672201	80064	30
Hepart	Vitamin B1 (H1101)	977301	80072	30
Hepart	Vitamin B1 (H1101)	977301	80116	50
Hepart	OPC Grape seed (H1066)	672201	80118	50

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Bioflavonoid complex (H1006)	683901	80124	50
Hepart	Glutathione (H1020)	955501	80125	50
Hepart	OPC Grape seed (H1066)	16201	80128	50
Hepart	Isoflavones (H1025)	955701	80163	50
Hepart	Isoflavones (H1025)	988301	80165	50
Hepart	Bioflavonoid complex (H1006)	948802	80170	40
Hepart	Antioxidants NAT complex (H1...	967901	80179	40
Hepart	Antioxidants NAT complex (H1...	11001	80182	40
Hepart	Bioflavonoid complex (H1006)	694301	80184	40
Hepart	Antioxidants NAT complex (H1...	980001	80188	40
Hepart	Calcium (H1008)	8901	80189	40
Hepart	Calcium (H1008)	956001	80190	40
Hepart	OPC Grape seed (H1066)	643901	80196	40
Hepart	Glutathione (H1020)	19703	80204	30
Hepart	Isoflavones (H1025)	591907	80208	30
Hepart	Glutathione (H1020)	918901	80217	30
Hepart	Antioxidants NAT complex (H1...	991301	80232	40
Hepart	OPC Grape seed (H1066)	18401	80233	40
Hepart	Antioxidants NAT complex (H1...	19901	80236	40
Hepart	Bioflavonoid complex (H1006)	19001	80252	40
Hepart	Vitamin B1 (H1101)	30501	80255	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	Isoflavones (H1025)	38801	80272	40
Hepart	Bioflavonoid complex (H1006)	42501	80275	30
Hepart	Bioflavonoid complex (H1006)	28501	80279	40
Hepart	Antioxidants NAT complex (H1...	19901	80282	40
Hepart	Glutathione (H1020)	40201	80288	40
Hepart	Calcium (H1008)	55301	80324	60
Hepart	Calcium (H1008)	55401	80325	60
Hepart	Calcium (H1008)	55501	80326	60
Hepart	OPC Grape seed (H1066)	70401	80380†	10
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	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	Bioflavonoid complex (H1006)	14001675	80492†	20
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	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	Vitamin B1 (H1101)	75001	80529†	20

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Isoflavones (H1025)	15000205	80556†	20
Hepart	Glutathione (H1020)	15000478	80583†	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	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

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Calcium (H1008)	15001674(B2)	80741†	20
Hepart	Calcium (H1008)	15001674(B1)	80742	60
Hepart	Calcium (H1008)	15001674(MM)	80743	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
Hepart	OPC Grape seed (H1066)	16001439(B1)	80865	40
Hepart	OPC Grape seed (H1066)	16001439(F1)	80866	40
Hepart	Bioflavonoid complex (H1006)	17000257	80879	40

- 22 156 spectra from a total of 480 batches from further 93 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 265 spectra from 19 *Apo-Ident* customers from 118 batches from the substance/substance group *HCK classification II*.

Supplier	Substance	Batch	Spectra
Unisan	Antioxidants NAT complex (H1…	67201	4
Unisan	Antioxidants NAT complex (H1…	1851	1
Hepart AG	Antioxidants NAT complex (H1…	67501	1
Hepart AG	Antioxidants NAT complex (H1…	67201	1
Unisan	Antioxidants NAT complex (H1…	14000044	1
UNISAN	Antioxidants NAT complex (H1…	14000042	1
Unisan	Antioxidants NAT complex (H1…	14000961	1
UNISAN	Antioxidants NAT complex (H1…	14000961	1
Unisan	Antioxidants NAT complex (H1…	14000963	2
UNISAN	Antioxidants NAT complex (H1…	14000963	3
Unisan	Antioxidants NAT complex (H1…	1400042	1
Unisan	Antioxidants NAT complex (H1…	14001847/0	2
Unisan	Antioxidants NAT complex (H1…	14001847/1	1
Unisan	Antioxidants NAT complex (H1…	14001848/0	1
Unisan 02.04.2016	Antioxidants NAT complex (H1…	15000874/0	2
Unisan	Antioxidants NAT complex (H1…	14001851/0	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	Antioxidants NAT complex (H1…	15000877	1
Unisan	Antioxidants NAT complex (H1…	15000877/0	1
Unisan	Antioxidants NAT complex (H1…	16000968/0	1
Unisan	Antioxidants NAT complex (H1…	15000880	1
Unisan	Antioxidants NAT complex (H1…	11001	1
Unisan	Antioxidants NAT complex (H1…	16000376	1
hepart ag	Antioxidants NAT complex (H1…	19901	1
Unisan	Antioxidants NAT complex (H1…	19901	3
Hepart AG	Antioxidants NAT complex (H1…	30901	1
Unisan	Antioxidants NAT complex (H1…	30901	1
Unisan	Antioxidants NAT complex (H1…	30902	1
Unisan	Antioxidants NAT complex (H1…	30903	3
Unisan	Antioxidants NAT complex (H1…	51901	4
Unisan	Antioxidants NAT complex (H1…	30904	1
Hedinger	Antioxidants NAT complex (H1…	51901	1
Unisan	Antioxidants NAT complex (H1…	51902	1
Hepart AG	Antioxidants NAT complex (H1…	51902	1
Unisan	Antioxidants NAT complex (H1…	52001	2
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
Unisan Gmbh, 78465 Kons…	Antioxidants NAT complex (H1…	52201	1
Hepart AG	Antioxidants NAT complex (H1…	52201	2
Unisan	Antioxidants NAT complex (H1…	52201	1
Hepart AG	Antioxidants NAT complex (H1…	67301	2
Unisan Gmbh, 78465 Kons…	Antioxidants NAT complex (H1…	67301	1
Unisan	Antioxidants NAT complex (H1…	67601	2
Unisan	Antioxidants NAT complex (H1…	67501	1
Unisan	Antioxidants NAT complex (H1…	68201	4
Hepart AG, CH-8280 Kreu…	Antioxidants NAT complex (H1…	1034019901	1
Hepart AG	Antioxidants NAT complex (H1…	1034019901	1
Hepart AG	Antioxidants NAT complex (H1…	1034030901	1
Hepart AG, CH-8280 Kreu…	Antioxidants NAT complex (H1…	1034030901	1
Unisan	Antioxidants NAT complex (H1…	1034030902	1
Unisan	Antioxidants NAT complex (H1…	1034019901	1
Hepart AG	Antioxidants NAT complex (H1…	1034030902	1
Unisan	Antioxidants NAT complex (H1…	1034030904	1
Hepart AG	Antioxidants NAT complex (H1…	1034030904	1
Hepart AG	Antioxidants NAT complex (H1…	1037030904	1
Unisan	Bioflavonoid complex (H1006)	68101	4
Hepart AG	Bioflavonoid complex (H1006)	68101	1
Unisan	Bioflavonoid complex (H1006)	14001675	2
Hepart AG	Bioflavonoid complex (H1006)	14001675/1	1
Unisan 2.10.2015	Bioflavonoid complex (H1006)	14001675/1	1
Hepart	Bioflavonoid complex (H1006)	14001675/5	1
Unisan	Bioflavonoid complex (H1006)	42501	2
Unisan 02.04.2016	Bioflavonoid complex (H1006)	14001675/2	1
Unisan	Bioflavonoid complex (H1006)	1281683901	1
Hepart AG	Bioflavonoid complex (H1006)	42501	1
Hepart AG	Bioflavonoid complex (H1006)	56001	2
Unisan	Bioflavonoid complex (H1006)	19001	1
Hepart AG	Bioflavonoid complex (H1006)	1284019001	1
Hepart AG	Bioflavonoid complex (H1006)	1284042501	1
Unisan	Bioflavonoid complex (H1006)	1284019001	1
Unisan	Bioflavonoid complex (H1006)	1284042501	2
Unisan	Bioflavonoid complex (H1006)	1284648802	1
Hepart AG, CH-8280 Kreu…	Bioflavonoid complex (H1006)	56001	1
Unisan	Bioflavonoid complex (H1006)		1
Unisan	Calcium (H1008)	8901	7
Hepart AG	Calcium (H1008)	8901	2

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Supplier	Substance	Batch	Spectra
Unisan/Hepart AG	Calcium (H1008)	8901	1
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
Hepart AG	Calcium (H1008)	55301	2
Unisan	Calcium (H1008)	55301	1
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
Hepart AG	Calcium (H1008)	1104008901	6
Unisan	Calcium (H1008)	1104008901	1
Unisan	Calcium (H1008)	1104956001	1
Unisan	Calcium (H1008)	14000106	1
Unisan	Calcium (H1008)	14000110	1
Unisan	Calcium (H1008)	1105008901	1
UNISAN	Calcium (H1008)	14000110	1
Unisan	Calcium (H1008)	14000108	1
Hepart AG	Calcium (H1008)	14001933	1
Unisan	Calcium (H1008)	14001934/0	1
Unisan	Calcium (H1008)	14001938/0	1
Sanacorp	Calcium (H1008)	Fehlt	1
Unisan	Calcium (H1008)	956001	1
Unisan	Calcium (H1008)	15001666	1
Unisan	Calcium (H1008)	15001666/0	1
Hepart	Calcium (H1008)	15001671	1
Unisan	Calcium (H1008)	15001667	1
Hepart	Calcium (H1008)	15001673	3
hepart	Calcium (H1008)	15001674	3
hepart	Calcium (H1008)	15001675	2
hepart	Calcium (H1008)	15001675/4	1
Hepart	Calcium (H1008)	15001676	3
Hepart	Calcium (H1008)	15001676/4	1
Hepart	Calcium (H1008)	15001677	1
Unisan	Glutathione (H1020)	25703	3
Hepart AG, CH-8280 Kreu...	Glutathione (H1020)	40201	1
Unisan	Glutathione (H1020)	40201	4
unisan	Glutathione (H1020)	74901	3
Hepart AG, CH-8280 Kreu...	Glutathione (H1020)	1251025703	1
Hepart AG, CH-8280 Kreu...	Glutathione (H1020)	1251019703	1
Unisan	Glutathione (H1020)	1251019703	2
UNISAN	Glutathione (H1020)	74901	1
Hepart AG	Glutathione (H1020)	1254025703	1
Hepart AG	Glutathione (H1020)	1254040201	1
Purren Apotheke	Glutathione (H1020)	1254955501	1
Unisan	Glutathione (H1020)	1254025703	1
Hepart AG	Isoflavones (H1025)	38801	1
Unisan/Hepart AG	Isoflavones (H1025)	38801	1
Hepart AG	Isoflavones (H1025)	56701	1
Unisan	Isoflavones (H1025)	25704	1
Unisan	Isoflavones (H1025)	56701	4
Unisan	Isoflavones (H1025)	1310988301	1
Hepart AG	Isoflavones (H1025)	1314025704	1

