

Validation documentation  
*HCK - nutritional supplements (Hepart)*

HiperScan GmbH

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## Introduction

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

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

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

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

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

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

## Context of this document

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

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

## Criteria for the inclusion of substances

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 core statement of this validation report is that the following criteria must be fulfilled for each database entry, so that *Apo-Ident* offers verification of identity by means of NIR for the relevant substance/substance group:

- The database is exclusively generated from spectra which have been recorded by *HiperScan GmbH* on traceable samples in pharmaceutical quality.
  - The samples are procured via typical pharmacy sources (*DAC III.2.: Bezugsquellennachweis für Rezepturbestandteile [reference source for prescription components]* [7]).
  - A valid manufacturer's certificate exists (content, purity and identity of the batch).
  - The identity was confirmed by a certified test laboratory or *HiperScan GmbH*.
- Each version of the reference database (every update) is validated in-full.
  - Calibration spectra (*Type A*), other spectra recorded under the control of *HiperScan GmbH* (*Type B*), and spectra from the field (*Type C*) are presented to the *IdentModule* for evaluation in three separately evaluated validation runs.
  - Here, no single *false positive* result may arise.
  - Here, the various substance classes are also tested for reciprocal rejection, where this is objectively justified (see *Summary* section).
- In the validation with spectra recorded under the control of *HiperScan GmbH*, spectra of at least one independent sample must be considered, i.e. spectra from a batch whose spectra have not been used for the generation of the database. In addition, the set of *Type A* and *Type B* spectra must originate from at least three different batches.
- Spectra of additional substances may be used for the generation of the database even though they will not be offered for identification by this database. The purpose is the reliable distinction from these substances.

- Any positive result of *Apo-Ident* confirms the identity of the substance/substance group and distinguishes it from all other substances of the database. In the case of substance groups, the result is ambiguous: Distinction from all substances not belonging to the group is proven. The substance is identified as a member of this group. However, within the substance group, it is not possible to reliably classify which substance has been tested.
- The criteria for clear identifiability are a [specificity](#) of 100 % ([true negative rate](#)) and a minimum distance in the distance matrix. See 2. d) under [Model creation procedure and validation runs](#).

## Validation concept

[Chemometrics](#) is a statistical technique for the extraction of relevant chemical information from spectra. In mathematics, this method is described as *multivariate data analysis*. Chemometrics proceeds here as follows:

1. Collection of spectra for the *calibration sample*. The results (identities) of the calibration sample must be known. The calibration samples must be representative for the samples which are to be evaluated later. Therefore, they must take the various possible (physical) compositions into account. (Therefore, sourcing calibration samples for NIR from the specialist trade is superior to the use of CRS reference substances.)
2. The first mathematical step is *calibration*. Here, the [chemometric model](#) is calculated from the *calibration sample spectra* ([reference spectra](#)) and limits as well as some parameters are stipulated. The chemometric model is used later to calculate the analysis result (*prediction*).
3. Collection of further spectra for the *validation sample* which should be independent of the *calibration sample*. The results (identities) of the *validation sample* must also be known. The textbook suggests a random sample with a normal scope of 25 % to 50 % of the *calibration sample* [8].
4. The second technical data step is *validation*. Here, the [chemometric model](#) created is evaluated based on the spectra of the *validation samples*. As validation parameters for the identification, the *Ph. Eur. Section 2.2.40* [3] specifies the [specificity](#) and [robustness](#).

The validation step according to the textbook has the target of estimating the performance capability of the model created based on a random sample. In order to achieve the best possible precision, attention is paid to the calibration sample. In the field of pharmaceuticals, the safety of the method has priority. In order to be able to [validate](#) the model within the regulatory scope, the validation step must include probative force. For this purpose, the validation sample must be *representative and complete* in order to enable the testing of all cases.

A *sufficient number of batches* must be secured for validation because validation finally proves whether the number of batches in calibration suffices.

Each substance is validated individually. The validation results are documented per substance in this document. Moreover, the documents show how many and which batches have been used for creating the model or model validation.

At least one certificate is taken in for each substance from an accredited test laboratory for the independent testing of identity of the sample. The identification number of the corresponding test certificate is listed in the report, enabling traceability of a substance tested according to the monographs in the Pharmacopoeia.

## Model creation procedure and validation runs

The safety of the [chemometric models](#) is guaranteed by several measures during model creation, of which the validation step is the final one. Normally, the procedure is as follows. It is in particular valid for the active pharmaceutical ingredients (APIs) *solid API excipients, liquid/semi-solid API excipients (with a test certificate), narcotics - solid medicinal substances and drugs*. If, for individual substance classes, variations are required, they are depicted in the section [Particularities of individual substance classes](#).

## 1. Collecting the reference spectra (calibration sample)

- a) Procurement of the samples from the same sources from which pharmacies source their raw material for compounding (Caelo, Fagron, Euro-OTC, . . . , see also *DAC III.2. Bezugsquellen-nachweis für Rezepturbestandteile* [Sources of supply for compounding] [7]).
- b) Testing the suitability according to *ApBetrO* [Pharmacies Rules and Regulations] §§ 6, 11, that is to say the availability of a valid manufacturer certificates via identity, purity and contents of the batch.
- c) Recording standard 40 spectra of the sample in different positions, as a standard on four instruments. Here, handling and presentation of the samples as later in the pharmacy.
- d) Visual checking for anomalies in the spectra. In case of indications of measurement errors, measurement must be repeated. If a signature is missing in the spectrum, the substance may be excluded from the start as not promising (the spectra are nonetheless entered in the database validation as independent *Type B* spectra).
- e) Testing identity. For each substance, a certificate of correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the respective following substance page of this validation documentation the *Mahalanobis distance* to this reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance. Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

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

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

## 2. Generating the chemometric models (calibration)

- a) Determination of the transformation matrix from the reference spectra using variance maximisation [8, 9]. (All reference spectra are always included, even if only a few spectra are added for an update.) All reference spectra receive the same data pre-treatment, which is also later applied to all measurement spectra in the field (in the pharmacies).
- b) Checking that the number of principal components used is still sufficient.
- c) Calculating the limits for each substance from the spread of the reference spectra. The calculation regulation is identical for each substance in a substance class.
- d) 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 generated. These also include spectra from substances which the *chemometric model* should not identify, but were also recorded during generation in order to increase selectivity. (As a result, the model “learns” to differentiate from other substances which are actually unknown to it.)
- b) *Type B*: Spectra recorded under the control of *HiperScan GmbH* and not used for the generation of the database. These also include reference spectra of other substance classes, and spectra that are not used as reference spectra. Samples are considered to be independent, if they originate from a batch, of which no spectra have been used for the generation of the database. (Up to *IdentModule 2018-01*, samples were still considered independent if the sampling was done independently, i.e. if they originate from another sales container.)
- c) *Type C*: Spectra from the field, which have not been recorded under the control of *HiperScan GmbH* and have not been used for the generation of the database. The spectra include not only substances of the substance class to be tested, but also substances from other classes.

All manufacturers’ batches from which spectra are used for the validation are listed by substance in this document: for substances included in the substance class *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 error in the spectrum can be proven. Here, the spectra are not deleted, but instead placed on a *blacklist* incorporating the reason, date and initials in the commentary.

The section *Particularities of individual substance classes* treats the other substance classes from which *Type B* and *Type C* spectra are cited for validation purposes.

### 4. Validation runs and approval

- a) Validation spectra are transferred holistically to the *IdentModule* for evaluation in the same way as the spectroscopy software *QuickStep* transfers measured spectra.
- b) Following the provision of each spectrum, the *IdentModule* responds as to whether it has recognised a substance and which substance was recognised.
- c) The correctness of this response is checked for each possible initial assumption (each measurable substance with the substance class) and counted according to *true negative*, *false negative*, *true positive* and *false positive*. These figures are provided for each substance and additionally in the section *Summary*, separated according to types *A*, *B* and *C*.
- d) No *false positive* results whatsoever are permissible.
- e) If the criterion is also met for all substance classes, the *IdentModule* is approved.

### Particularities of individual substance classes

Basically, *HiperScan GmbH* procures and tests the manufacturer’s certificate for the batch, commissions external testing of the identity of the sample or carries it out independently and stores the certificates. As described, this process is established for the Pharmacopoeia substances, that is to say for substance classes **APIs & excipients, solid**, **APIs & excipients, liquid/semi-solid (with analysis certificate)**, **Narcotic substances, liquid/semi-solid** and **Drugs**. Therefore, *HiperScan GmbH* is able to furnish proof of the identity of the reference samples. In case of manufacturer-specific substance classes and others, individual steps are organised differently in-part:

The substance class **APIs & excipients, liquid/semi-solid (other)** (often described as cosmetics) incorporates substances for which no specification of the requirements of the pharmaceutical quality is determined, neither in a Pharmacopoeia monograph, a DAC/NRF monograph nor via a manufacturer’s specification. Consequently, neither the identity nor contents can be tested independently. No certificates whatsoever exist for the reference samples. So here, merely the matching of the sample with former samples of this product is established and confusion with the other substances

is ruled-out. (If the manufacturer of such a substance prepares a specification, determines testing methods and provides manufacturer's certificates in accordance with *ApBetrO* [Pharmacies Rules and Regulations] §§ 6, 11, *HiperScan GmbH* can assign the substance to the substance class *APIs & excipients, liquid/semi-solid (with analysis certificate)* again in the future).

Substance class **HCK – nutritional supplements (Hepart)** contains the HCK micro-nutrients from the Swiss company *Hepart AG*. *HiperScan GmbH* receives the reference samples directly from the manufacturer. For each reference sample, *HiperScan GmbH* also receives manufacturer's certificates and keeps these. New checking of the identity of the reference sample is not carried out by *HiperScan GmbH*. The identity of the reference samples is therefore documented by *Hepart AG*. The spectra of all batches provided by *Hepart AG* are recorded by *HiperScan GmbH* and entered in the database.

All the manufacturer's batches are used for the generation and validation of the substance class *HCK*. The expected variation is also represented in the generation and validation if there are less than three batches.

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

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

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

If, for example 14000 spectra not belonging to the substance are presented and no *false positive* classification is made, a hypothetical number of three *false positive* results is assumed (*Rule of Three* [10, 11]) and the *specificity* is defined with 100.0000 % (> 99.9786 %). Here, it applies that the higher the number of validation spectra which form the statistical basis, the better the *specificity* calculated via the lower *specificity* limit will be approximated.