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Supplier	Substance	Batch	Spectra
Unisan	Isoflavones (H1025)	1310025704	1
Purren Apotheke	Isoflavones (H1025)	1314955701	1
Unisan	Isoflavones (H1025)	15000205	1
Unisan 2.10.2015	Isoflavones (H1025)	15000205/0	3
Unisan	Isoflavones (H1025)	15000205/3	1
Hepart AG	Isoflavones (H1025)	1314038801	1
Unisan 02.04.2016	Isoflavones (H1025)	15000205/1	1
Unisan	OPC Grape seed (H1066)		1
UNISAN	OPC Grape seed (H1066)	70401	1
Hepart	OPC Grape seed (H1066)	15000215	1
Unisan	OPC Grape seed (H1066)	70401	2
Hepart AG	OPC Grape seed (H1066)	70401	2
Unisan	OPC Grape seed (H1066)	18401	2
Unisan	OPC Grape seed (H1066)	68301	4
Hepart AG	OPC Grape seed (H1066)	18401	1
Hepart AG, CH-8280 Kreu…	OPC Grape seed (H1066)	130208	1
Unisan	OPC Grape seed (H1066)	1504018401	1
Hepart AG	OPC Grape seed (H1066)	1504018401	2
Hepart AG	Rhodiola (H1064)	70501	1
Unisan/Hepart AG	Vitamin B1 (H1101)	53301	1
Unisan	Vitamin B1 (H1101)	30202	4
Unisan	Vitamin B1 (H1101)	53301	1
Hepart AG	Vitamin B1 (H1101)	53301	2
Hepart AG, CH-8280 Kreu…	Vitamin B1 (H1101)	53301	1
UNISAN	Vitamin B1 (H1101)	75001	1
Unisan	Vitamin B1 (H1101)	15001620/0	1
Unisan	Vitamin B1 (H1101)	14001112/0	1
Unisan	Vitamin B1 (H1101)	15001622/0	1
Hepart AG, Unisan GmbH	Vitamin B1 (H1101)	15001622/0	1
Hepart AG	Vitamin B1 (H1101)	1622030202	2
Hepart AG	Vitamin B1 (H1101)	1621030202	1
Unisan	Vitamin B1 (H1101)	1621030202	1
Unisan	Vitamin B1 (H1101)	1622977301	1
Unisan	Vitamin B1 (H1101)	977301	2

- 1348 spectra from 18 *Apo-Ident* customers from a total of 490 batches from a further 52 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance 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 II* can clearly be 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 II* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	3120	0	11 494
Type B	0	5502	547	22 121
Type C	0	244	21	1348

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9124 %)	100.0000 % (> 99.8077 %)
Type B	100.0000 % (> 99.9004 %)	90.9572 % (> 90.9076 %)
Type C	100.0000 % (> 98.9715 %)	92.0755 % (> 90.9434 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	39.36
80313	80313	0.00	32.94
80315	80315	0.00	38.82
80316	80316	0.00	21.64
80317	80317	0.00	41.69
80318	80318	0.00	35.75
80322	80322	0.00	40.38
80323	80323	0.00	40.34
80327	80327	0.00	40.69
80329	80329	0.00	31.85
80337	80337	0.00	39.92
80342	80342	0.00	21.72
80345	80345	0.00	32.19
80352	80352	0.00	15.17
80380	80380	0.00	22.45
80390	80390	0.00	31.54
80392	80392	0.00	35.71
80398	80398	0.00	23.52
80404	80404	0.00	31.07
80405	80405	0.00	30.09
80412	80412	0.00	44.69
80419	80419	0.00	28.88
80422	80422	0.00	45.31
80430	80430	0.00	26.95
80469	80469	0.00	33.41
80473	80473	0.00	35.34
80479	80479	0.00	40.93
80480	80480	0.00	19.16
80481	80481	0.00	19.64

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80492	80492	0.00	34.93
80504	80504	0.00	28.46
80505	80505	0.00	26.65
80506	80506	0.00	27.08
80507	80507	0.00	24.88
80508	80508	0.00	27.31
80509	80509	0.00	26.19
80521	80521	0.00	45.98
80522	80522	0.00	46.12
80525	80525	0.00	42.14
80526	80526	0.00	42.52
80527	80527	0.00	43.59
80529	80529	0.00	37.34
80556	80556	0.00	32.27
80583	80583	0.00	24.42
80607	80607	0.00	31.31
80609	80609	0.00	33.84
80613	80613	0.00	32.19
80616	80616	0.00	34.35
80618	80618	0.00	31.95
80619	80619	0.00	33.74
80621	80621	0.00	33.74
80624	80624	0.00	30.31
80632	80632	0.00	34.70
80672	80672	0.00	26.29
80707	80707	0.00	46.74
80709	80709	0.00	45.55
80711	80711	0.00	42.33
80712	80712	0.00	43.18
80715	80715	0.00	43.78
80719	80719	0.00	40.65
80722	80722	0.00	42.93
80724	80724	0.00	43.78
80729	80729	0.00	46.09
80732	80732	0.00	47.41
80734	80734	0.00	44.23
80740	80740	0.00	46.60
80741	80741	0.00	46.07
80783	80783	0.00	31.22
80813	80813	0.00	27.04
80815	80815	0.00	42.61
80853	80853	0.00	36.03
80864	80864	0.00	23.59
80878	80878	0.00	34.46

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Inositol hexanicotinate (H1022)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80087-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Inositol hexanicotinate (H1022)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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	from supplier

Validation samples

A total of 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Inositol hexanicotinate (H1022)*. These samples are listed above in the *calibration samples* section.

- 14 434 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 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…	652206	80087	40
Hepart	Inositol hexanicotinate (H10…	979201	80106	50
Hepart	Inositol hexanicotinate (H10…	15000013	80554†	20

- 28 055 spectra from a total of 617 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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…	46001	1
unisan	Inositol hexanicotinate (H10…	15000013	1
Unisan/Hepart AG	Inositol hexanicotinate (H10…	46001	1
Unisan	Inositol hexanicotinate (H10…	1810046001	1
Unisan	Inositol hexanicotinate (H10…	1810979201	1
Fagron	Inositol hexanicotinate (H10…	1811046001	1
Hepart AG	Inositol hexanicotinate (H10…	1811979201	2
Unisan	Inositol hexanicotinate (H10…	14000920	1
Purren Apotheke	Inositol hexanicotinate (H10…	1811979201	1

- 1603 spectra from 20 *Apo-Ident* customers from a total of 600 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	180	0	14 434
Type B	0	70	80	28 055
Type C	0	10	0	1603

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 % (> 99.9133 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8998 %)	46.6667 % (> 44.6667 %)
Type C	100.0000 % (> 99.0035 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80320	80320	0.00	84.91
80465	80465	0.00	90.04
80554	80554	0.00	91.08
80814	80814	0.00	86.73

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Iron (H1015) / Copper (H1032)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80341-2017-11-17
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Iron (H1015) / Copper (H1032); Copper (H1032); Iron (H1015)

Special notes

When selecting the *Iron (H1015) / 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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Iron (H1015) / Copper (H1032)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Copper (H1032)	130415	80341	40	from supplier
Hepart	Iron (H1015)	14000285	80510	40	from supplier
Hepart	Iron (H1015)	040901	80511	40	from supplier
Hepart	Copper (H1032)	15000211	80536	40	from supplier
Hepart	Iron (H1015)	040901	80568	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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
Hepart	Copper (H1032)	15000211/5	80875	40	from supplier

Validation samples

A total of 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 10 reference samples from the substance/substance group *Iron (H1015) / Copper (H1032)*. These samples are listed above in the *calibration samples* section.

- 14 214 spectra from a total of 314 batches from further 75 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 850 spectra of 24 reference samples from the substance/substance group *Iron (H1015) / Copper (H1032)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Iron (H1015)	603206	80002	40
Hepart	Iron (H1015)	998701	80035	40
Hepart	Copper (H1032)	933901	80044	40
Hepart	Copper (H1032)	933901	80154	50
Hepart	Iron (H1015)	928101	80162	50
Hepart	Iron (H1015)	998701	80183	40
Hepart	Copper (H1032)	7901	80200	20
Hepart	Iron (H1015)	603206	80213	30
Hepart	Iron (H1015)	40901	80276	40
Hepart	Copper (H1032)	7901	80277	40
Hepart	Copper (H1032)	46401	80305	40
Hepart	Copper (H1032)	46401	80306	40
Hepart	Iron (H1015)	14000285	80413	40
Hepart	Iron (H1015)	14000285	80510†	20
Hepart	Iron (H1015)	40901	80511†	20
Hepart	Copper (H1032)	15000211	80536†	20
Hepart	Iron (H1015)	40901	80568†	20
Hepart	Iron (H1015)	14000285	80569†	20

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Supplier	Substance	Batch	Sample ID	Spectra
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

- 27 355 spectra from a total of 605 batches from further 99 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 71 spectra from 15 *Apo-Ident* customers from 22 batches from the substance/substance group *Iron (H1015) / Copper (H1032)*.

Supplier	Substance	Batch	Spectra
Unisan	Iron (H1015)	40901	11
Unisan/Hepart AG	Iron (H1015)	40901	1
Hepart AG	Iron (H1015)	40901	3
Hepart AG, Unisan GmbH	Iron (H1015)	40901	5
Unisan	Iron (H1015)	1114040901	2
Hepart AG	Iron (H1015)	1114040901	2
Unisan	Iron (H1015)	1114603206	1
Hepart AG, CH-8280 Kreu…	Iron (H1015)	1114998701	1
Hepart AG	Iron (H1015)	1114998701	1
Unisan	Iron (H1015)	1114998701	5
UNISAN	Iron (H1015)	14000285	1
Unisan	Iron (H1015)	14000285/2	1
Unisan 11.08.2105	Iron (H1015)	14000285/2	1
Unisan	Iron (H1015)	14000285/1	2
Unisan 2.10.2015	Iron (H1015)	14000285/3	2
Unisan	Iron (H1015)	14000285/5	1
Unisan	Iron (H1015)	998701	6
Unisan 02.04.2016	Iron (H1015)	15001258/0	1
Unisan	Iron (H1015)	15001259	1
Unisan	Iron (H1015)	15001258/0	1
Unisan	Iron (H1015)	15001258/2	2
Unisan	Iron (H1015)	14000285	1
Unisan	Copper (H1032)	7901	1
Unisan/Hepart AG	Copper (H1032)	46401	2
Hepart AG	Copper (H1032)	46401	1
Hepart AG	Copper (H1032)	13041501	1
Unisan	Copper (H1032)	933901	1
Unisan	Copper (H1032)	13041501	5
Unisan/Hepart AG	Copper (H1032)	13041501	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	Copper (H1032)	1542933901	1
Unisan	Copper (H1032)	1542933901	1
Hepart AG	Copper (H1032)	130415-K1	1
Unisan	Copper (H1032)	15000211/0	1
Caelo	Copper (H1032)	933901	1
Hepart AG	Copper (H1032)	1544007901	1
Hepart AG	Copper (H1032)	1544046401	1

- 1542 spectra from 20 *Apo-Ident* customers from a total of 585 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 *Iron (H1015) / 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 *Iron (H1015) / 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	400	0	14 214
Type B	0	686	164	27 355
Type C	0	64	7	1542

The substance/substance group *Iron (H1015) / 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 % (> 99.9128 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.8993 %)	80.7059 % (> 80.3529 %)
Type C	100.0000 % (> 98.9749 %)	90.1408 % (> 85.9155 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80341	80341	0.00	40.71
80510	80510	0.00	17.72
80511	80511	0.00	17.30
80536	80536	0.00	37.10
80568	80568	0.00	15.88
80569	80569	0.00	19.84
80650	80650	0.00	11.75
80651	80651	0.00	12.61
80653	80653	0.00	12.44
80875	80875	0.00	30.49

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Isoleucine (L-) (H1045)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80134-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Isoleucine (L-) (H1045)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Isoleucine (L-) (H1045)*. These samples are listed above in the *calibration samples* section.

- 14 454 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 7 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)	968701	80134	50
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

- 27 985 spectra from a total of 614 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Hepart AG	Isoleucine (L-) (H1045)	66301	1
Unisan	Isoleucine (L-) (H1045)	27701	2
Hepart AG, CH-8280 Kreu…	Isoleucine (L-) (H1045)	66301	1
Fritz Schiele	Isoleucine (L-) (H1045)	1805027701	1
Unisan	Isoleucine (L-) (H1045)	1804027701	2
Unisan	Isoleucine (L-) (H1045)	66301	2
Hepart AG	Isoleucine (L-) (H1045)	1805027701	2
Hepart AG, CH-8280 Kreu…	Isoleucine (L-) (H1045)	1804968701	1
Unisan	Isoleucine (L-) (H1045)	1805027701	1
Unisan	Isoleucine (L-) (H1045)	1805968701	1

- 1599 spectra from 20 *Apo-Ident* customers from a total of 601 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	160	0	14 454
Type B	0	101	119	27 985
Type C	0	4	10	1599

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 % (> 99.9134 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8996 %)	45.9091 % (> 44.5455 %)
Type C	100.0000 % (> 98.9940 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80368	80368	0.00	40.10
80498	80498	0.00	36.05
80678	80678	0.00	39.09
80679	80679	0.00	35.83

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Juniper (H1112)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80702-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Juniper (H1112)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Juniper (H1112)	15001004	80702	40	from supplier
Hepart	Juniper (H1112)	16000683	80891	40	from supplier

Validation samples

A total of 44 432 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 *Juniper (H1112)*. These samples are listed above in the *calibration samples* section.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 185 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	80	0	14 534
Type B	0	20	0	28 185
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	17.18
80891	80891	0.00	9.18

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**L-5-HTP (H1035)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80111-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *L-5-HTP (H1035)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-5-HTP (H1035)	16000441	80797	40	from supplier
Hepart	L-5-HTP (H1035)	16000441/0	80851	40	from supplier

Validation samples

A total of 44 432 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 L-*5-HTP (H1035)*. These samples are listed above in the *calibration samples* section.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 L-*5-HTP (H1035)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	L-5-HTP (H1035)	pending	80047	40
Hepart	L-5-HTP (H1035)	968801	80111	50
Hepart	L-5-HTP (H1035)	999801	80148	40

- 28 075 spectra from a total of 618 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Hepart AG	L-5-HTP (H1035)	1837025006	1
Unisan	L-5-HTP (H1035)	1836025006	1
Hepart AG	L-5-HTP (H1035)	1837999801	2

- 1605 spectra from 20 *Apo-Ident* customers from a total of 602 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	80	0	14 534
Type B	0	0	130	28 075
Type C	0	0	8	1605

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8999 %)	0.0000 % (≥ 0.0000 %)
Type C	100.0000 % (> 99.0118 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80797	80797	0.00	32.10
80851	80851	0.00	28.97

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

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Leucine (L-) (H1046)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80150-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Leucine (L-) (H1046)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Leucine (L-) (H1046)*. These samples are listed above in the *calibration samples* section.

- 14 474 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Leucine (L-) (H1046)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Leucine (L-) (H1046)	pending	80052	40
Hepart	Leucine (L-) (H1046)	965101	80150	50
Hepart	Leucine (L-) (H1046)	994101	80203	30
Hepart	Leucine (L-) (H1046)	15000283	80570†	20

- 28 065 spectra from a total of 617 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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
Hepart AG, CH-8280 Kreu…	Leucine (L-) (H1046)	52601	2
Unisan	Leucine (L-) (H1046)	1809965101	1
Unisan	Leucine (L-) (H1046)	52601	1
Purren Apotheke	Leucine (L-) (H1046)	1809965101	1
Hepart AG	Leucine (L-) (H1046)	1809994101	2
Unisan/Hepart AG	Leucine (L-) (H1046)	52601	1
Unisan	Leucine (L-) (H1046)	994101	1

- 1603 spectra from 20 *Apo-Ident* customers from a total of 602 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	140	0	14 474
Type B	0	140	0	28 065
Type C	0	8	2	1603

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 % (> 99.9136 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.8998 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 99.0035 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80333	80333	0.00	40.81
80410	80410	0.00	45.61
80570	80570	0.00	47.57

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Lipoic acid (a-) (H1000)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80022-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 395 spectra from a total of 317 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 27 664 spectra from a total of 607 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in 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)	14000497	1
UNISAN	Lipoic acid (a-) (H1000)	14001726	2
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

- 1588 spectra from 20 *Apo-Ident* customers from a total of 598 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	14 395
Type B	0	526	15	27 664
Type C	0	25	0	1588

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 % (> 99.9132 %)	100.0000 % (> 97.2603 %)
Type B	100.0000 % (> 99.8994 %)	97.2274 % (> 96.6728 %)
Type C	100.0000 % (> 98.9835 %)	100.0000 % (> 76.0000 %)

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	54.08
80482	80482	0.00	76.43
80491	80491	0.00	55.51
80681	80681	0.00	56.37
80682	80682	0.00	56.00

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Lysine (L-) (H1047)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80151-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 334 spectra from a total of 317 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 27 935 spectra from a total of 614 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Hepart AG	Lysine (L-) (H1047)	65401	1
Unisan/Hepart AG	Lysine (L-) (H1047)	65401	1
Unisan	Lysine (L-) (H1047)	65401/4	1
Unisan	Lysine (L-) (H1047)	1800017302	3
Unisan	Lysine (L-) (H1047)	14000944	1
Hepart AG, CH-8280 Kreu…	Lysine (L-) (H1047)	1800955002	1
Hepart AG	Lysine (L-) (H1047)	1800017302	1
Unisan	Lysine (L-) (H1047)	15000372/0	1
Unisan	Lysine (L-) (H1047)	28801	2
Unisan	Lysine (L-) (H1047)	1801028801	1

- 1600 spectra from 20 *Apo-Ident* customers from a total of 599 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	14 334
Type B	0	97	173	27 935
Type C	0	9	4	1600

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 % (> 99.9130 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.8995 %)	35.9259 % (> 34.8148 %)
Type C	100.0000 % (> 98.9958 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	51.68
80360	80360	0.00	60.61
80453	80453	0.00	52.83
80458	80458	0.00	61.38
80468	80468	0.00	62.80
80562	80562	0.00	59.22
80847	80847	0.00	70.86

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Magnesium (H1060)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80061-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 404 spectra from a total of 317 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Magnesium (H1060)	16001704	80858	40
Hepart	Magnesium (H1060)	16001705	80859	40
Hepart	Magnesium (H1060)	16001706	80860	40

- 26 865 spectra from a total of 592 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 64 spectra from 15 *Apo-Ident* customers from 19 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)	43501	2
Unisan	Magnesium (H1060)	16000265/0	1
unbekannt	Magnesium (H1060)	16000264	1
Unisan	Magnesium (H1060)	16000265/1	1
Hepart AG	Magnesium (H1060)	43501	1
Unisan	Magnesium (H1060)	43601	3
Hepart AG	Magnesium (H1060)	43601	2
Hepart AG	Magnesium (H1060)	43602	4
Unisan	Magnesium (H1060)	43602	1
Hepart AG, CH-8280 Kreu…	Magnesium (H1060)	43602	1
Hepart AG	Magnesium (H1060)	43701	1
Unisan/Hepart AG	Magnesium (H1060)	43601	1
Unisan	Magnesium (H1060)	43701	3
unisan	Magnesium (H1060)	43702	1
Unisan	Magnesium (H1060)	43702	1
Unisan Gmbh, 78465 Kons…	Magnesium (H1060)	43702	1
Unisan	Magnesium (H1060)	69701	3
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
Hepart AG, CH-8280 Kreu…	Magnesium (H1060)	1134043601	1
Unisan/Hepart AG	Magnesium (H1060)	973501	1
Hepart AG	Magnesium (H1060)	1134973501	5
Unisan	Magnesium (H1060)	1134973501	4
Hepart AG, CH-8280 Kreu…	Magnesium (H1060)	1134973501	2
unisan	Magnesium (H1060)	14001895	1
Unisan	Magnesium (H1060)	H106021	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*.