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

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

## Significance of testing with *Apo-Ident*

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

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

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

1. The spectrum of the sample measured matches spectra of the defined substance.

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

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

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

## Conclusion

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

## Explanation of terminology

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

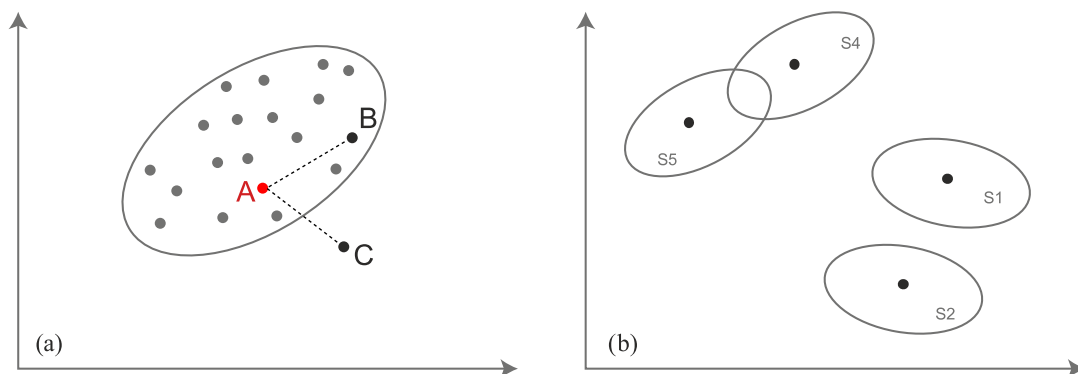


**Figure 1:** (a) The *Mahalanobis distance* from *A* to *B* is less than from *A* to *C*. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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

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

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

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

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

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

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

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



## Summary

A total of 49 390 spectra from 1461 different batches for a total of 123 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) | 76         | 336     | 15 224  |

From category *A* a total of 15 224 spectra from 336 batches for a total of 76 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) | 122        | 747     | 32 377  |

From category *B* a total of 32 377 spectra from 747 batches for a total of 122 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) | 62         | 690     | 1789    |

From category *C* a total of 1789 spectra from 690 batches for a total of 62 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              | 15 224        | 0              | 901 552       |
| Type B | 0              | 22 780        | 6117           | 1 919 560     |
| Type C | 0              | 1270          | 490            | 103 786       |

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 73 %) | 100.000 00 % (> 99.923 93 %) |
| Type B | 100.000 00 % (> 99.998 73 %) | 70.133 54 % (> 70.091 17 %)  |
| Type C | 100.000 00 % (> 99.980 43 %) | 57.041 88 % (> 56.733 84 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 1.3-2018-04

Validated substance/substance group **Amino V complex (H1400)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80745-2018-07-18  
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 |
|----------|-----------|-------|-----------|---------|-------------|
|----------|-----------|-------|-----------|---------|-------------|

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

### Type A All calibration spectra.

- 0 spectra of 0 reference samples from the substance/substance group *Amino V complex (H1400)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 0 different batches.
- 15 544 spectra from a total of 343 batches from further 77 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

### Type B Spectra recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 0 spectra from 0 reference samples of the substance/substance group *Amino V complex (H1400)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 33 057 spectra from a total of 736 batches from further 123 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Amino V complex (H1400)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.

- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 0             | 0              | 15 224        |
| <b>Type B</b> | 0              | 0             | 0              | 32 273        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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 |
|---------------|--------------------------|------------------|
| <b>Type A</b> | 100.0000 % (> 99.9245 %) | n/a (n/a)        |
| <b>Type B</b> | 100.0000 % (> 99.9262 %) | n/a (n/a)        |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)        |

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

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



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Aminomix NAC (H1002)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80003-2018-07-18  
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 |

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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 50 390 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 section [calibration samples](#). The reference samples originate from 9 different batches.
- 15 124 spectra from a total of 334 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 1070 spectra from 26 reference samples of the substance/substance group *Aminomix NAC (H1002)*.
- These include spectra of independent samples from 18 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance            | Batch    | Sample ID | Spectra |
|----------|----------------------|----------|-----------|---------|
| Hepart   | Aminomix NAC (H1002) | 946501   | 80003     | 40      |
| Hepart   | Aminomix NAC (H1002) | 0971701  | 80024     | 40      |
| Hepart   | Aminomix NAC (H1002) | 0971701  | 80186     | 40      |
| Hepart   | Aminomix NAC (H1002) | 019101   | 80199     | 20      |
| Hepart   | Aminomix NAC (H1002) | 936401   | 80220     | 30      |
| Hepart   | Aminomix NAC (H1002) | 14000259 | 80408     | 40      |
| Hepart   | Aminomix NAC (H1002) | 041401   | 80457     | 40      |
| Hepart   | Aminomix NAC (H1002) | 15000295 | 80537     | 60      |

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| Supplier | Substance            | Batch         | Sample ID          | Spectra |
|----------|----------------------|---------------|--------------------|---------|
| Hepart   | Aminomix NAC (H1002) | 15000295 (B1) | 80538 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Aminomix NAC (H1002) | 15000320      | 80545 <sup>†</sup> | 20      |
| Hepart   | Aminomix NAC (H1002) | 15000321      | 80546 <sup>†</sup> | 20      |
| Hepart   | Aminomix NAC (H1002) | 15000321 (B1) | 80547              | 60      |
| Hepart   | Aminomix NAC (H1002) | 15000319      | 80548              | 60      |
| Hepart   | Aminomix NAC (H1002) | 15000319 (F2) | 80549 <sup>†</sup> | 20      |
| Hepart   | Aminomix NAC (H1002) | 17000771      | 80937              | 40      |
| Hepart   | Aminomix NAC (H1002) | 17000770      | 80947              | 40      |
| Hepart   | Aminomix NAC (H1002) | 17000769      | 80948              | 40      |
| Hepart   | Aminomix NAC (H1002) | 17000768      | 80949              | 40      |
| Hepart   | Aminomix NAC (H1002) | 17000767      | 80950              | 40      |
| Hepart   | Aminomix NAC (H1002) | 17000766      | 80951              | 40      |

- 31 987 spectra from a total of 711 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 41 spectra from 9 *Apo-Ident* customers from 18 batches from the substance/substance group *Aminomix NAC (H1002)*.
- These include spectra of independent samples from 15 batches, of which no spectra have been used for the generation of the database.

| Supplier          | Substance            | Batch      | Spectra |
|-------------------|----------------------|------------|---------|
| unisan            | Aminomix NAC (H1002) |            | 1       |
| Unisan            | Aminomix NAC (H1002) | 140000259  | 1       |
| Hepart AG         | Aminomix NAC (H1002) | 41401      | 3       |
| Unisan            | Aminomix NAC (H1002) | 14000258   | 4       |
| Unisan            | Aminomix NAC (H1002) | 14000259   | 1       |
| Unisan            | Aminomix NAC (H1002) | 15000295/0 | 3       |
| Unisan            | Aminomix NAC (H1002) | 1400258    | 2       |
| unisan            | Aminomix NAC (H1002) | 15000297   | 1       |
| Hepart AG         | Aminomix NAC (H1002) | 15000320   | 1       |
| Unisan            | Aminomix NAC (H1002) | 15000320   | 1       |
| Unisan            | Aminomix NAC (H1002) | 15000298/0 | 1       |
| Unisan 02.04.2016 | Aminomix NAC (H1002) | 15000320/0 | 1       |
| Unisan            | Aminomix NAC (H1002) | 15000320/0 | 1       |

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

continued from previous page

| Supplier                   | Substance            | Batch      | Spectra |
|----------------------------|----------------------|------------|---------|
| Euro OTC                   | Aminomix NAC (H1002) | 16001017/0 | 1       |
| Unisan                     | Aminomix NAC (H1002) | 16001017/0 | 1       |
| Hepart                     | Aminomix NAC (H1002) | 16001453/0 | 1       |
| Hepart AG                  | Aminomix NAC (H1002) | 16001452   | 1       |
| Unisan                     | Aminomix NAC (H1002) | 19101      | 1       |
| Unisan                     | Aminomix NAC (H1002) | 41401      | 3       |
| Unisan                     | Aminomix NAC (H1002) | 41402      | 5       |
| Unisan/Hepart AG           | Aminomix NAC (H1002) | 41402      | 1       |
| Hepart AG                  | Aminomix NAC (H1002) | 41402      | 2       |
| Hepart AG                  | Aminomix NAC (H1002) | 1054019101 | 2       |
| Hepart AG, CH-8280 Kreu... | Aminomix NAC (H1002) | 1054019101 | 1       |
| Unisan                     | Aminomix NAC (H1002) | 971701     | 1       |

- 1748 spectra from 20 *Apo-Ident* customers from a total of 666 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

## Validation results

The validation runs checked whether the substance/substance group *Aminomix NAC (H1002)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Aminomix NAC (H1002)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 420           | 0              | 15 124        |
| <b>Type B</b> | 0              | 992           | 78             | 31 987        |
| <b>Type C</b> | 0              | 28            | 13             | 1748          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9243 %) | 100.0000 % (> 98.5714 %) |
| <b>Type B</b> | 100.0000 % (> 99.9241 %) | 92.7103 % (> 92.4299 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8383 %) | 68.2927 % (> 60.9756 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 23.60                           |
| 80314     | 80314               | 0.00                         | 32.34                           |
| 80407     | 80407               | 0.00                         | 32.11                           |
| 80444     | 80444               | 0.00                         | 29.28                           |
| 80447     | 80447               | 0.00                         | 29.49                           |
| 80538     | 80538               | 0.00                         | 31.71                           |
| 80544     | 80544               | 0.00                         | 32.79                           |
| 80545     | 80545               | 0.00                         | 31.31                           |
| 80546     | 80546               | 0.00                         | 32.69                           |
| 80549     | 80549               | 0.00                         | 31.54                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Antibiosis forte complex (H1115)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80675-2018-07-18  
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 |
| Hepart   | Antibiosis forte... | 17001137 | 80912     | 40      | from supplier |

## Validation samples

A total of 50 390 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 forte complex (H1115)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 60 spectra from 2 reference samples of the substance/substance group *Antibiosis forte complex (H1115)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                       | Batch    | Sample ID          | Spectra |
|----------|---------------------------------|----------|--------------------|---------|
| Hepart   | Antibiosis forte complex (H1... | 15001169 | 80675 <sup>†</sup> | 20      |
| Hepart   | Antibiosis forte complex (H1... | 17001151 | 81019              | 40      |

- 32 997 spectra from a total of 734 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details

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

provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Antibiosis forte complex (H1115)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 60            | 0              | 32 997        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 90.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 141.24                          |
| 80912     | 80912               | 0.00                         | 104.19                          |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Antibiosis mite complex (H1113)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80898-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 160 spectra from 4 reference samples of the substance/substance group *Antibiosis mite complex (H1113)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| 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      |

- 32 897 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Antibiosis mite complex (H1113)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 157           | 3              | 32 897        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 98.1250 % (> 96.2500 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 37.36                           |
| 80903     | 80903               | 0.00                         | 39.45                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Argentum (H1116)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80674-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 20 spectra from 1 reference samples of the substance/substance group *Argentum (H1116)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance        | Batch    | Sample ID          | Spectra |
|----------|------------------|----------|--------------------|---------|
| Hepart   | Argentum (H1116) | 15001151 | 80674 <sup>†</sup> | 20      |

- 33 037 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Argentum (H1116)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

## 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 20            | 0              | 33 037        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9268 %) | 100.0000 % (> 70.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 13.64                           |
| 80890     | 80890               | 0.00                         | 20.07                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Arginine (L-) (H1036)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80026-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 3 different batches.
- 15 374 spectra from a total of 340 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 500 spectra from 13 reference samples of the substance/substance group *Arginine (L-) (H1036)*.
- These include spectra of independent samples from 10 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance             | Batch    | Sample ID          | Spectra |
|----------|-----------------------|----------|--------------------|---------|
| Hepart   | Arginine (L-) (H1036) | 0999001  | 80026              | 40      |
| Hepart   | Arginine (L-) (H1036) | 950601   | 80129              | 50      |
| Hepart   | Arginine (L-) (H1036) | 0999001  | 80157              | 50      |
| Hepart   | Arginine (L-) (H1036) | 928302   | 80212              | 30      |
| Hepart   | Arginine (L-) (H1036) | 027802   | 80256              | 40      |
| Hepart   | Arginine (L-) (H1036) | 044301   | 80280              | 40      |
| Hepart   | Arginine (L-) (H1036) | 052401   | 80330              | 60      |
| Hepart   | Arginine (L-) (H1036) | 066501   | 80373 <sup>†</sup> | 10      |
| Hepart   | Arginine (L-) (H1036) | 14000563 | 80446              | 20      |
| Hepart   | Arginine (L-) (H1036) | 14000564 | 80448              | 40      |
| Hepart   | Arginine (L-) (H1036) | 16000950 | 80808              | 40      |
| Hepart   | Arginine (L-) (H1036) | 17000878 | 80928              | 40      |
| Hepart   | Arginine (L-) (H1036) | 17000877 | 80929              | 40      |