- 1549 spectra from 20 *Apo-Ident* customers from a total of 588 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 *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	14 404
Type B	0	1050	290	26 865
Type C	0	24	40	1549

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 % (> 99.9132 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8993 %)	78.3582 % (> 78.1343 %)
Type C	100.0000 % (> 98.9754 %)	37.5000 % (> 32.8125 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	31.36
80515	80515	0.00	40.57
80767	80767	0.00	32.72
80770	80770	0.00	32.64
80856	80856	0.00	26.07

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Methylsulfonylmethane (MSM) (H1062)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80102-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 4 reference samples from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*. These samples are listed above in the *calibration samples* section.

- 14 394 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 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) ...	979401	80102	50
Hepart	Methylsulfonylmethane (MSM) ...	964001	80115	50
Hepart	Methylsulfonylmethane (MSM) ...	15001371	80703†	40

- 28 035 spectra from a total of 617 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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) …	979401	1
Unisan	Methylsulfonylmethane (MSM) …	15001371	1
Unisan	Methylsulfonylmethane (MSM) …	25013	2
HCK	Methylsulfonylmethane (MSM) …	1400921/1	1
Unisan	Methylsulfonylmethane (MSM) …	26101	1
Hepart AG	Methylsulfonylmethane (MSM) …	1819026101	1
Unisan/Hepart AG	Methylsulfonylmethane (MSM) …	1819025013	1
Unisan	Methylsulfonylmethane (MSM) …	1818025013	1

- 1602 spectra from 20 *Apo-Ident* customers from a total of 598 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	220	0	14 394
Type B	0	170	0	28 035
Type C	0	6	5	1602

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 % (> 99.9132 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.8997 %)	100.0000 % (> 96.4706 %)
Type C	100.0000 % (> 99.0004 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80332	80332	0.00	81.70
80467	80467	0.00	91.67
80703	80703	0.00	86.35
80782	80782	0.00	79.23

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Ornithine (L-) (H1048)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80175-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Ornithine (L-) (H1048)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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	from supplier

Validation samples

A total of 44 432 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 *Ornithine (L-) (H1048)*. These samples are listed above in the *calibration samples* section.

- 14 454 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 8 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)	979301	80175	40
Hepart	Ornithine (L-) (H1048)	646703	80195	40
Hepart	Ornithine (L-) (H1048)	1202	80206	30
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

- 27 935 spectra from a total of 613 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 13 spectra from 7 *Apo-Ident* customers from 6 batches from the substance/substance group *Ornithine (L-) (H1048)*.

Supplier	Substance	Batch	Spectra
Unisan/Hepart AG	Ornithine (L-) (H1048)	27001	2
Unisan	Ornithine (L-) (H1048)	27001	3
Unisan	Ornithine (L-) (H1048)	979301	2
Hepart	Ornithine (L-) (H1048)	16000935/0	2
Unisan	Ornithine (L-) (H1048)	1816979301	2
Purren Apotheke	Ornithine (L-) (H1048)	1817979301	1
Hepart AG	Ornithine (L-) (H1048)	1817025008	1

- 1600 spectra from 20 *Apo-Ident* customers from a total of 601 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	160	0	14 454
Type B	0	195	75	27 935
Type C	0	3	10	1600

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 % (> 99.9134 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8995 %)	72.2222 % (> 71.1111 %)
Type C	100.0000 % (> 98.9958 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80629	80629	0.00	78.94
80667	80667	0.00	78.35
80669	80669	0.00	82.35
80811	80811	0.00	68.41

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Orthovimin Neutral Complex (H1403)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80744-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Orthovimin Neutral Complex (H1403)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Orthovimin Neutr…	15001850	80744	40	from supplier

Validation samples

A total of 44 432 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.

- 14 574 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 185 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 574
Type B	0	20	0	28 185
Type C	0	0	0	1613

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 % (> 99.9166 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	26.14

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**PET basis (H1503)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80566-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 534 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 165 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 534
Type B	0	40	0	28 125
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	28.96
80636	80636	0.00	25.13

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**PET coenzyme Q10 (H0022)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80561-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 534 spectra from a total of 322 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 165 spectra from a total of 620 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 534
Type B	0	40	0	28 165
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9013 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	20.74
80635	80635	0.00	23.84

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**PET immune system (H1502)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80564-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 534 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 165 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 534
Type B	0	40	0	28 125
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	29.61
80634	80634	0.00	28.50

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**PET joints (H1501)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80567-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 534 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 165 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 534
Type B	0	40	0	28 125
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	18.99
80630	80630	0.00	20.39

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**PET skin and hair (H1504)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80565-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 534 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 165 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 534
Type B	0	40	0	28 125
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	48.45
80633	80633	0.00	46.94

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**PET well-aging (H1500)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80563-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *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 44 432 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.

- 14 534 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 165 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 534
Type B	0	40	0	28 165
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9013 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	14.78
80631	80631	0.00	14.14

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Phenylalanine (L-) (H1049)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80090-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Phenylalanine (L-) (H1049)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Phenylalanine (L...	074401	80400	40	from supplier
Hepart	Phenylalanine (L...	16001096	80852	40	from supplier

Validation samples

A total of 44 432 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 *Phenylalanine (L-) (H1049)*. These samples are listed above in the *calibration samples* section.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 175 spectra of 4 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	55
Hepart	Phenylalanine (L-) (H1049)	1201	80198	60
Hepart	Phenylalanine (L-) (H1049)	19707	80202	30

- 28 030 spectra from a total of 617 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Unisan	Phenylalanine (L-) (H1049)	74401/0	1
Unisan	Phenylalanine (L-) (H1049)	1828019707	1

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Supplier	Substance	Batch	Spectra
Unisan/Hepart AG	Phenylalanine (L-) (H1049)	1828025009	1
Hepart AG	Phenylalanine (L-) (H1049)	1828025009	1

- 1602 spectra from 20 *Apo-Ident* customers from a total of 603 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	80	0	14 534
Type B	0	0	175	28 030
Type C	0	1	10	1602

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8997 %)	0.0000 % (≥ 0.0000 %)
Type C	100.0000 % (> 99.0004 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80400	80400	0.00	49.98
80852	80852	0.00	50.48

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Potassium (H1030)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80043-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Potassium (H1030)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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
Hepart	Potassium (H1030)	16001645	80868	40	from supplier

Validation samples

A total of 44 432 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.

- 14 364 spectra from a total of 316 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 759 spectra of 19 reference samples from the substance/substance group *Potassium (H1030)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Potassium (H1030)	944201	80043	40
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
Hepart	Potassium (H1030)	16001646	80869	40
Hepart	Potassium (H1030)	16001647	80870	40

- 27 446 spectra from a total of 603 batches from further 100 substances. These spectra were

†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*.

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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)	28903	2
Unisan	Potassium (H1030)	39301	5
Unisan/Hepart AG	Potassium (H1030)	39301	3
Hepart AG	Potassium (H1030)	39301	1
Fagron	Potassium (H1030)	39301	1
Unisan/Hepart AG	Potassium (H1030)	39302	1
Hepart AG	Potassium (H1030)	39302	1
Unisan	Potassium (H1030)	39302	1
Unisan	Potassium (H1030)	69201	4
UNISAN	Potassium (H1030)	69201	1
Unisan	Potassium (H1030)	69301	3
Unisan	Potassium (H1030)	944201	4
Unisan	Potassium (H1030)	69401/0	1
Unisan	Potassium (H1030)	69401	1
Hepart AG	Potassium (H1030)	1124028903	1
Unisan	Potassium (H1030)	1124028903	1
Hepart AG	Potassium (H1030)	1124944201	1
Unisan	Potassium (H1030)	1124944201	1
Unisan	Potassium (H1030)	130328001	3
Unisan	Potassium (H1030)	15000597/0	1
Unisan	Potassium (H1030)	15000599	1

- 1574 spectra from 20 *Apo-Ident* customers from a total of 593 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	14 364
Type B	0	701	58	27 446
Type C	0	32	7	1574

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 % (> 99.9131 %)	100.0000 % (> 97.6000 %)
Type B	100.0000 % (> 99.8993 %)	92.3584 % (> 91.9631 %)
Type C	100.0000 % (> 98.9788 %)	82.0513 % (> 74.3590 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80372	80372	0.00	36.72
80571	80571	0.00	48.42
80574	80574	0.00	49.27
80576	80576	0.00	49.74
80578	80578	0.00	49.58
80868	80868	0.00	49.88

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Silymarin (H1071)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80068-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Silymarin (H1071)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Silymarin (H1071)	15001046	80671	40	from supplier
Hepart	Silymarin (H1071)	16001084	80861	40	from supplier

Validation samples

A total of 44 432 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 *Silymarin (H1071)*. These samples are listed above in the *calibration samples* section.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 230 spectra of 6 reference samples from the substance/substance group *Silymarin (H1071)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Silymarin (H1071)	950401	80068	30
Hepart	Silymarin (H1071)	950401	80138	50
Hepart	Silymarin (H1071)	915601	80210	30
Hepart	Silymarin (H1071)	29901	80265	40
Hepart	Silymarin (H1071)	67701	80375	60
Hepart	Silymarin (H1071)	15001046	80671†	20

- 27 975 spectra from a total of 615 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

†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	Silymarin (H1071)	67701/7	1
Hepart AG, CH-8280 Kreu…	Silymarin (H1071)	29901	2
Unisan/Hepart AG	Silymarin (H1071)	29901	1
Unisan	Silymarin (H1071)	29901	3
Unisan	Silymarin (H1071)	46101	1
unisan	Silymarin (H1071)	67701	2
Hepart AG	Silymarin (H1071)	67701	1
Unisan	Silymarin (H1071)	950401	2
UNISAN	Silymarin (H1071)	67701	1
Hepart AG, CH-8280 Kreu…	Silymarin (H1071)	1241046101	1
Unisan	Silymarin (H1071)	46101/0	1
Unisan	Silymarin (H1071)	1241950401	2
hepart ag	Silymarin (H1071)	1244950401	1
Hepart AG	Silymarin (H1071)	1244029901	1
Hepart AG, CH-8280 Kreu…	Silymarin (H1071)	1241950401	1

- 1592 spectra from 20 *Apo-Ident* customers from a total of 597 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	80	0	14 534
Type B	0	80	150	27 975
Type C	0	0	21	1592

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8996 %)	34.7826 % (> 33.4783 %)
Type C	100.0000 % (> 98.9861 %)	0.0000 % (≥ 0.0000 %)

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
80671	80671	0.00	33.00
80861	80861	0.00	26.21

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Stomach complex (H1120)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80666-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Stomach complex (H1120)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Stomach complex ...	15001350	80666	40	from supplier
Hepart	Stomach complex ...	16001138	80888	40	from supplier
Hepart	Stomach complex ...	16001139	80889	40	from supplier

Validation samples

A total of 44 432 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 *Stomach complex (H1120)*. These samples are listed above in the *calibration samples* section.

- 14 494 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 185 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	120	0	14 494
Type B	0	20	0	28 185
Type C	0	0	0	1613

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 % (> 99.9138 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9035 %)	100.0000 % (> 70.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	30.55
80888	80888	0.00	37.61
80889	80889	0.00	37.54

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Taurine (H1084)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80071-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Taurine (H1084)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Taurine (H1084)	14001767	80497	40	from supplier
Hepart	Taurine (H1084)	16000946	80809	40	from supplier
Hepart	Taurine (H1084)	16000946	80887	40	from supplier

Validation samples

A total of 44 432 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 *Taurine (H1084)*. These samples are listed above in the *calibration samples* section.

- 14 494 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 260 spectra of 7 reference samples from the substance/substance group *Taurine (H1084)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Taurine (H1084)	960201	80071	30
Hepart	Taurine (H1084)	960201	80088	50
Hepart	Taurine (H1084)	17301	80142	50
Hepart	Taurine (H1084)	600402	80216	30
Hepart	Taurine (H1084)	28001	80250	40
Hepart	Taurine (H1084)	14001767	80497†	20
Hepart	Taurine (H1084)	16000947	80810	40

- 27 945 spectra from a total of 614 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

†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, CH-8280 Kreu…	Taurine (H1084)	25710	3
Unisan	Taurine (H1084)	25710	1
Unisan/Hepart AG	Taurine (H1084)	28001	1
Unisan	Taurine (H1084)	28001	8
Hepart AG	Taurine (H1084)	28001	2
Unisan	Taurine (H1084)	1294028001	1
Unisan	Taurine (H1084)	1294960201	2
Hepart AG	Taurine (H1084)	1294028001	1
Unisan	Taurine (H1084)	14001767/0	1
unisan	Taurine (H1084)	14001767	1

- 1592 spectra from 20 *Apo-Ident* customers from a total of 601 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	120	0	14 494
Type B	0	92	168	27 945
Type C	0	3	18	1592

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 % (> 99.9138 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8995 %)	35.3846 % (> 34.2308 %)
Type C	100.0000 % (> 98.9861 %)	14.2857 % (≥ 0.0000 %)

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
80497	80497	0.00	69.66
80809	80809	0.00	71.80
80887	80887	0.00	70.89

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Threonine (L-) (H1052)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80107-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Threonine (L-) (H1052)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Threonine (L-) (...	14001718	80496	40	from supplier

Validation samples

A total of 44 432 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 *Threonine (L-) (H1052)*. These samples are listed above in the *calibration samples* section.

- 14 574 spectra from a total of 321 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 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)	638802	80107	50
Hepart	Threonine (L-) (H1052)	14901	80122	50
Hepart	Threonine (L-) (H1052)	14001718	80496†	20

- 28 055 spectra from a total of 617 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

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	Threonine (L-) (H1052)	25708	2
unisan	Threonine (L-) (H1052)	25708	1
UNISAN	Threonine (L-) (H1052)	25708	1
Unisan	Threonine (L-) (H1052)	14001718	1
Unisan	Threonine (L-) (H1052)	14001718/1	1
Hepart AG	Threonine (L-) (H1052)	1832014901	1
Purren Apotheke	Threonine (L-) (H1052)	1833014901	1
Unisan	Threonine (L-) (H1052)	1832014901	1

- 1601 spectra from 20 *Apo-Ident* customers from a total of 602 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	40	0	14 574
Type B	0	20	130	28 055
Type C	0	2	10	1601

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 % (> 99.9166 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8998 %)	13.3333 % (> 11.3333 %)
Type C	100.0000 % (> 98.9979 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80496	80496	0.00	47.43

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Trace elements BAG (H1078)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80205-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Trace elements BAG (H1078)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Trace elements B...	16000795	80799	40	from supplier
Hepart	Trace elements B...	16000796	80800	40	from supplier

Validation samples

A total of 44 432 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.

- 14 534 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 28 165 spectra from a total of 619 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 1613 spectra from 20 *Apo-Ident* customers from a total of 607 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	14 534
Type B	0	40	0	28 165
Type C	0	0	0	1613

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 % (> 99.9145 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9013 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.9702 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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	15.39
80800	80800	0.00	14.87

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Trace elements JK (H1080)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80069-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Trace elements JK (H1080)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Trace elements JK (H1080)*. These samples are listed above in the *calibration samples* section.

- 14 414 spectra from a total of 318 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 250 spectra of 7 reference samples from the substance/substance group *Trace elements JK (H1080)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Trace elements JK (H1080)	956901	80069	30
Hepart	Trace elements JK (H1080)	956901	80137	50
Hepart	Trace elements JK (H1080)	919701	80223	30
Hepart	Trace elements JK (H1080)	11701	80235	40
Hepart	Trace elements JK (H1080)	15000525	80673	60
Hepart	Trace elements JK (H1080)	72901	80701†	20
Hepart	Trace elements JK (H1080)	15000526	80766†	20

- 27 955 spectra from a total of 614 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 35 spectra from 12 *Apo-Ident* customers from 9 batches from the substance/substance group *Trace elements JK (H1080)*.

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)	15000525/0	1
Unisan	Trace elements JK (H1080)	15000526	1
Euro OTC	Trace elements JK (H1080)	15000526/0	1
Unisan/Hepart AG	Trace elements JK (H1080)	11701	3
Hepart AG	Trace elements JK (H1080)	11701	8
Unisan	Trace elements JK (H1080)	72701	1
Hepart AG	Trace elements JK (H1080)	1026011701	2
Unisan	Trace elements JK (H1080)	1026919701	1
Unisan	Trace elements JK (H1080)	1026011701	2
Unisan	Trace elements JK (H1080)	1026956901	1
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

- 1578 spectra from 20 *Apo-Ident* customers from a total of 598 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	200	0	14 414
Type B	0	100	150	27 955
Type C	0	6	29	1578

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 % (> 99.9132 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8995 %)	40.0000 % (> 38.8000 %)
Type C	100.0000 % (> 98.9797 %)	17.1429 % (> 8.5714 %)

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80387	80387	0.00	29.56
80388	80388	0.00	28.50
80389	80389	0.00	29.89
80701	80701	0.00	24.93
80766	80766	0.00	21.09

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Trace elements SE (H1082)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80070-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Trace elements SE (H1082)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 9 reference samples from the substance/substance group *Trace elements SE (H1082)*. These samples are listed above in the *calibration samples* section.

- 14 254 spectra from a total of 314 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 1140 spectra of 25 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)	937201	80070	30
Hepart	Trace elements SE (H1082)	937201	80092	50
Hepart	Trace elements SE (H1082)	12401	80141	50
Hepart	Trace elements SE (H1082)	929202	80172	40
Hepart	Trace elements SE (H1082)	31301	80263	40
Hepart	Trace elements SE (H1082)	42301	80278	55
Hepart	Trace elements SE (H1082)	42301	80290	55
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
Hepart	Trace elements SE (H1082)	15000557(F2)	80596	60

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Supplier	Substance	Batch	Sample ID	Spectra
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

- 27 065 spectra from a total of 598 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 33 spectra from 12 *Apo-Ident* customers from 13 batches from the substance/substance group *Trace elements SE (H1082)*.

Supplier	Substance	Batch	Spectra
Unisan	Trace elements SE (H1082)	31301	5
Unisan	Trace elements SE (H1082)	42301	2
Unisan	Trace elements SE (H1082)	14000720	3
Hepart AG	Trace elements SE (H1082)	120435-14	1
Unisan	Trace elements SE (H1082)	14000722	1
Unisan	Trace elements SE (H1082)	14000721	1
Unisan	Trace elements SE (H1082)	14000721/0	1
Unisan	Trace elements SE (H1082)	15000553	1
Unisan	Trace elements SE (H1082)	15000556/0	1
Hepart AG, CH-8280 Kreu…	Trace elements SE (H1082)	31301	1
Hepart AG	Trace elements SE (H1082)	31301	2
Hepart AG	Trace elements SE (H1082)	42301	3
Unisan	Trace elements SE (H1082)	1024042301	1
Unisan	Trace elements SE (H1082)	1024012401	2
Unisan	Trace elements SE (H1082)	1024929202	1
Hepart AG	Trace elements SE (H1082)	937201	4
Unisan	Trace elements SE (H1082)	937201	2
Hepart AG, CH-8280 Kreu…	Trace elements SE (H1082)	937201	1

- 1580 spectra from 20 *Apo-Ident* customers from a total of 594 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	360	0	14 254
Type B	0	780	360	27 065
Type C	0	9	24	1580

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 % (> 99.9129 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.8993 %)	68.4211 % (> 68.1579 %)
Type C	100.0000 % (> 98.9803 %)	27.2727 % (> 18.1818 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80459	80459	0.00	30.72
80460	80460	0.00	32.86
80461	80461	0.00	32.11
80464	80464	0.00	32.73
80588	80588	0.00	58.68
80592	80592	0.00	51.75
80594	80594	0.00	54.73
80597	80597	0.00	64.38
80601	80601	0.00	58.97

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

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Tryptophan (L-) (H1053)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80127-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Tryptophan (L-) (H1053)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Tryptophan (L-) (H1053)*. These samples are listed above in the *calibration samples* section.