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

- 32 557 spectra from a total of 724 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 30 spectra from 11 *Apo-Ident* customers from 14 batches from the substance/substance group *Arginine (L-) (H1036)*.
- These include spectra of independent samples from 14 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance             | Batch      | Spectra |
|----------------------------|-----------------------|------------|---------|
| Unisan                     | Arginine (L-) (H1036) | 27802      | 1       |
| Unisan                     | Arginine (L-) (H1036) | 14000564/0 | 1       |
| Unisan                     | Arginine (L-) (H1036) | 16000949/0 | 1       |
| Unisan                     | Arginine (L-) (H1036) | 44301      | 2       |
| Hepart AG, CH-8280 Kreu... | Arginine (L-) (H1036) | 52401      | 2       |
| unisan                     | Arginine (L-) (H1036) | 52401      | 1       |
| Unisan                     | Arginine (L-) (H1036) | 52401      | 1       |
| Hepart AG, Unisan GmbH     | Arginine (L-) (H1036) | 52401      | 2       |
| Unisan                     | Arginine (L-) (H1036) | 66501      | 6       |
| UNISAN                     | Arginine (L-) (H1036) | 66501      | 1       |
| Hepart AG                  | Arginine (L-) (H1036) | 66501      | 3       |
| Unisan                     | Arginine (L-) (H1036) | 1320025705 | 1       |
| Unisan                     | Arginine (L-) (H1036) | 1320550101 | 1       |
| Unisan/Hepart AG           | Arginine (L-) (H1036) | 1324044301 | 1       |
| Fagron                     | Arginine (L-) (H1036) | 1324044301 | 1       |
| Hepart AG                  | Arginine (L-) (H1036) | 1324027802 | 1       |
| Unisan                     | Arginine (L-) (H1036) | 1324950601 | 1       |
| Unisan                     | Arginine (L-) (H1036) | 14000563   | 1       |
| Hepart AG                  | Arginine (L-) (H1036) | 14000563/1 | 1       |
| Unisan                     | Arginine (L-) (H1036) | 1320999001 | 1       |

- 1759 spectra from 20 *Apo-Ident* customers from a total of 668 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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              | 15 374        |
| Type B | 0              | 200           | 300            | 32 557        |
| Type C | 0              | 15            | 15             | 1759          |

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 % (> 99.9250 %) | 100.0000 % (> 96.4706 %) |
| Type B | 100.0000 % (> 99.9242 %) | 40.0000 % (> 39.4000 %)  |
| Type C | 100.0000 % (> 98.8408 %) | 50.0000 % (> 40.0000 %)  |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 80373     | 80373               | 0.00                         | 52.75                           |
| 80807     | 80807               | 0.00                         | 51.94                           |
| 80867     | 80867               | 0.00                         | 44.09                           |
| 80876     | 80876               | 0.00                         | 46.41                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Cabbage extract (H1121)</b>                                  |
| Substance class                     | HCK - nutritional supplements (Hepart)                          |
| Report date                         | 18/07/2018                                                      |
| Report number                       | 80676-2018-07-18                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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 | <i>European Pharmacopoeia 8th Edition, Basic Version 2014</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]          |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>        |
| Anhang F          | <a href="#">Zusatz zu den Modellen der zweiten Stufe</a>          |

### Validation method

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

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

Finally, 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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 80 spectra from 2 reference samples of the substance/substance group *Cabbage extract (H1121)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance               | Batch    | Sample ID          | Spectra |
|----------|-------------------------|----------|--------------------|---------|
| Hepart   | Cabbage extract (H1121) | 15001355 | 80676 <sup>†</sup> | 20      |
| Hepart   | Cabbage extract (H1121) | 15001474 | 80677              | 60      |

- 32 977 spectra from a total of 734 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Cabbage extract (H1121)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

## 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 80            | 0              | 32 977        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9248 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 45.45                           |
| 80819     | 80819               | 0.00                         | 15.30                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Carnitine (L-) (H1038)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80013-2018-07-18  
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 |
| Hepart   | Carnitine (L-) (...) | 18000538  | 81045     | 40      | from supplier |

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

### Type A All calibration spectra.

- 290 spectra of 7 reference samples from the substance/substance group *Carnitine (L-) (H1038)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 7 different batches.
- 15 254 spectra from a total of 336 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 723 spectra from 18 reference samples of the substance/substance group *Carnitine (L-) (H1038)*.
- These include spectra of independent samples from 11 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance              | Batch     | Sample ID          | Spectra |
|----------|------------------------|-----------|--------------------|---------|
| Hepart   | Carnitine (L-) (H1038) | 938501    | 80013              | 40      |
| Hepart   | Carnitine (L-) (H1038) | 965901    | 80081              | 30      |
| Hepart   | Carnitine (L-) (H1038) | 008501    | 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) | 026001    | 80243              | 40      |
| Hepart   | Carnitine (L-) (H1038) | 130605300 | 80371 <sup>†</sup> | 10      |
| Hepart   | Carnitine (L-) (H1038) | 130605302 | 80483 <sup>†</sup> | 20      |
| Hepart   | Carnitine (L-) (H1038) | 15000052  | 80557 <sup>†</sup> | 20      |
| Hepart   | Carnitine (L-) (H1038) | 15000053  | 80558              | 60      |
| Hepart   | Carnitine (L-) (H1038) | 15000054  | 80559 <sup>†</sup> | 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      |
| Hepart   | Carnitine (L-) (H1038) | 18000539  | 81046              | 40      |
| Hepart   | Carnitine (L-) (H1038) | 18000418  | 81047              | 40      |

- 32 334 spectra from a total of 721 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 54 spectra from 12 *Apo-Ident* customers from 21 batches from the substance/substance group *Carnitine (L-) (H1038)*.
- These include spectra of independent samples from 18 batches, of which no spectra have been used for the generation of the database.

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

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

- 1735 spectra from 20 *Apo-Ident* customers from a total of 662 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 290           | 0              | 15 254        |
| <b>Type B</b> | 0              | 592           | 131            | 32 334        |
| <b>Type C</b> | 0              | 47            | 7              | 1735          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9245 %) | 100.0000 % (> 97.9310 %) |
| <b>Type B</b> | 100.0000 % (> 99.9242 %) | 81.8811 % (> 81.4661 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8367 %) | 87.0370 % (> 81.4815 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 43.43                           |
| 80371     | 80371               | 0.00                         | 45.70                           |
| 80483     | 80483               | 0.00                         | 41.16                           |
| 80557     | 80557               | 0.00                         | 36.65                           |
| 80559     | 80559               | 0.00                         | 37.19                           |
| 80787     | 80787               | 0.00                         | 39.95                           |
| 81045     | 81045               | 0.00                         | 36.34                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Carnosine (L-) (H1014)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80153-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 424 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 110 spectra from 3 reference samples of the substance/substance group *Carnosine (L-) (H1014)*.
- These include spectra of independent samples from 2 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance              | Batch       | Sample ID          | Spectra |
|----------|------------------------|-------------|--------------------|---------|
| Hepart   | Carnosine (L-) (H1014) | zu erfassen | 80048              | 40      |
| Hepart   | Carnosine (L-) (H1014) | 979202      | 80153              | 50      |
| Hepart   | Carnosine (L-) (H1014) | 074801      | 80655 <sup>†</sup> | 20      |

- 32 947 spectra from a total of 734 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details

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

provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 11 spectra from 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Carnosine (L-) (H1014)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

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

- 1778 spectra from 20 *Apo-Ident* customers from a total of 677 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 120           | 0              | 15 424        |
| <b>Type B</b> | 0              | 67            | 43             | 32 947        |
| <b>Type C</b> | 0              | 7             | 4              | 1778          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9254 %) | 100.0000 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9246 %) | 60.9091 % (> 58.1818 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8568 %) | n/a (n/a)                |

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 62.70                           |
| 80452     | 80452               | 0.00                         | 79.53                           |
| 80655     | 80655               | 0.00                         | 71.40                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Catechin extract (H1010)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80031-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 6 different batches.
- 15 304 spectra from a total of 337 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 240 spectra from 6 reference samples of the substance/substance group *Catechin extract (H1010)*.
- These include spectra of independent samples from 3 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                | Batch    | Sample ID          | Spectra |
|----------|--------------------------|----------|--------------------|---------|
| Hepart   | Catechin extract (H1010) | 0681501  | 80031              | 40      |
| Hepart   | Catechin extract (H1010) | 638201   | 80139              | 50      |
| Hepart   | Catechin extract (H1010) | 0681501  | 80140              | 50      |
| Hepart   | Catechin extract (H1010) | 018601   | 80240              | 40      |
| Hepart   | Catechin extract (H1010) | 15000206 | 80555 <sup>†</sup> | 20      |
| Hepart   | Catechin extract (H1010) | 15000206 | 80872              | 40      |

- 32 817 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B*

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

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 22 spectra from 9 *Apo-Ident* customers from 11 batches from the substance/substance group *Catechin extract (H1010)*.
- These include spectra of independent samples from 10 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance                | Batch      | Spectra |
|----------------------------|--------------------------|------------|---------|
| Unisan                     | Catechin extract (H1010) | 62901      | 1       |
| Hepart AG                  | Catechin extract (H1010) | 62901      | 1       |
| Hepart AG                  | Catechin extract (H1010) | 130208020  | 1       |
| Unisan                     | Catechin extract (H1010) | 18601      | 1       |
| Hepart AG                  | Catechin extract (H1010) | 18601      | 3       |
| Hepart                     | Catechin extract (H1010) | 17000409/0 | 1       |
| Unisan/Hepart AG           | Catechin extract (H1010) | 18601      | 1       |
| Hepart AG, CH-8280 Kreu... | Catechin extract (H1010) | 18601      | 1       |
| Unisan                     | Catechin extract (H1010) | 130208020  | 2       |
| Unisan                     | Catechin extract (H1010) | 62801      | 1       |
| Unisan                     | Catechin extract (H1010) | 1571025702 | 2       |
| Unisan                     | Catechin extract (H1010) | 25702      | 1       |
| Hepart AG, CH-8280 Kreu... | Catechin extract (H1010) | 62901      | 1       |
| Hepart AG, CH-8280 Kreu... | Catechin extract (H1010) | 1571025702 | 1       |
| Hepart AG                  | Catechin extract (H1010) | 1574018601 | 1       |
| Unisan                     | Catechin extract (H1010) | 1571681501 | 1       |
| Unisan                     | Catechin extract (H1010) | 681501     | 1       |
| Unisan                     | Catechin extract (H1010) | 208020     | 1       |

- 1767 spectra from 20 *Apo-Ident* customers from a total of 671 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 15 304        |
| <b>Type B</b> | 0              | 64            | 176            | 32 817        |
| <b>Type C</b> | 0              | 5             | 17             | 1767          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9247 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 26.6667 % (> 25.4167 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8442 %) | 22.7273 % (> 9.0909 %)   |