- 14 414 spectra from a total of 317 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 210 spectra of 6 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)	950001	80127	50
Hepart	Tryptophan (L-) (H1053)	978501	80135	50
Hepart	Tryptophan (L-) (H1053)	27901	80251	40
Hepart	Tryptophan (L-) (H1053)	15000441	80581†	20
Hepart	Tryptophan (L-) (H1053)	15000443	80582†	20

- 27 995 spectra from a total of 615 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Unisan	Tryptophan (L-) (H1053)	27901	2
Unisan/Hepart AG	Tryptophan (L-) (H1053)	27901	1
Hepart AG	Tryptophan (L-) (H1053)	27901	4
Hepart AG, CH-8280 Kreu...	Tryptophan (L-) (H1053)	27901	1
Unisan	Tryptophan (L-) (H1053)	27902	2
Unisan	Tryptophan (L-) (H1053)	1824025011	1
Hepart AG	Tryptophan (L-) (H1053)	27902	1
Hepart AG	Tryptophan (L-) (H1053)	1824025011	1
Hepart AG	Tryptophan (L-) (H1053)	1824027901	2
Unisan	Tryptophan (L-) (H1053)	1824950001	2
Unisan	Tryptophan (L-) (H1053)	950001	1
Purren Apotheke	Tryptophan (L-) (H1053)	978501	1
Purren Apotheke	Tryptophan (L-) (H1053)	1825950001	1

- 1586 spectra from 20 *Apo-Ident* customers from a total of 594 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	200	0	14 414
Type B	0	40	170	27 995
Type C	0	6	21	1586

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 % (> 99.9132 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8996 %)	19.0476 % (> 17.6190 %)
Type C	100.0000 % (> 98.9825 %)	22.2222 % (> 11.1111 %)

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
80401	80401	0.00	61.02
80581	80581	0.00	69.38
80582	80582	0.00	71.97
80845	80845	0.00	57.71
80846	80846	0.00	66.20

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Tyrosine (L-) (H1054)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80121-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Tyrosine (L-) (H1054)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Tyrosine (L-) (H...	074601	80386	80	from supplier
Hepart	Tyrosine (L-) (H...	15001380	80704	40	from supplier

Validation samples

A total of 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *Tyrosine (L-) (H1054)*. These samples are listed above in the *calibration samples* section.

- 14 494 spectra from a total of 320 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Tyrosine (L-) (H1054)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Tyrosine (L-) (H1054)	pending	80059	30
Hepart	Tyrosine (L-) (H1054)	979102	80121	50
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

- 28 005 spectra from a total of 616 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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)	29501	4
Unisan	Tyrosine (L-) (H1054)	29502	5
Hepart AG	Tyrosine (L-) (H1054)	29502	1
Unisan	Tyrosine (L-) (H1054)	74601/3	1
Unisan	Tyrosine (L-) (H1054)	979102	2
Unisan	Tyrosine (L-) (H1054)	1826029501	2
Hepart AG	Tyrosine (L-) (H1054)	74601	1
UNISAN	Tyrosine (L-) (H1054)	74601	1
Hepart AG	Tyrosine (L-) (H1054)	1827029501	1

- 1595 spectra from 20 *Apo-Ident* customers from a total of 600 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	120	0	14 494
Type B	0	40	160	28 005
Type C	0	3	15	1595

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 % (> 99.9138 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8996 %)	20.0000 % (> 18.5000 %)
Type C	100.0000 % (> 98.9887 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80386	80386	0.00	89.22
80704	80704	0.00	93.19

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Valine (L-) (H1056)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80145-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Valine (L-) (H1056)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 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 *Valine (L-) (H1056)*. These samples are listed above in the *calibration samples* section.

- 14 494 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 230 spectra of 7 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)	961101	80145	50
Hepart	Valine (L-) (H1056)	916201	80226	30
Hepart	Valine (L-) (H1056)	936701	80228	40
Hepart	Valine (L-) (H1056)	25012	80291	40
Hepart	Valine (L-) (H1056)	14001947	80520†	20
Hepart	Valine (L-) (H1056)	15001436	80670†	20

- 27 975 spectra from a total of 614 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Hepart AG	Valine (L-) (H1056)	1807025012	1
Unisan	Valine (L-) (H1056)	1806025012	2
Unisan	Valine (L-) (H1056)	15001436	1
Purren Apotheke	Valine (L-) (H1056)	1807936701	1
Unisan	Valine (L-) (H1056)	1807961101	1

- 1605 spectra from 20 *Apo-Ident* customers from a total of 601 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	120	0	14 494
Type B	0	127	103	27 975
Type C	0	4	4	1605

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 % (> 99.9138 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8996 %)	55.2174 % (> 53.9130 %)
Type C	100.0000 % (> 99.0118 %)	n/a (n/a)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80520	80520	0.00	71.46
80670	80670	0.00	73.65
80844	80844	0.00	65.28

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Vitamin B6 (H1103)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80074-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Vitamin B6 (H1103)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin B6 (H1103)	15000279	80550	40	from supplier
Hepart	Vitamin B6 (H1103)	14001576	80798	40	from supplier
Hepart	Vitamin B6 (H1103)	16001239	80886	40	from supplier

Validation samples

A total of 44 432 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 B6 (H1103)*. These samples are listed above in the *calibration samples* section.

- 14 494 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 200 spectra of 5 reference samples from the substance/substance group *Vitamin B6 (H1103)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin B6 (H1103)	960401	80074	30
Hepart	Vitamin B6 (H1103)	960401	80110	50
Hepart	Vitamin B6 (H1103)	938001	80192	40
Hepart	Vitamin B6 (H1103)	15000279	80550†	20
Hepart	Vitamin B6 (H1103)	15000279	80781	60

- 28 005 spectra from a total of 617 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

†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	Vitamin B6 (H1103)	20101	1
Unisan	Vitamin B6 (H1103)	25711	7
Hepart AG, CH-8280 Kreu…	Vitamin B6 (H1103)	25711	1
Hepart AG	Vitamin B6 (H1103)	25711	1
Unisan	Vitamin B6 (H1103)	14001576/2	1
Euro OTC	Vitamin B6 (H1103)	15000279/1	1
Unisan	Vitamin B6 (H1103)	1552020101	1
Hepart AG, Unisan GmbH	Vitamin B6 (H1103)	15000279/0	1
Unisan	Vitamin B6 (H1103)	1554025711	1
Hepart AG	Vitamin B6 (H1103)	1552025711	1
Purren Apotheke	Vitamin B6 (H1103)	1554938001	1
Unisan	Vitamin B6 (H1103)	14001576	1
Hepart AG	Vitamin B6 (H1103)	1554020101	1
Unisan	Vitamin B6 (H1103)	15000279/2	1
Hepart AG, CH-8280 Kreu…	Vitamin B6 (H1103)	1552025711	1

- 1592 spectra from 20 *Apo-Ident* customers from a total of 595 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	120	0	14 494
Type B	0	78	122	28 005
Type C	0	10	11	1592

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 % (> 99.9138 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8996 %)	39.0000 % (> 37.5000 %)
Type C	100.0000 % (> 98.9861 %)	47.6190 % (> 33.3333 %)

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
80550	80550	0.00	68.98
80798	80798	0.00	61.47
80886	80886	0.00	69.92

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Vitamin C (H1104)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80009-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Vitamin C (H1104)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin C (H1104)	044502	80363	40	from supplier
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

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 600 spectra of 15 reference samples from the substance/substance group *Vitamin C (H1104)*. These samples are listed above in the *calibration samples* section.

- 14 014 spectra from a total of 308 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 859 spectra of 22 reference samples from the substance/substance group *Vitamin C (H1104)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin C (H1104)	946901	80009	40
Hepart	Vitamin C (H1104)	960901	80076	29
Hepart	Vitamin C (H1104)	946901	80112	50
Hepart	Vitamin C (H1104)	960901	80123	50
Hepart	Vitamin C (H1104)	13201	80161	50
Hepart	Vitamin C (H1104)	13202	80229	40
Hepart	Vitamin C (H1104)	44501	80296	40
Hepart	Vitamin C (H1104)	25020	80304	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

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin C (H1104)	16000198	80753†	20
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

- 27 346 spectra from a total of 600 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 67 spectra from 12 *Apo-Ident* customers from 26 batches from the substance/substance group *Vitamin C (H1104)*.