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

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

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80338            | 80338                      | 0.00                                | 33.64                                  |
| 80339            | 80339                      | 0.00                                | 37.78                                  |
| 80340            | 80340                      | 0.00                                | 25.33                                  |
| 80555            | 80555                      | 0.00                                | 44.55                                  |
| 80849            | 80849                      | 0.00                                | 40.22                                  |
| 80880            | 80880                      | 0.00                                | 30.77                                  |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Chaga (H1011)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80032-2018-07-18  
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 |
| Hepart   | Chaga (H1011) | 17001560 | 80952     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Chaga (H1011)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 384 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 200 spectra from 5 reference samples of the substance/substance group *Chaga (H1011)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance     | Batch    | Sample ID          | Spectra |
|----------|---------------|----------|--------------------|---------|
| Hepart   | Chaga (H1011) | 0675601  | 80032              | 40      |
| Hepart   | Chaga (H1011) | 975601   | 80180              | 40      |
| Hepart   | Chaga (H1011) | 046701   | 80310              | 40      |
| Hepart   | Chaga (H1011) | 14001688 | 80493 <sup>†</sup> | 20      |
| Hepart   | Chaga (H1011) | 16000235 | 80763              | 60      |

- 32 857 spectra from a total of 731 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 7 spectra from 3 *Apo-Ident* customers from 6 batches from the substance/substance group *Chaga (H1011)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| Supplier         | Substance     | Batch      | Spectra |
|------------------|---------------|------------|---------|
| Unisan/Hepart AG | Chaga (H1011) | 46701      | 1       |
| Unisan           | Chaga (H1011) | 14001688   | 1       |
| Unisan           | Chaga (H1011) | 64001      | 2       |
| Unisan           | Chaga (H1011) | 151467601  | 1       |
| Purren Apotheke  | Chaga (H1011) | 1514675601 | 1       |
| Hepart AG        | Chaga (H1011) | 14000951   | 1       |

- 1782 spectra from 20 *Apo-Ident* customers from a total of 676 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 200           | 0              | 32 857        |
| <b>Type C</b> | 0              | 7             | 0              | 1782          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 100.0000 % (> 97.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8712 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 109.65                          |
| 80493     | 80493               | 0.00                         | 80.21                           |
| 80825     | 80825               | 0.00                         | 54.02                           |
| 80952     | 80952               | 0.00                         | 60.74                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Chondroitin sulfate (Sodium-) (H1065)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80093-2018-07-18  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Chondroitin sulfate (Sodium-) (H1065); Chondroitin sulphate (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 50 390 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 section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 384 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 330 spectra from 9 reference samples of the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                      | Batch       | Sample ID          | Spectra |
|----------|--------------------------------|-------------|--------------------|---------|
| Hepart   | Chondroitin sulfate (Sodium... | zu erfassen | 80063              | 30      |
| Hepart   | Chondroitin sulfate (Sodium... | 001801      | 80093              | 50      |
| Hepart   | Chondroitin sulfate (Sodium... | 964101      | 80119              | 50      |
| Hepart   | Chondroitin sulfate (Sodium... | 031801      | 80269              | 40      |
| Hepart   | Chondroitin sulfate (Sodium... | 031801      | 80271              | 40      |
| Hepart   | Chondroitin sulfate (Sodium... | 14001985    | 80532 <sup>†</sup> | 20      |
| Hepart   | Chondroitin sulfate (Sodium... | 14001991    | 80533 <sup>†</sup> | 20      |
| Hepart   | Chondroitin sulfate (Sodium... | 031801      | 80584              | 60      |
| Hepart   | Chondroitin sulfate (Sodium... | 14001985/2  | 80779 <sup>†</sup> | 20      |

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

- 32 727 spectra from a total of 730 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 23 spectra from 11 *Apo-Ident* customers from 8 batches from the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*.
- These include spectra of independent samples from 8 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance                      | Batch      | Spectra |
|----------------------------|--------------------------------|------------|---------|
| Unisan                     | Chondroitin sulfate (Sodium... | 1801       | 2       |
| Hepart AG                  | Chondroitin sulfate (Sodium... | 31801      | 4       |
| Hepart                     | Chondroitin sulfate (Sodium... | 14001985/5 | 1       |
| hepart ag                  | Chondroitin sulfate (Sodium... | 31801      | 1       |
| Unisan                     | Chondroitin sulfate (Sodium... | 31801      | 5       |
| Hepart AG, CH-8280 Kreu... | 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       |

- 1766 spectra from 20 *Apo-Ident* customers from a total of 674 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 60            | 270            | 32 727        |
| <b>Type C</b> | 0              | 1             | 22             | 1766          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 18.1818 % (> 17.2727 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8436 %) | 4.3478 % (≥ 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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80532            | 80532                      | 0.00                                | 40.82                                  |
| 80533            | 80533                      | 0.00                                | 31.99                                  |
| 80779            | 80779                      | 0.00                                | 45.43                                  |
| 80871            | 80871                      | 0.00                                | 54.79                                  |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Coenzyme Q10 (H1013)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80015-2018-07-18  
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 |

*continued on the next page*

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| Supplier | Substance           | Batch      | Sample ID | Spectra | Certificate   |
|----------|---------------------|------------|-----------|---------|---------------|
| Hepart   | Coenzyme Q10 (H1... | 16001598/4 | 80854     | 40      | from supplier |
| Hepart   | Coenzyme Q10 (H1... | 16001598   | 80881     | 40      | from supplier |
| Hepart   | Coenzyme Q10 (H1... | 18000792/0 | 81048     | 40      | from supplier |
| Hepart   | Coenzyme Q10 (H1... | 18000806   | 81049     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Coenzyme Q10 (H1013)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 7 different batches.
- 15 184 spectra from a total of 336 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 350 spectra from 10 reference samples of the substance/substance group *Coenzyme Q10 (H1013)*.
- These include spectra of independent samples from 7 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance            | Batch       | Sample ID          | Spectra |
|----------|----------------------|-------------|--------------------|---------|
| Hepart   | Coenzyme Q10 (H1013) | 943001      | 80015              | 40      |
| Hepart   | Coenzyme Q10 (H1013) | zu erfassen | 80021              | 40      |
| Hepart   | Coenzyme Q10 (H1013) | 0992501     | 80065              | 30      |
| Hepart   | Coenzyme Q10 (H1013) | 0992501     | 80133              | 50      |
| Hepart   | Coenzyme Q10 (H1013) | 926101      | 80209              | 30      |
| Hepart   | Coenzyme Q10 (H1013) | 015601      | 80241              | 40      |
| Hepart   | Coenzyme Q10 (H1013) | 14001546    | 80484 <sup>†</sup> | 20      |
| Hepart   | Coenzyme Q10 (H1013) | 14001546    | 80587 <sup>†</sup> | 20      |
| Hepart   | Coenzyme Q10 (H1013) | 16000402/4  | 80795              | 40      |
| Hepart   | Coenzyme Q10 (H1013) | 16000402    | 80882              | 40      |

- 32 707 spectra from a total of 729 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 55 spectra from 16 *Apo-Ident* customers from 14 batches from the substance/substance group *Coenzyme Q10 (H1013)*.
- These include spectra of independent samples from 11 batches, of which no spectra have been used for the generation of the database.

| 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) | 14001446/1 | 1       |
| Hepart AG                  | Coenzyme Q10 (H1013) | 14001546   | 1       |
| Unisan                     | Coenzyme Q10 (H1013) | 14001546/1 | 2       |
| Unisan 02.04.2016          | Coenzyme Q10 (H1013) | 14001546/3 | 1       |
| Unisan 2.10.2015           | Coenzyme Q10 (H1013) | 14001546/2 | 1       |
| Unisan                     | Coenzyme Q10 (H1013) | 16000402/0 | 2       |
| Hepart AG                  | Coenzyme Q10 (H1013) | 16000402/0 | 1       |
| hepart                     | Coenzyme Q10 (H1013) | 16000402   | 1       |
| 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       |
| Hepart AG, CH-8280 Kreu... | Coenzyme Q10 (H1013) | 1194015601 | 1       |
| Unisan                     | Coenzyme Q10 (H1013) | 119405601  | 1       |
| Unisan                     | Coenzyme Q10 (H1013) | 992501     | 1       |
| Unisan                     | Coenzyme Q10 (H1013) | H101311    | 1       |

- 1734 spectra from 20 *Apo-Ident* customers from a total of 668 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

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

## 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 360           | 0              | 15 184        |
| <b>Type B</b> | 0              | 120           | 230            | 32 707        |
| <b>Type C</b> | 0              | 28            | 27             | 1734          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9244 %) | 100.0000 % (> 98.3333 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 34.2857 % (> 33.4286 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8366 %) | 50.9091 % (> 45.4545 %)  |

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

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

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

## Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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                         | 29.05                           |
| 80484     | 80484               | 0.00                         | 26.38                           |
| 80587     | 80587               | 0.00                         | 41.57                           |
| 80794     | 80794               | 0.00                         | 25.95                           |
| 80850     | 80850               | 0.00                         | 22.80                           |
| 80854     | 80854               | 0.00                         | 23.84                           |
| 80881     | 80881               | 0.00                         | 43.24                           |
| 81048     | 81048               | 0.00                         | 33.46                           |
| 81049     | 81049               | 0.00                         | 35.34                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Creatine (H1031)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80149-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 384 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 160 spectra from 5 reference samples of the substance/substance group *Creatine (H1031)*.
- These include spectra of independent samples from 3 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance        | Batch       | Sample ID          | Spectra |
|----------|------------------|-------------|--------------------|---------|
| Hepart   | Creatine (H1031) | zu erfassen | 80045              | 40      |
| Hepart   | Creatine (H1031) | 0965201     | 80149              | 40      |
| Hepart   | Creatine (H1031) | 15000749    | 80627 <sup>†</sup> | 20      |
| Hepart   | Creatine (H1031) | 15000750    | 80628 <sup>†</sup> | 20      |
| Hepart   | Creatine (H1031) | 17001177    | 80918              | 40      |

- 32 897 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples

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

are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 10 spectra from 5 *Apo-Ident* customers from 7 batches from the substance/substance group *Creatine (H1031)*.
- These include spectra of independent samples from 6 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance        | Batch      | Spectra |
|----------------------------|------------------|------------|---------|
| Hepart AG                  | Creatine (H1031) | 25004      | 3       |
| Unisan                     | Creatine (H1031) | 1830025005 | 1       |
| Unisan GmbH, 78465 Kons... | Creatine (H1031) | 1830025003 | 1       |
| Unisan                     | Creatine (H1031) | 25003      | 1       |
| Purren Apotheke            | Creatine (H1031) | 965201     | 2       |
| Hepart AG                  | Creatine (H1031) | 1831025005 | 1       |
| Hepart AG                  | Creatine (H1031) | 15000749   | 1       |