Supplier	Substance	Batch	Spectra
unisan	Vitamin C (H1104)	14001794	1
unbekannt	Vitamin C (H1104)	16000199	1
unbekannt	Vitamin C (H1104)	16000200	1
unbekannt	Vitamin C (H1104)	16000197	1
unbekannt	Vitamin C (H1104)	16000198	1
Unisan	Vitamin C (H1104)	16000198	1
unbekannt	Vitamin C (H1104)	16000201	1
Unisan	Vitamin C (H1104)	14001797	1
unbekannt	Vitamin C (H1104)	16000229	1
unbekannt	Vitamin C (H1104)	16000203	1
unbekannt	Vitamin C (H1104)	16000202	1
unbekannt	Vitamin C (H1104)	16000231	1
Unisan	Vitamin C (H1104)	44501	7
Unisan	Vitamin C (H1104)	25020	2
unbekannt	Vitamin C (H1104)	16000230	1
Hepart AG	Vitamin C (H1104)	44501	3
Unisan/Hepart AG	Vitamin C (H1104)	44501	1
Unisan Gmbh, 78465 Kons…	Vitamin C (H1104)	25020	1
Unisan	Vitamin C (H1104)	44502	4
Unisan	Vitamin C (H1104)	44601	1
Fagron	Vitamin C (H1104)	44502	1
Hepart AG	Vitamin C (H1104)	44502	3
Hepart AG	Vitamin C (H1104)	44601	2
Unisan/Hepart AG	Vitamin C (H1104)	44602	2
Unisan	Vitamin C (H1104)	73901	3
Hepart AG	Vitamin C (H1104)	73901	3
Falcento	Vitamin C (H1104)	44602	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	1
Unisan	Vitamin C (H1104)	74001	2
Unisan	Vitamin C (H1104)	74201	2
Hepart AG, CH-8280 Kreu…	Vitamin C (H1104)	1084025019	1
Unisan	Vitamin C (H1104)	1085025020	5
Unisan	Vitamin C (H1104)	1084025020	1
Hepart AG	Vitamin C (H1104)	1084025020	3
Unisan	Vitamin C (H1104)	74101	1
Hepart AG	Vitamin C (H1104)	1085025020	2
Unisan	Vitamin C (H1104)	14001780/0	1
Unisan	Vitamin C (H1104)	14001788	1

- 1546 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 *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	600	0	14 014
Type B	0	788	71	27 346
Type C	0	53	14	1546

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 % (> 99.9127 %)	100.0000 % (> 99.0000 %)
Type B	100.0000 % (> 99.8993 %)	91.7346 % (> 91.3853 %)
Type C	100.0000 % (> 98.9752 %)	79.1045 % (> 74.6269 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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
80363	80363	0.00	52.92
80394	80394	0.00	32.13
80395	80395	0.00	30.09
80396	80396	0.00	45.41
80397	80397	0.00	29.11
80418	80418	0.00	45.23
80438	80438	0.00	54.44
80499	80499	0.00	30.72
80500	80500	0.00	32.40
80501	80501	0.00	34.45
80502	80502	0.00	48.88
80751	80751	0.00	49.88
80753	80753	0.00	53.58
80756	80756	0.00	50.87
80760	80760	0.00	49.80

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Vitamin complex (H1100)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80073-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

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

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin complex …	14001589	80486	40	from supplier
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 44 432 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.

- 13 974 spectra from a total of 306 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin complex (H1100)	15001276(B1)	80637†	20
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

- 27 200 spectra from a total of 594 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 69 spectra from 13 *Apo-Ident* customers from 27 batches from the substance/substance group *Vitamin complex (H1100)*.

Supplier	Substance	Batch	Spectra
Unisan	Vitamin complex (H1100)	74101	1
Unisan	Vitamin complex (H1100)	77201	3
Hepart AG	Vitamin complex (H1100)	77201	3
Unisan	Vitamin complex (H1100)	77001	1
Unisan	Vitamin complex (H1100)	14001589	1
Unisan/Hepart AG	Vitamin complex (H1100)	48301	1
Unisan	Vitamin complex (H1100)	1400159/0	1
Unisan	Vitamin complex (H1100)	16000958/0	1
Unisan	Vitamin complex (H1100)	14001590/1	1
Unisan	Vitamin complex (H1100)	15001277/0	1
Unisan	Vitamin complex (H1100)	25101	1
Unisan	Vitamin complex (H1100)	15001275/0	1
Unisan	Vitamin complex (H1100)	25201	1
Hepart AG	Vitamin complex (H1100)	49201	4
Unisan	Vitamin complex (H1100)	49201	2
Unisan	Vitamin complex (H1100)	15001276/0	1
Hepart AG	Vitamin complex (H1100)	49202	5
Hepart AG, CH-8280 Kreu…	Vitamin complex (H1100)	49301	5

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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/Hepart AG	Vitamin complex (H1100)	49201	1
Unisan	Vitamin complex (H1100)	14001590/0	1
Unisan	Vitamin complex (H1100)	49202	2
Unisan	Vitamin complex (H1100)	49301	8
Hepart AG	Vitamin complex (H1100)	49301	7
unisan	Vitamin complex (H1100)	49302	1
Unisan	Vitamin complex (H1100)	49302	2
Hepart AG	Vitamin complex (H1100)	1014025101	1
Hepart AG, CH-8280 Kreu…	Vitamin complex (H1100)	1014025101	1
Unisan	Vitamin complex (H1100)	1014009901	1
Unisan	Vitamin complex (H1100)	1014025301	1
Unisan	Vitamin complex (H1100)	1014025401	1
hepart ag	Vitamin complex (H1100)	1015954801	2
hepart ag	Vitamin complex (H1100)	10159548011	1
Unisan	Vitamin complex (H1100)	H110031	2
Unisan	Vitamin complex (H1100)	4966901	1
Hepart AG	Vitamin complex (H1100)	1014025301	1
Unisan	Vitamin complex (H1100)	904006	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 *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	13 974
Type B	0	957	48	27 200
Type C	0	66	3	1544

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 % (> 99.9126 %)	100.0000 % (> 99.0625 %)
Type B	100.0000 % (> 99.8993 %)	95.2239 % (> 94.9254 %)
Type C	100.0000 % (> 98.9751 %)	95.6522 % (> 91.3043 %)

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	47.61
80411	80411	0.00	47.73
80431	80431	0.00	48.61
80432	80432	0.00	45.67
80485	80485	0.00	47.09
80486	80486	0.00	50.55
80487	80487	0.00	49.06
80637	80637	0.00	49.48
80638	80638	0.00	50.54
80640	80640	0.00	50.68
80642	80642	0.00	49.25
80643	80643	0.00	49.11
80646	80646	0.00	49.30
80647	80647	0.00	50.75
80648	80648	0.00	49.21
80827	80827	0.00	49.86

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Vitamin E NAT (H1107)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80010-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

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

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin E NAT (H...	15001558	80688	40	from supplier
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 44 432 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.

- 14 179 spectra from a total of 311 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin E NAT (H1107)	15001558	80688†	20
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

- 26 885 spectra from a total of 595 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 48 spectra from 13 *Apo-Ident* customers from 20 batches from the substance/substance group *Vitamin E NAT (H1107)*.

Supplier	Substance	Batch	Spectra
Unisan	Vitamin E NAT (H1107)	71501	5
UNISAN	Vitamin E NAT (H1107)	71701	1
Unisan	Vitamin E NAT (H1107)	71701	2
Unisan 2.10.2015	Vitamin E NAT (H1107)	14001821/0	1
Unisan	Vitamin E NAT (H1107)	14001821	1
HCK	Vitamin E NAT (H1107)	14001822/0	1
Unisan	Vitamin E NAT (H1107)	14001821/0	1
Unisan	Vitamin E NAT (H1107)	65001	5
Unisan 02.04.2016	Vitamin E NAT (H1107)	15001558/0	1
Unisan	Vitamin E NAT (H1107)	15001659/0	1
Unisan	Vitamin E NAT (H1107)	15001558	1
Hepart	Vitamin E NAT (H1107)	16000591/0	1
Hepart	Vitamin E NAT (H1107)	160005910	1
Unisan	Vitamin E NAT (H1107)	17901	1
Purren Apotheke	Vitamin E NAT (H1107)	945901	1
Unisan	Vitamin E NAT (H1107)	25021	1
Unisan	Vitamin E NAT (H1107)	25022	10
Hepart AG	Vitamin E NAT (H1107)	25022	2
Hepart AG, CH-8280 Kreu…	Vitamin E NAT (H1107)	65001	1
Hepart AG	Vitamin E NAT (H1107)	65101	3
Unisan	Vitamin E NAT (H1107)	1094017701	1
Hepart AG, CH-8280 Kreu…	Vitamin E NAT (H1107)	1094017701	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)	1094025021	2
Hepart AG	Vitamin E NAT (H1107)	1094025021	1
Unisan	Vitamin E NAT (H1107)	1095961301	1
Hepart AG	Vitamin E NAT (H1107)	1094025022	1

- 1565 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 *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	14 179
Type B	0	1320	0	26 885
Type C	0	48	0	1565

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 % (> 99.9128 %)	100.0000 % (> 98.6207 %)
Type B	100.0000 % (> 99.8993 %)	100.0000 % (> 99.5455 %)
Type C	100.0000 % (> 98.9772 %)	100.0000 % (> 87.5000 %)

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	20.02
80426	80426	0.00	21.15
80512	80512	0.00	22.91
80513	80513	0.00	21.60
80514	80514	0.00	21.00
80688	80688	0.00	28.16
80690	80690	0.00	26.52
80693	80693	0.00	28.01
80694	80694	0.00	26.37
80697	80697	0.00	28.94
80826	80826	0.00	20.88

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

VALIDATION REPORT

IdentModul 1.3-2017-06

Validated substance/substance group	**Zinc (H1110)**
Substance class	HCK - nutritional supplements (Hepart)
Report date	17/11/2017
Report number	80011-2017-11-17
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* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*
Anhang F	Zusatz zu den Modellen der zweiten Stufe

Validation method

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

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

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

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

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Zinc (H1110)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 44 432 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Zinc (H1110)*. These samples are listed above in the *calibration samples* section.

- 14 494 spectra from a total of 319 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 †.