- 1779 spectra from 20 *Apo-Ident* customers from a total of 675 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 160           | 0              | 32 897        |
| <b>Type C</b> | 0              | 10            | 0              | 1779          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 100.0000 % (> 96.2500 %) |
| <b>Type C</b> | 100.0000 % (> 98.8593 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 47.04                           |
| 80441     | 80441               | 0.00                         | 53.74                           |
| 80627     | 80627               | 0.00                         | 43.52                           |
| 80628     | 80628               | 0.00                         | 49.98                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Curcumin and piperine (H1014)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80034-2018-07-18  
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... | 17000258 | 80883     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Curcumin and piperine (H1014)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 3 different batches.
- 15 424 spectra from a total of 340 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 220 spectra from 6 reference samples of the substance/substance group *Curcumin and piperine (H1014)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                     | Batch    | Sample ID          | Spectra |
|----------|-------------------------------|----------|--------------------|---------|
| Hepart   | Curcumin and piperine (H1014) | 0002201  | 80034              | 40      |
| Hepart   | Curcumin and piperine (H1014) | 002201   | 80166              | 50      |
| Hepart   | Curcumin and piperine (H1014) | 929601   | 80225              | 30      |
| Hepart   | Curcumin and piperine (H1014) | 013901   | 80234              | 40      |
| Hepart   | Curcumin and piperine (H1014) | 15001589 | 80705 <sup>†</sup> | 20      |
| Hepart   | Curcumin and piperine (H1014) | 16000369 | 80796              | 40      |

- 32 837 spectra from a total of 730 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 19 spectra from 8 *Apo-Ident* customers from 6 batches from the substance/substance group *Curcumin and piperine (H1014)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance                     | Batch      | Spectra |
|----------------------------|-------------------------------|------------|---------|
| Unisan                     | Curcumin and piperine (H1014) | 72001      | 3       |
| Unisan                     | Curcumin and piperine (H1014) | 14001017   | 1       |
| Hepart AG                  | Curcumin and piperine (H1014) | 72001      | 4       |
| Hepart AG                  | Curcumin and piperine (H1014) | 13901      | 3       |
| Hepart AG                  | Curcumin and piperine (H1014) | 14001017   | 1       |
| Hepart AG, CH-8280 Kreu... | Curcumin and piperine (H1014) | 13901      | 1       |
| Unisan                     | Curcumin and piperine (H1014) | 13901      | 2       |
| Hepart AG                  | Curcumin and piperine (H1014) | 15001589   | 1       |
| Hepart AG                  | Curcumin and piperine (H1014) | 1534002201 | 1       |
| Unisan                     | Curcumin and piperine (H1014) | 1534002201 | 1       |
| Unisan                     | Curcumin and piperine (H1014) | 1534013901 | 1       |

- 1770 spectra from 20 *Apo-Ident* customers from a total of 676 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 120           | 0              | 15 424        |
| <b>Type B</b> | 0              | 43            | 177            | 32 837        |
| <b>Type C</b> | 0              | 3             | 16             | 1770          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9254 %) | 100.0000 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 19.5455 % (> 18.1818 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8461 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 42.23                           |
| 80705     | 80705               | 0.00                         | 41.13                           |
| 80883     | 80883               | 0.00                         | 38.34                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Detox complex (H1111) / Juniper (H1112)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80702-2018-07-18  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Detox complex (H1111) / Juniper (H1112); Detox complex (H1118); Juniper (H1112)

### Special notes

When selecting the *Detox complex (H1111) / 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 *Detox complex (H1111) / 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 |
| Hepart   | Detox complex (H... | 16001075(MM) | 80894     | 40      | from supplier |
| Hepart   | Detox complex (H... | 16001076     | 80895     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Detox complex (H1111) / Juniper (H1112)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 384 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 100 spectra from 3 reference samples of the substance/substance group *Detox complex (H1111) / Juniper (H1112)*.
- These include spectra of independent samples from 2 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance             | Batch            | Sample ID          | Spectra |
|----------|-----------------------|------------------|--------------------|---------|
| Hepart   | Juniper (H1112)       | 15001004         | 80702 <sup>†</sup> | 20      |
| Hepart   | Detox complex (H1118) | 16001075(Nr.5-7) | 80892              | 40      |
| Hepart   | Detox complex (H1118) | 16001075(Nr.1-4) | 80893              | 40      |

- 32 957 spectra from a total of 733 batches from further 121 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Detox complex (H1111) / Juniper (H1112)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 (H1111) / 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 *Detox complex (H1111) / 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 100           | 0              | 32 957        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

The substance/substance group *Detox complex (H1111) / 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9246 %) | 100.0000 % (> 94.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 29.39                           |
| 80891     | 80891               | 0.00                         | 31.51                           |
| 80894     | 80894               | 0.00                         | 21.92                           |
| 80895     | 80895               | 0.00                         | 21.64                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Garcinia Cambogia (H1017)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80037-2018-07-18  
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 |
| Hepart   | Garcinia Cambogi... | 17000873      | 80956     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Garcinia Cambogia* (H1017). These samples are listed above in the section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 344 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 380 spectra from 7 reference samples of the substance/substance group *Garcinia Cambogia* (H1017).
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| 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 <sup>†</sup> | 20      |
| Hepart   | Garcinia Cambogia (H1017) | 15001048(F2) | 80660 <sup>†</sup> | 20      |
| Hepart   | Garcinia Cambogia (H1017) | 15001048     | 80661              | 60      |
| Hepart   | Garcinia Cambogia (H1017) | 15001048(B1) | 80662              | 60      |

- 32 677 spectra from a total of 730 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 10 spectra from 4 *Apo-Ident* customers from 5 batches from the substance/substance group *Garcinia Cambogia (H1017)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier  | Substance                 | Batch      | Spectra |
|-----------|---------------------------|------------|---------|
| Hepart AG | Garcinia Cambogia (H1017) | 14001098   | 3       |
| Unisan    | Garcinia Cambogia (H1017) | 56601      | 1       |
| Hepart    | Garcinia Cambogia (H1017) | 16001252/1 | 1       |
| Hepart AG | Garcinia Cambogia (H1017) | 7401       | 2       |
| Hepart AG | Garcinia Cambogia (H1017) | 1221007401 | 1       |
| Unisan    | Garcinia Cambogia (H1017) | 1221007401 | 2       |

- 1779 spectra from 20 *Apo-Ident* customers from a total of 677 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 15 344        |
| <b>Type B</b> | 0              | 250           | 130            | 32 677        |
| <b>Type C</b> | 0              | 5             | 5              | 1779          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9248 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9242 %) | 65.7895 % (> 65.0000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8593 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 43.07                           |
| 80477     | 80477               | 0.00                         | 42.22                           |
| 80490     | 80490               | 0.00                         | 32.52                           |
| 80660     | 80660               | 0.00                         | 25.00                           |
| 80956     | 80956               | 0.00                         | 28.85                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Ginkgo (H1024)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80391-2018-07-18  
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 |
| Hepart   | Ginkgo (H1024) | 17001832     | 81005     | 40      | from supplier |

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

### Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Ginkgo (H1024)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 5 different batches.
- 15 264 spectra from a total of 338 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 120 spectra from 4 reference samples of the substance/substance group *Ginkgo (H1024)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance      | Batch         | Sample ID          | Spectra |
|----------|----------------|---------------|--------------------|---------|
| Hepart   | Ginkgo (H1024) | 15001039      | 80656 <sup>†</sup> | 20      |
| Hepart   | Ginkgo (H1024) | 15001038 (F3) | 80657 <sup>†</sup> | 20      |
| Hepart   | Ginkgo (H1024) | 15001038      | 80658 <sup>†</sup> | 20      |
| Hepart   | Ginkgo (H1024) | 15001038 (F1) | 80659              | 60      |

- 32 937 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 2 spectra from 1 *Apo-Ident* customers from 2 batches from the substance/substance group *Ginkgo (H1024)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier  | Substance      | Batch    | Spectra |
|-----------|----------------|----------|---------|
| Hepart AG | Ginkgo (H1024) | 67901    | 1       |
| Hepart AG | Ginkgo (H1024) | 15001038 | 1       |

- 1787 spectra from 20 *Apo-Ident* customers from a total of 680 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 280           | 0              | 15 264        |
| <b>Type B</b> | 0              | 120           | 0              | 32 917        |
| <b>Type C</b> | 0              | 2             | 0              | 1787          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9246 %) | 100.0000 % (> 97.8571 %) |
| <b>Type B</b> | 100.0000 % (> 99.9259 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.9703 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 42.93                           |
| 80476     | 80476               | 0.00                         | 32.60                           |
| 80656     | 80656               | 0.00                         | 16.55                           |
| 80657     | 80657               | 0.00                         | 31.23                           |
| 80658     | 80658               | 0.00                         | 39.26                           |
| 81005     | 81005               | 0.00                         | 13.34                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Glucosamine sulfate (H1019)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80094-2018-07-18  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Glucosamine sulfate (H1019); Glucosamine sulphate (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 50 390 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 section [calibration samples](#). The reference samples originate from 3 different batches.
- 15 364 spectra from a total of 340 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 380 spectra from 9 reference samples of the substance/substance group *Glucosamine sulfate (H1019)*.
- These include spectra of independent samples from 8 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                   | Batch       | Sample ID | Spectra |
|----------|-----------------------------|-------------|-----------|---------|
| Hepart   | Glucosamine sulfate (H1019) | zu erfassen | 80039     | 40      |
| Hepart   | Glucosamine sulfate (H1019) | 0978401     | 80094     | 50      |
| Hepart   | Glucosamine sulfate (H1019) | 954901      | 80131     | 50      |
| Hepart   | Glucosamine sulfate (H1019) | 034001      | 80254     | 40      |
| Hepart   | Glucosamine sulfate (H1019) | 025002      | 80262     | 40      |
| Hepart   | Glucosamine sulfate (H1019) | 034001      | 80454     | 40      |
| Hepart   | Glucosamine sulfate (H1019) | 17000073    | 80877     | 40      |
| Hepart   | Glucosamine sulfate (H1019) | 17001387    | 80954     | 40      |
| Hepart   | Glucosamine sulfate (H1019) | 17001245    | 80955     | 40      |

- 32 677 spectra from a total of 729 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 14 spectra from 8 *Apo-Ident* customers from 7 batches from the substance/substance group *Glucosamine sulfate (H1019)*.
- These include spectra of independent samples from 7 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance                   | Batch      | Spectra |
|----------------------------|-----------------------------|------------|---------|
| Unisan                     | Glucosamine sulfate (H1019) | 38001      | 2       |
| Hepart AG                  | Glucosamine sulfate (H1019) | 38001      | 2       |
| Unisan/Hepart AG           | Glucosamine sulfate (H1019) | 38001      | 1       |
| Hepart                     | Glucosamine sulfate (H1019) | 17000073   | 1       |
| UNISAN                     | Glucosamine sulfate (H1019) | 34001      | 1       |
| Unisan GmbH, 78465 Kons... | Glucosamine sulfate (H1019) | 38001      | 1       |
| Hepart AG                  | Glucosamine sulfate (H1019) | 1823038001 | 1       |
| Hepart AG                  | Glucosamine sulfate (H1019) | 1822038001 | 1       |
| Unisan                     | Glucosamine sulfate (H1019) | 1822038001 | 1       |
| Unisan                     | Glucosamine sulfate (H1019) | 1823954901 | 2       |
| Unisan                     | Glucosamine sulfate (H1019) | 1822025002 | 1       |

- 1775 spectra from 20 *Apo-Ident* customers from a total of 675 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 15 364        |
| <b>Type B</b> | 0              | 157           | 223            | 32 677        |
| <b>Type C</b> | 0              | 8             | 6              | 1775          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9249 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9242 %) | 41.3158 % (> 40.5263 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8514 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 104.93                          |
| 80362     | 80362               | 0.00                         | 104.21                          |
| 80402     | 80402               | 0.00                         | 90.71                           |
| 80812     | 80812               | 0.00                         | 81.32                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Glutamine (L-) (H1043)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80089-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 384 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 480 spectra from 13 reference samples of the substance/substance group *Glutamine (L-) (H1043)*.
- These include spectra of independent samples from 11 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance              | Batch       | Sample ID          | Spectra |
|----------|------------------------|-------------|--------------------|---------|
| Hepart   | Glutamine (L-) (H1043) | zu erfassen | 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) | 026901      | 80242              | 40      |
| Hepart   | Glutamine (L-) (H1043) | 026904      | 80245              | 40      |
| Hepart   | Glutamine (L-) (H1043) | 026903      | 80246              | 40      |
| Hepart   | Glutamine (L-) (H1043) | 15000017    | 80551 <sup>†</sup> | 20      |
| Hepart   | Glutamine (L-) (H1043) | 15000018    | 80552 <sup>†</sup> | 20      |
| Hepart   | Glutamine (L-) (H1043) | 16000941    | 80803              | 40      |
| Hepart   | Glutamine (L-) (H1043) | 16000942    | 80804              | 40      |
| Hepart   | Glutamine (L-) (H1043) | 17000902    | 80930              | 40      |
| Hepart   | Glutamine (L-) (H1043) | 17000901    | 80931              | 40      |

<sup>†</sup>These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*).

- 32 577 spectra from a total of 724 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 39 spectra from 9 *Apo-Ident* customers from 14 batches from the substance/substance group *Glutamine (L-) (H1043)*.
- These include spectra of independent samples from 13 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance              | Batch      | Spectra |
|----------------------------|------------------------|------------|---------|
| Unisan                     | Glutamine (L-) (H1043) | 16000940/0 | 2       |
| Unisan                     | Glutamine (L-) (H1043) |            | 1       |
| Unisan                     | Glutamine (L-) (H1043) | 26903      | 2       |
| Unisan/Hepart AG           | Glutamine (L-) (H1043) | 26901      | 1       |
| Unisan                     | Glutamine (L-) (H1043) | 26904      | 2       |
| Unisan GmbH, 78465 Kons... | Glutamine (L-) (H1043) | 26904      | 1       |
| Hepart AG                  | Glutamine (L-) (H1043) | 26904      | 1       |
| Unisan                     | Glutamine (L-) (H1043) | 61501      | 10      |
| UNISAN                     | Glutamine (L-) (H1043) | 61501      | 2       |
| Hepart AG                  | Glutamine (L-) (H1043) | 61501/4    | 1       |
| Unisan                     | Glutamine (L-) (H1043) | 61501/4    | 1       |
| Unisan                     | Glutamine (L-) (H1043) | 15000017/0 | 1       |
| Hepart AG                  | Glutamine (L-) (H1043) | 15000017/1 | 1       |
| UNISAN                     | Glutamine (L-) (H1043) | 15000017/0 | 1       |
| Unisan                     | Glutamine (L-) (H1043) | 15000017   | 1       |
| Unisan                     | Glutamine (L-) (H1043) | 1814026901 | 8       |
| Unisan                     | Glutamine (L-) (H1043) | 1814026903 | 1       |
| Hepart AG                  | Glutamine (L-) (H1043) | H104331    | 1       |
| Hepart AG                  | Glutamine (L-) (H1043) | 1815026901 | 1       |

- 1750 spectra from 20 *Apo-Ident* customers from a total of 669 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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.

Hence, these spectra are not independent and are not of *Type B*.

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

|        | False positive | True positive | False negative | True negative |
|--------|----------------|---------------|----------------|---------------|
| Type A | 0              | 160           | 0              | 15 384        |
| Type B | 0              | 408           | 72             | 32 577        |
| Type C | 0              | 29            | 10             | 1750          |

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 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| Type B | 100.0000 % (> 99.9242 %) | 85.0000 % (> 84.3750 %)  |
| Type C | 100.0000 % (> 98.8387 %) | 74.3590 % (> 66.6667 %)  |

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

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

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

### Identity according to identity test using NIR spectroscopy

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

| Sample ID | Reference sample ID | Distance to reference sample | Distance to next foreign sample |
|-----------|---------------------|------------------------------|---------------------------------|
| 80336     | 80336               | 0.00                         | 40.91                           |
| 80551     | 80551               | 0.00                         | 37.40                           |
| 80552     | 80552               | 0.00                         | 40.47                           |
| 80802     | 80802               | 0.00                         | 40.38                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Glycine (H1021)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80168-2018-07-18  
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 |
| Hepart   | Glycine (H1021) | 18000449 | 81027     | 40      | from supplier |

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

### Type A All calibration spectra.

- 280 spectra of 7 reference samples from the substance/substance group *Glycine (H1021)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 7 different batches.
- 15 264 spectra from a total of 336 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 451 spectra from 12 reference samples of the substance/substance group *Glycine (H1021)*.
- These include spectra of independent samples from 9 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance       | Batch       | Sample ID          | Spectra |
|----------|-----------------|-------------|--------------------|---------|
| Hepart   | Glycine (H1021) | zu erfassen | 80050              | 40      |
| Hepart   | Glycine (H1021) | 965401      | 80168              | 51      |
| Hepart   | Glycine (H1021) | 993401      | 80197              | 40      |
| Hepart   | Glycine (H1021) | 028101      | 80253              | 40      |
| Hepart   | Glycine (H1021) | 14001730    | 80494 <sup>†</sup> | 20      |
| Hepart   | Glycine (H1021) | 14001731    | 80495              | 60      |
| Hepart   | Glycine (H1021) | 16000239    | 80764 <sup>†</sup> | 20      |
| Hepart   | Glycine (H1021) | 16000238    | 80765 <sup>†</sup> | 20      |
| Hepart   | Glycine (H1021) | 16000934    | 80806              | 40      |
| Hepart   | Glycine (H1021) | 17001658    | 80981              | 40      |
| Hepart   | Glycine (H1021) | 17001660    | 80982              | 40      |
| Hepart   | Glycine (H1021) | 18000451/0  | 81028              | 40      |

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

- 32 606 spectra from a total of 725 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 16 spectra from 6 *Apo-Ident* customers from 7 batches from the substance/substance group *Glycine (H1021)*.
- These include spectra of independent samples from 6 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance       | Batch      | Spectra |
|----------------------------|-----------------|------------|---------|
| Hepart AG, CH-8280 Kreu... | Glycine (H1021) | 28101      | 1       |
| Unisan                     | Glycine (H1021) | 28101      | 6       |
| Unisan/Hepart AG           | Glycine (H1021) | 28101      | 1       |
| Hepart AG                  | Glycine (H1021) | 61801      | 1       |
| Hepart AG                  | Glycine (H1021) | 75501      | 2       |
| Hepart                     | Glycine (H1021) | 14001730/0 | 1       |
| Hepart AG                  | Glycine (H1021) | 1803028101 | 1       |
| Unisan                     | Glycine (H1021) | 14001730   | 1       |
| Euro OTC                   | Glycine (H1021) | 16000239/0 | 1       |
| Hepart AG                  | Glycine (H1021) | 16000239/0 | 1       |

- 1773 spectra from 20 *Apo-Ident* customers from a total of 675 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 280           | 0              | 15 264        |
| <b>Type B</b> | 0              | 361           | 90             | 32 606        |
| <b>Type C</b> | 0              | 14            | 2              | 1773          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9246 %) | 100.0000 % (> 97.8571 %) |
| <b>Type B</b> | 100.0000 % (> 99.9242 %) | 80.0443 % (> 79.3792 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8489 %) | n/a (n/a)                |

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

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

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80348            | 80348                      | 0.00                                | 92.47                                  |
| 80436            | 80436                      | 0.00                                | 101.54                                 |
| 80494            | 80494                      | 0.00                                | 95.12                                  |
| 80764            | 80764                      | 0.00                                | 96.80                                  |
| 80765            | 80765                      | 0.00                                | 98.31                                  |
| 80805            | 80805                      | 0.00                                | 93.84                                  |
| 81027            | 81027                      | 0.00                                | 95.49                                  |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>HCK classification I</b>                                     |
| Substance class                     | HCK - nutritional supplements (Hepart)                          |
| Report date                         | 18/07/2018                                                      |
| Report number                       | 80331-2018-07-18                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>Germany |

### Relevant substance names

HCK classification I; Biotin (H1007); Chromium (H1012); Folic acid (H1016); Ginseng (H1018); Lycopene (H1058); Selenium (H1067); 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 | <i>European Pharmacopoeia 8th Edition, Basic Version 2014</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]          |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>        |
| Anhang F          | <a href="#">Zusatz zu den Modellen der zweiten Stufe</a>          |

### Validation method

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

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

Finally, 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   | Folic acid (H1016)  | 052301 | 80331     | 60      | from supplier |
| Hepart   | Lycopene (H1058)    | 053501 | 80335     | 40      | from supplier |
| Hepart   | Vitamin B12 (H11... | 025017 | 80353     | 40      | from supplier |
| Hepart   | Selenium (H1067)    | 065601 | 80361     | 40      | from supplier |

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| Supplier | Substance           | Batch        | Sample ID | Spectra | Certificate   |
|----------|---------------------|--------------|-----------|---------|---------------|
| 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 (H1105) | 15000993     | 80603     | 40      | from supplier |
| Hepart   | Vitamin B12 (H1105) | 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 |
| Hepart   | Vitamin B12 (H1105) | 17000277     | 80910     | 40      | from supplier |
| Hepart   | Lycopene (H1058)    | 17000619     | 80913     | 40      | from supplier |
| Hepart   | Lycopene (H1058)    | 17000619/0   | 81024     | 40      | from supplier |
| Hepart   | Selenium (H1067)    | 18000578     | 81025     | 40      | from supplier |

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

**Type A** All calibration spectra.

- 1510 spectra of 37 reference samples from the substance/substance group *HCK classification*. These samples are listed above in the section *calibration samples*. The reference samples originate from 32 different batches.
- 14034 spectra from a total of 311 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 2035 spectra from 57 reference samples of the substance/substance group *HCK classification I*.
- These include spectra of independent samples from 28 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance           | Batch    | Sample ID | Spectra |
|----------|---------------------|----------|-----------|---------|
| Hepart   | Vitamin B12 (H1102) | 944101   | 80008     | 40      |
| Hepart   | Selenium (H1067)    | 933301   | 80014     | 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)    | 0933301  | 80066     | 30      |
| Hepart   | Vitamin B12 (H1102) | 0966201  | 80075     | 30      |
| Hepart   | Vitamin D3 (H1105)  | 0959601  | 80078     | 30      |
| Hepart   | Selenium (H1067)    | 010201   | 80086     | 45      |
| Hepart   | Ginseng (H1018)     | 701602   | 80099     | 50      |
| Hepart   | Selenium (H1067)    | 010201   | 80105     | 50      |
| Hepart   | Vitamin D3 (H1105)  | 0959601  | 80108     | 50      |
| Hepart   | Lycopene (H1058)    | 927601   | 80132     | 40      |
| Hepart   | Lycopene (H1058)    | 999101   | 80144     | 50      |
| Hepart   | Folic acid (H1016)  | 977701   | 80146     | 40      |
| Hepart   | Lycopene (H1058)    | 004501   | 80159     | 50      |
| Hepart   | Vitamin B12 (H1102) | 944101   | 80173     | 40      |
| Hepart   | Vitamin B12 (H1102) | 0966201  | 80174     | 40      |
| Hepart   | Chromium (H1012)    | 977201   | 80181     | 40      |
| Hepart   | Biotin (H1007)      | 983601   | 80187     | 40      |
| Hepart   | Ginseng (H1018)     | 630706   | 80191     | 40      |
| Hepart   | Vitamin D3 (H1105)  | 008101   | 80201     | 25      |
| Hepart   | Selenium (H1067)    | 601901   | 80211     | 30      |
| Hepart   | Vitamin D3 (H1105)  | 940201   | 80215     | 30      |
| Hepart   | Lycopene (H1058)    | 927601   | 80239     | 40      |
| Hepart   | Biotin (H1007)      | 029603   | 80247     | 40      |
| Hepart   | Selenium (H1067)    | 010201   | 80268     | 40      |
| Hepart   | Ginseng (H1018)     | 038802   | 80270     | 40      |
| Hepart   | Selenium (H1067)    | 010201   | 80297     | 40      |
| Hepart   | Vitamin B12 (H1102) | 026401   | 80307     | 40      |
| Hepart   | Ginseng (H1018)     | 018502   | 80308     | 40      |
| Hepart   | Vitamin D3 (H1105)  | 008101   | 80309     | 40      |
| Hepart   | Biotin (H1007)      | 029601   | 80385†    | 10      |
| Hepart   | Ginseng (H1018)     | 067801   | 80403     | 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      |