- 430 spectra of 11 reference samples from the substance/substance group *Zinc (H1110)*.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Zinc (H1110)	949701	80011	40
Hepart	Zinc (H1110)	pending	80018	40
Hepart	Zinc (H1110)	991001	80100	50
Hepart	Zinc (H1110)	949701	80143	50
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

- 27 775 spectra from a total of 611 batches from further 100 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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
Hepart AG	Zinc (H1110)	1164991001	4
Unisan	Zinc (H1110)	99101	2
Unisan	Zinc (H1110)	1164949701	1
Unisan	Zinc (H1110)	1164991001	3
Unisan	Zinc (H1110)	14001753	1
Hepart AG, CH-8280 Kreu…	Zinc (H1110)	1164991001	1
Unisan	Zinc (H1110)	14001803	3
Unisan	Zinc (H1110)	14001753/0	1
Hepart AG	Zinc (H1110)	991001	3
Unisan	Zinc (H1110)	14001803/1	1
Unisan Gmbh, 78465 Kons…	Zinc (H1110)	991001	1
Unisan	Zinc (H1110)	16000196	1
unbekannt	Zinc (H1110)	16000196	1

- 1559 spectra from 20 *Apo-Ident* customers from a total of 596 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	120	0	14 494
Type B	0	396	34	27 775
Type C	0	30	24	1559

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 % (> 99.9138 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8994 %)	92.0930 % (> 91.3953 %)
Type C	100.0000 % (> 98.9764 %)	55.5556 % (> 50.0000 %)

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
80503	80503	0.00	13.45
80761	80761	0.00	11.10
80789	80789	0.00	13.22

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

Appendix A: Additional calibration samples (*Type A*)

Not required.

Appendix B: Additional validation samples (*Type B*)

It is necessary that spectra also enter the validation which cannot be identified with this model. In this manner, it is verified that the model also rejects unknown substances. The spectra for these samples were recorded by *HiperScan GmbH*. They are allocated to the *Type B*. They also include the calibration spectra for other models.

The samples originate from 55 batches. From these 2398 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)	048401	40	from supplier
Hepart	Guar (H1023)	048501	40	from supplier
Hepart	Guar (H1023)	703603	50	from supplier
Hepart	Guar (H1023)	073701	40	from supplier
Hepart	Guar (H1023)	130514-GG3	40	from supplier
Hepart	Guar (H1023)	699304	50	from supplier
Hepart	Guar (H1023)	130506-GG1	40	from supplier
Hepart	Guar (H1023)	048502	40	from supplier
Hepart	Guar (H1023)	048001	40	from supplier
Hepart	Guar (H1023)	701401	50	from supplier
Hepart	Guar (H1023)	130513-GG2	40	from supplier
Hepart	Guar (H1023)	970001	30	from supplier
Hepart	Guar (H1023)	048402	40	from supplier
Hepart	Guar (H1023)	130514-GG5	48	from supplier
Hepart	Guar (H1023)	130514-GG4	40	from supplier
Hepart	Histamine block ...	16001078	39	from supplier
Hepart	Histamine block ...	16001079	40	from supplier
Hepart	Melatonin (H1061)	069101	60	from supplier
Hepart	Melatonin (H1061)	069101	60	from supplier
Hepart	Omega-3-fish oil...	30011403	30	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	748901	60	from supplier
Hepart	Orthovimin B w. ...	699308	50	from supplier
Hepart	Orthovimin B w. ...	706303	50	from supplier
Hepart	Orthovimin B w. ...	700208	50	from supplier
Hepart	Probiotic capcon	12-01	40	from supplier
Hepart	Proline (-L) (H1...	066401	60	from supplier
Hepart	Proline (-L) (H1...	pending	30	from supplier
Hepart	Proline (-L) (H1...	025707	40	from supplier
Hepart	Proline (-L) (H1...	596805	50	from supplier
Hepart	Proline (-L) (H1...	0695301	50	from supplier
Hepart	Proline (-L) (H1...	707801	40	from supplier
Hepart	Proline (-L) NF ...	16000951	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	Silicium (H1070)	17000326	40	from supplier
Hepart	TopFlora multi f...	15001135	60	from supplier
Hepart	Vegetable proteins	041001	40	from supplier
Hepart	Vitamin K2 (75μg...	16001559	40	from supplier

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Supplier	Substance	Batch	Spectra	Certificate
Hepart	Vitamin K2-Ca-Mn…	069001	50	from supplier
Hepart	Vitamin K2-Ca-Mn…	15000836	60	from supplier
Hepart	Vitamin K2-Ca-Mn…	15000836	60	from supplier
Hepart	Vitamin K2-Ca-Mn…	16000403	60	from supplier
Hepart	Vitamins BAG (H1…	14000037	40	from supplier
Hepart	Vitamins BAG (H1…	952201	30	from supplier
Hepart	Walnut leaf (H11…	16001149	40	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 5 batches. From these, 9 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
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
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).

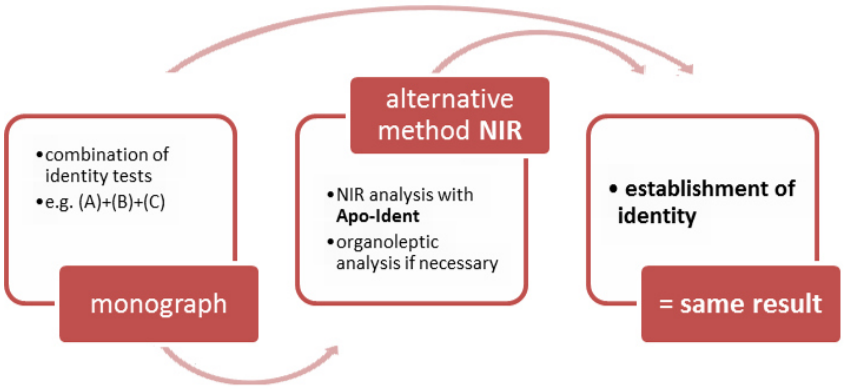

Figure 2: The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

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].

Anhang F: Zusatz zu den Modellen der zweiten Stufe

Wie im allgemeinen Teil der Validierungsdokumentation des *Apo-Ident* im Abschnitt Ablauf von Modellerstellung und Validierungsläufen unter *2. Generieren der chemometrischen Modelle (Kalibrierung)* in *f)* beschrieben, besteht die Möglichkeit für bestimmte Substanzen ein weiteres *chemometrisches Modell* zu erstellen (Zweite-Stufe-Modell) und die Bewertung in mehreren Stufen vorzunehmen.

Substanzen in Stufe-Zwei-Modellen

Im *Apo-Ident Update 2017-06* werden folgende Substanzen in den aufgeführten Stufe-Zwei-Modellen differenziert:

Submodell 1

Betamethason, mikronisiert
Betamethasonvalerat
Budesonid, mikronisiert
Dexamethason
Erythromycin
Hydrocortisonbutyrat
Norethisteronacetat
Prednicarbat, mikronisiert
Prednisolon, mikronisiert
Triamcinolonacetonid

Submodell 2

Beclometasondipropionat, wasserfreies
Betamethasondipropionat, mikronisiert
Clobetasolpropionat
Diphenylcyclopropenon
Gentamicinsulfat
Natriumbenzoat
Natriumcitrat
Oxybutyninhydrochlorid

Submodell 3

Alfatradiol
Chininhydrochlorid
Chininsulfat Dihydrat
Estriol
Pregnenolon
Progesteron, mikronisiert
Spironolacton
Testosteronpropionat

Submodell flüssig

2-Ethylhexyllaurat
Basiscreme DAC
Hydrophile Creme, nichtionisch DAB
Lanette®-Salbe (konserviert)
Squalan
Wollwachsalkoholcreme DAB/SR

References

[1] ABDA – Bundesvereinigung Deutscher Apothekerverbände: Verordnung über den Betrieb von Apotheken (Apothekenbetriebsordnung – ApBetrO), 2012

[2] Reimann, B. ; Regierungspräsidium Darmstadt: Hinweise zur ordnungsgemäßen Prüfung von Arzneimitteln und Ausgangsstoffen (§§ 6 und 11 *ApBetrO*), 2007

[3] *Europäisches Arzneibuch, Grundwerk 2014 einschließlich 1. bis 4. Nachtrag.* 8. Ausgabe. Deutscher Apotheker Verlag (978-3-7692-6508-8)

[4] HiperScan GmbH: Erfüllung von 2.2.40 Ph. Eur. durch Apo-Ident, 2013

[5] Arbeitsgemeinschaft der Pharmazieräte Deutschlands (APD): Resolution in Verbindung mit §§ 6 und 11 *ApBetrO* Verwendung eines Nah-Infrarot-Spektrometers (NIR) zur Identitätsprüfung, 16. 10. 2013, DAZ 48, November 2013

[6] Arbeitsgemeinschaft der Pharmazieräte Deutschlands (APD): Resolution 2014, Arbeitsgemeinschaft der Pharmazieräte Deutschlands (APD), Oktober 2014

[7] *DAC/NRF.* Govi-Verlag (978-3-7741-0044-2)

[8] Kessler, W.: *Multivariate Datenanalyse.* WILEY-VCH Verlag, 2007 (978-3-527-31262-7)

[9] Næs, T. ; Isaksson, T. ; Fearn, T. ; Davies, T.: *Multivariate Calibration and Classification.* NIR Publications, 2002 (978 0 9528666 2 6)

[10] Hanley, J. A. ; Lippman-Hand, A.: If nothing goes wrong, is everything all right? In: *Journal of the American Medical Association* 249 (1983), S. 1743–1745

[11] Jovanovic, B. D. ; Levy, P. S.: A Look at the Rule of Three. In: *The American Statistician* 51 (1997), S. 137–139

[12] Bronstein, I. N. ; Semendjajew, K. A. ; Musiol, G. ; Mühlig, H.: *Taschenbuch der Mathematik.* 5. überarbeitete und erweiterte Auflage. Verlag Harri Deutsch, 2000 (3-8171-2015-2)

[13] Mahalanobis, P.: On the generalized distance in statistics. In: *Proc. Nat. Inst. Sci. India (Calcutta)* 2 (1936), S. 49–55

[14] Yambor, B. ; Draper, W. ; Beveridge, R.: Analyzing PCA-based face recognition algorithms: Eigenvector selection and distance measures. In: *Second Workshop Empirical Evaluation in Computer Vision* (2000)

[15] HiperScan GmbH: Identifikationsmethodik Apo-Ident, 2012

[16] HiperScan GmbH: Datenvorbehandlung des Identifikationssystems Apo-Ident, 2012

[17] Cyran ; Rotta: Apothekenbetriebsordnung, Kommentar § 6 Rn. 10, 2010

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