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| Supplier | Substance           | Batch        | Sample ID          | Spectra |
|----------|---------------------|--------------|--------------------|---------|
| Hepart   | Biotin (H1007)      | 15000735     | 80586 <sup>†</sup> | 20      |
| Hepart   | Vitamin B12 (H1102) | 15000993     | 80603 <sup>†</sup> | 20      |
| Hepart   | Vitamin B12 (H1102) | 15000993(B1) | 80604 <sup>†</sup> | 20      |
| Hepart   | Vitamin B12 (H1102) | 15000993(F2) | 80605              | 60      |
| Hepart   | Ginseng (H1018)     | 15001047     | 80663 <sup>†</sup> | 20      |
| Hepart   | Selenium (H1067)    | 065501       | 80706 <sup>†</sup> | 20      |
| Hepart   | Ginseng (H1018)     | 15001047     | 80780 <sup>†</sup> | 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      |
| Hepart   | Vitamin B12 (H1102) | 17000276     | 80911              | 40      |
| Hepart   | Vitamin D3 (H1105)  | 17000874     | 80959              | 40      |
| Hepart   | Selenium (H1067)    | 18000422     | 81026              | 40      |

- 31 022 spectra from a total of 693 batches from further 115 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 310 spectra from 16 *Apo-Ident* customers from 84 batches from the substance/substance group *HCK classification I*.
- These include spectra of independent samples from 73 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance      | Batch      | Spectra |
|----------------------------|----------------|------------|---------|
| Hepart AG                  | Biotin (H1007) | 29601      | 3       |
| Unisan                     | Biotin (H1007) | 29601      | 2       |
| Unisan                     | Biotin (H1007) | 29603      | 7       |
| Hepart AG                  | Biotin (H1007) | 29603      | 3       |
| Unisan                     | Biotin (H1007) | 14000862   | 2       |
| Hepart AG                  | Biotin (H1007) | 14000862   | 2       |
| Unisan                     | Biotin (H1007) | 14000862/2 | 2       |
| Unisan                     | Biotin (H1007) | 15000735/0 | 1       |
| Unisan                     | Biotin (H1007) | 15000735   | 1       |
| Unisan                     | Biotin (H1007) | 1591983601 | 1       |
| Hepart AG                  | Biotin (H1007) | 1592029603 | 3       |
| Ichthyol Gesellschaft C... | Biotin (H1007) | 1591983601 | 1       |
| Hepart AG, CH-8280 Kreu... | Biotin (H1007) | 1592029603 | 1       |
| Unisan                     | Biotin (H1007) | 1592983601 | 1       |
| Unisan                     | Biotin (H1007) | 983601     | 1       |
| Hepart                     | Biotin (H1007) | 16001396   | 1       |

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

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| Supplier                   | Substance          | Batch      | Spectra |
|----------------------------|--------------------|------------|---------|
| Unisan                     | Biotin (H1007)     | H100721    | 1       |
| unisan                     | Chromium (H1012)   |            | 1       |
| Unisan                     | Chromium (H1012)   | 14000429   | 6       |
| Hepart AG                  | Chromium (H1012)   | 14000429   | 1       |
| Unisan                     | Chromium (H1012)   | 1582977201 | 3       |
| Unisan                     | Chromium (H1012)   | 1581977201 | 2       |
| Hepart AG                  | Chromium (H1012)   | 1582977201 | 4       |
| Unisan                     | Chromium (H1012)   | 977201     | 7       |
| Hepart AG                  | Chromium (H1012)   | 977201     | 5       |
| Hepart AG, CH-8280 Kreu... | Chromium (H1012)   | 977201     | 2       |
| Hepart AG                  | Chromium (H1012)   | 14000429/4 | 1       |
| Unisan                     | Chromium (H1012)   | 16000520/0 | 1       |
| Hepart AG                  | Folic acid (H1016) | 16000931   | 1       |
| Hepart AG                  | Folic acid (H1016) | 15000125   | 1       |
| Unisan                     | Folic acid (H1016) | 30201      | 8       |
| Hepart AG                  | Folic acid (H1016) | 16001098   | 1       |
| Unisan                     | Folic acid (H1016) | 16000931   | 1       |
| 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       |
| Hepart AG                  | Folic acid (H1016) | 14000639/1 | 1       |
| Hepart AG                  | Folic acid (H1016) | 14000638   | 1       |
| Unisan                     | Folic acid (H1016) | 1611030201 | 1       |
| Unisan                     | Folic acid (H1016) | 14000639/1 | 1       |
| Hepart AG                  | Folic acid (H1016) | 1613030201 | 5       |
| Unisan Gmbh, 78465 Kons... | Folic acid (H1016) | 1611030201 | 1       |
| Unisan                     | Folic acid (H1016) | 1613030201 | 3       |
| Unisan                     | Folic acid (H1016) | 1613977701 | 2       |
| Unisan                     | Folic acid (H1016) | 977701     | 2       |
| Bombastus                  | Folic acid (H1016) | 1613052301 | 1       |
| Hepart AG                  | Folic acid (H1016) | 4000638    | 1       |
| Unisan                     | Folic acid (H1016) | H101621    | 1       |
| Unisan                     | Ginseng (H1018)    | 38802      | 2       |
| Unisan/Hepart AG           | Ginseng (H1018)    | 38802      | 1       |
| Hepart AG                  | Ginseng (H1018)    | 38802      | 1       |
| Hepart AG                  | Ginseng (H1018)    | 67801      | 1       |
| Unisan                     | Ginseng (H1018)    | 14002047/1 | 1       |
| Unisan                     | Ginseng (H1018)    | 67801      | 1       |
| Hepart AG                  | Ginseng (H1018)    | 15001047   | 1       |
| Hepart AG                  | Ginseng (H1018)    | 17000285/0 | 1       |
| UNISAN                     | Ginseng (H1018)    | 67801      | 1       |
| Hepart                     | Ginseng (H1018)    | 14002047/0 | 1       |
| Euro OTC                   | Ginseng (H1018)    | 15001047/0 | 1       |
| Unisan                     | Lycopene (H1058)   | 47301      | 2       |
| Unisan                     | Lycopene (H1058)   | 53501      | 6       |
| Hepart AG                  | Lycopene (H1058)   | 47301      | 1       |
| Unisan/Hepart AG           | Lycopene (H1058)   | 47301      | 1       |
| Hepart AG                  | Lycopene (H1058)   | 53501      | 1       |
| Unisan                     | Lycopene (H1058)   | 1195004501 | 1       |
| Unisan                     | Lycopene (H1058)   | 4501       | 4       |
| Unisan                     | Lycopene (H1058)   | 14000803   | 1       |
| Hepart                     | Lycopene (H1058)   | 17000619   | 1       |
| Unisan                     | Lycopene (H1058)   | H105811    | 1       |
| Unisan                     | Selenium (H1067)   | 10201      | 21      |
| Hedinger                   | Selenium (H1067)   | 10201      | 10      |
| Hepart AG, CH-8280 Kreu... | Selenium (H1067)   | 10201      | 1       |
| Unisan                     | Selenium (H1067)   | 65501      | 1       |

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| <b>Supplier</b>            | <b>Substance</b>    | <b>Batch</b> | <b>Spectra</b> |
|----------------------------|---------------------|--------------|----------------|
| UNISAN                     | Selenium (H1067)    | 65501        | 1              |
| Unisan                     | Selenium (H1067)    | 65601        | 4              |
| Unisan                     | Selenium (H1067)    | 65501/2      | 1              |
| UNISAN                     | Selenium (H1067)    | 65601        | 3              |
| Unisan                     | Selenium (H1067)    | 65601/2      | 2              |
| Unisan                     | Selenium (H1067)    | 65601/1      | 1              |
| Unisan                     | Selenium (H1067)    | 65701        | 5              |
| Hepart AG                  | Selenium (H1067)    | 65701        | 2              |
| Hepart AG                  | Selenium (H1067)    | 933301       | 1              |
| Unisan                     | Selenium (H1067)    | 1144010201   | 2              |
| Hepart AG                  | Selenium (H1067)    | 1144010201   | 3              |
| Bombastus                  | Selenium (H1067)    | 1144010201   | 1              |
| Unisan                     | Selenium (H1067)    | 1144933301   | 2              |
| Hepart AG, CH-8280 Kreu... | Selenium (H1067)    | 1144010201   | 1              |
| Unisan                     | Selenium (H1067)    | 15000157     | 2              |
| Hepart                     | Selenium (H1067)    | 15000158/1   | 1              |
| Hepart                     | Selenium (H1067)    | 15000158     | 1              |
| Unisan                     | Selenium (H1067)    | 15000158     | 1              |
| Unisan                     | Vitamin B12 (H1102) | 75301        | 6              |
| Hepart AG                  | Vitamin B12 (H1102) | 75301        | 2              |
| Unisan                     | Vitamin B12 (H1102) | 75301/2      | 2              |
| Hepart AG                  | Vitamin B12 (H1102) | 15000993/0   | 1              |
| Unisan                     | Vitamin B12 (H1102) | 15000993     | 1              |
| Unisan                     | Vitamin B12 (H1102) | 15000993/3   | 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) | 26401        | 2              |
| Hepart AG                  | Vitamin B12 (H1102) | 1064025017   | 1              |
| Unisan                     | Vitamin B12 (H1102) | 1061025017   | 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              |
| HCK                        | Vitamin D3 (H1105)  | 8101         | 1              |
| Unisan                     | Vitamin D3 (H1105)  | 6108129      | 1              |
| UNISAN                     | Vitamin D3 (H1105)  | 63601        | 1              |
| Unisan Gmbh, 78465 Kons... | Vitamin D3 (H1105)  | 63701        | 1              |
| Hepart AG                  | Vitamin D3 (H1105)  | 63701        | 3              |
| Unisan                     | Vitamin D3 (H1105)  | 63701        | 5              |
| Fagron                     | Vitamin D3 (H1105)  | 63701        | 1              |
| Unisan                     | Vitamin D3 (H1105)  | 64801        | 6              |
| Hepart AG                  | Vitamin D3 (H1105)  | 64801        | 4              |
| Hepart AG, CH-8280 Kreu... | Vitamin D3 (H1105)  | 64801        | 1              |
| Hepart AG, Unisan GmbH     | Vitamin D3 (H1105)  | 64801        | 1              |
| Unisan                     | Vitamin D3 (H1105)  | 1335008101   | 4              |
| Hepart AG                  | Vitamin D3 (H1105)  | 1335008101   | 2              |
| Unisan                     | Vitamin D3 (H1105)  | 1335008108   | 1              |
| Unisan                     | Vitamin D3 (H1105)  | 1335959601   | 2              |
| Unisan                     | Vitamin D3 (H1105)  | 14000481     | 1              |
| Hepart AG, CH-8280 Kreu... | Vitamin D3 (H1105)  | 1336008101   | 2              |
| Hepart AG                  | Vitamin D3 (H1105)  | 14000481     | 1              |
| UNISAN                     | Vitamin D3 (H1105)  | 14000481     | 3              |
| Unisan                     | Vitamin D3 (H1105)  | 14000481/2   | 3              |
| Hepart                     | Vitamin D3 (H1105)  | 14000481/2   | 1              |
| Unisan                     | Vitamin D3 (H1105)  | 15000490     | 2              |
| Unisan                     | Vitamin D3 (H1105)  | 15000490/0   | 3              |

- 1479 spectra from 20 *Apo-Ident* customers from a total of 599 batches from a further 54 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 1510          | 0              | 14 034        |
| <b>Type B</b> | 0              | 1693          | 342            | 30 428        |
| <b>Type C</b> | 0              | 293           | 17             | 1474          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9240 %) | 100.0000 % (> 99.6026 %) |
| <b>Type B</b> | 100.0000 % (> 99.9266 %) | 83.1941 % (> 83.0467 %)  |
| <b>Type C</b> | 100.0000 % (> 98.9270 %) | 94.5161 % (> 93.5484 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 80331     | 80331               | 0.00                         | 32.75                           |
| 80335     | 80335               | 0.00                         | 26.85                           |
| 80353     | 80353               | 0.00                         | 26.82                           |
| 80361     | 80361               | 0.00                         | 48.11                           |
| 80364     | 80364               | 0.00                         | 51.32                           |
| 80365     | 80365               | 0.00                         | 36.11                           |
| 80366     | 80366               | 0.00                         | 49.84                           |

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| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80385            | 80385                      | 0.00                                | 26.55                                  |
| 80442            | 80442                      | 0.00                                | 29.42                                  |
| 80443            | 80443                      | 0.00                                | 32.26                                  |
| 80449            | 80449                      | 0.00                                | 30.69                                  |
| 80451            | 80451                      | 0.00                                | 30.82                                  |
| 80455            | 80455                      | 0.00                                | 24.86                                  |
| 80456            | 80456                      | 0.00                                | 25.40                                  |
| 80478            | 80478                      | 0.00                                | 33.61                                  |
| 80530            | 80530                      | 0.00                                | 34.90                                  |
| 80531            | 80531                      | 0.00                                | 35.79                                  |
| 80534            | 80534                      | 0.00                                | 10.53                                  |
| 80535            | 80535                      | 0.00                                | 30.72                                  |
| 80553            | 80553                      | 0.00                                | 31.45                                  |
| 80580            | 80580                      | 0.00                                | 35.55                                  |
| 80586            | 80586                      | 0.00                                | 30.81                                  |
| 80603            | 80603                      | 0.00                                | 29.11                                  |
| 80604            | 80604                      | 0.00                                | 28.30                                  |
| 80663            | 80663                      | 0.00                                | 21.16                                  |
| 80706            | 80706                      | 0.00                                | 38.92                                  |
| 80780            | 80780                      | 0.00                                | 21.97                                  |
| 80791            | 80791                      | 0.00                                | 38.07                                  |
| 80792            | 80792                      | 0.00                                | 34.63                                  |
| 80816            | 80816                      | 0.00                                | 38.81                                  |
| 80822            | 80822                      | 0.00                                | 30.98                                  |
| 80855            | 80855                      | 0.00                                | 29.90                                  |
| 80863            | 80863                      | 0.00                                | 35.79                                  |
| 80910            | 80910                      | 0.00                                | 34.41                                  |
| 80913            | 80913                      | 0.00                                | 30.07                                  |
| 81024            | 81024                      | 0.00                                | 25.73                                  |
| 81025            | 81025                      | 0.00                                | 34.75                                  |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>HCK classification II</b>                                    |
| Substance class                     | HCK - nutritional supplements (Hepart)                          |
| Report date                         | 18/07/2018                                                      |
| Report number                       | 80311-2018-07-18                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>Germany |

### Relevant substance names

HCK classification II; Antioxidants NAT complex (H1004); Bioflavonoid complex (H1006); Calcium (H1008); Flavour orange (H1405); Glutathione (H1020); Isoflavones (H1025); OPC Grape seed (H1066); Orthocolon complex (H1800); 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 | <i>European Pharmacopoeia 8th Edition, Basic Version 2014</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]          |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>        |
| Anhang F          | <a href="#">Zusatz zu den Modellen der zweiten Stufe</a>          |

### Validation method

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

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

Finally, 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   | 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   | 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 |
| 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 |

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| Supplier | Substance            | Batch         | Sample ID | Spectra | Certificate   |
|----------|----------------------|---------------|-----------|---------|---------------|
| Hepart   | Calcium (H1008)      | 15001674 (B2) | 80741     | 40      | from supplier |
| Hepart   | Flavour orange (...) | 16000262      | 80768     | 40      | from supplier |
| Hepart   | Antioxidants NAT...  | 16000378      | 80783     | 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 |
| Hepart   | Antioxidants NAT...  | 17000260      | 80946     | 40      | from supplier |
| Hepart   | Vitamin B1 (H1101)   | 17000914      | 80953     | 40      | from supplier |
| Hepart   | Vitamin B1 (H1101)   | 17001075      | 80980     | 40      | from supplier |
| Hepart   | Antioxidants NAT...  | 17000261      | 80986     | 40      | from supplier |
| Hepart   | Antioxidants NAT...  | 17001756      | 80987     | 40      | from supplier |
| Hepart   | OPC Grape seed (...) | 17001805      | 81001     | 40      | from supplier |
| Hepart   | Flavour orange (...) | 17000491/0    | 81016     | 40      | from supplier |
| Hepart   | Orthocolon compl...  | 18000636      | 81041     | 40      | from supplier |
| Hepart   | Orthocolon compl...  | 18000641      | 81042     | 40      | from supplier |

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

**Type A** All calibration spectra.

- 3360 spectra of 79 reference samples from the substance/substance group *HCK classification II*. These samples are listed above in the section *calibration samples*. The reference samples originate from 75 different batches.
- 12 184 spectra from a total of 268 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 7149 spectra from 177 reference samples of the substance/substance group *HCK classification II*.
- These include spectra of independent samples from 128 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                       | Batch       | Sample ID          | Spectra |
|----------|---------------------------------|-------------|--------------------|---------|
| Hepart   | Calcium (H1008)                 | 956001      | 80005              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | zu erfassen | 80016              | 40      |
| Hepart   | Bioflavonoid complex (H1006)    | zu erfassen | 80017              | 30      |
| Hepart   | Calcium (H1008)                 | zu erfassen | 80020              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 2401        | 80025              | 40      |
| Hepart   | Bioflavonoid complex (H1006)    | 0683901     | 80027              | 40      |
| Hepart   | Calcium (H1008)                 | 0956001     | 80029              | 40      |
| Hepart   | Glutathione (H1020)             | 0955501     | 80040              | 40      |
| Hepart   | Isoflavones (H1025)             | 988301      | 80041              | 40      |
| Hepart   | OPC Grape seed (H1066)          | 0672201     | 80064              | 30      |
| Hepart   | Vitamin B1 (H1101)              | 977301      | 80072              | 30      |
| Hepart   | Vitamin B1 (H1101)              | 977301      | 80116              | 50      |
| Hepart   | OPC Grape seed (H1066)          | 0672201     | 80118              | 50      |
| Hepart   | Bioflavonoid complex (H1006)    | 0683901     | 80124              | 50      |
| Hepart   | Glutathione (H1020)             | 0955501     | 80125              | 50      |
| Hepart   | OPC Grape seed (H1066)          | 016201      | 80128              | 50      |
| Hepart   | Isoflavones (H1025)             | 0955701     | 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... | 011001      | 80182              | 40      |
| Hepart   | Bioflavonoid complex (H1006)    | 694301      | 80184              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 0980001     | 80188              | 40      |
| Hepart   | Calcium (H1008)                 | 008901      | 80189              | 40      |
| Hepart   | Calcium (H1008)                 | 0956001     | 80190              | 40      |
| Hepart   | OPC Grape seed (H1066)          | 643901      | 80196              | 40      |
| Hepart   | Glutathione (H1020)             | 019703      | 80204              | 30      |
| Hepart   | Isoflavones (H1025)             | 591907      | 80208              | 30      |
| Hepart   | Glutathione (H1020)             | 918901      | 80217              | 30      |
| Hepart   | Antioxidants NAT complex (H1... | 0991301     | 80232              | 40      |
| Hepart   | OPC Grape seed (H1066)          | 018401      | 80233              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 019901      | 80236              | 40      |
| Hepart   | Bioflavonoid complex (H1006)    | 019001      | 80252              | 40      |
| Hepart   | Vitamin B1 (H1101)              | 030501      | 80255              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 030901      | 80258              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 030903      | 80259              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 030902      | 80260              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 030904      | 80261              | 40      |
| Hepart   | Isoflavones (H1025)             | 038801      | 80272              | 40      |
| Hepart   | Bioflavonoid complex (H1006)    | 042501      | 80275              | 30      |
| Hepart   | Bioflavonoid complex (H1006)    | 028501      | 80279              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 019901      | 80282              | 40      |
| Hepart   | Glutathione (H1020)             | 040201      | 80288              | 40      |
| Hepart   | Calcium (H1008)                 | 055301      | 80324              | 60      |
| Hepart   | Calcium (H1008)                 | 055401      | 80325              | 60      |
| Hepart   | Calcium (H1008)                 | 055501      | 80326              | 60      |
| Hepart   | OPC Grape seed (H1066)          | 070401      | 80380 <sup>†</sup> | 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   | Vitamin B1 (H1101)              | 14001112    | 80480              | 40      |
| Hepart   | Vitamin B1 (H1101)              | 14001113    | 80481              | 40      |
| Hepart   | Bioflavonoid complex (H1006)    | 14001675    | 80492 <sup>†</sup> | 20      |

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| Supplier | Substance                       | Batch        | Sample ID          | Spectra |
|----------|---------------------------------|--------------|--------------------|---------|
| Hepart   | Antioxidants NAT complex (H1... | 14001849     | 80504 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 14001850     | 80505 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 14001851     | 80506 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 14001846     | 80507 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 14001848     | 80508 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 14001847     | 80509 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 14001933     | 80521 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 14001934     | 80522 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 14001935     | 80523              | 60      |
| Hepart   | Calcium (H1008)                 | 14001936     | 80524              | 60      |
| Hepart   | Calcium (H1008)                 | 14001937     | 80525 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 14001938     | 80526 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 14001939     | 80527 <sup>†</sup> | 20      |
| Hepart   | Vitamin B1 (H1101)              | 075001       | 80529 <sup>†</sup> | 20      |
| Hepart   | Isoflavones (H1025)             | 15000205     | 80556              | 60      |
| Hepart   | Glutathione (H1020)             | 15000478     | 80583 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 15000875     | 80606              | 60      |
| Hepart   | Antioxidants NAT complex (H1... | 15000875(B1) | 80607 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 15000875(F2) | 80608              | 60      |
| Hepart   | Antioxidants NAT complex (H1... | 15000880     | 80609 <sup>†</sup> | 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 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 15000878(F2) | 80617              | 60      |
| Hepart   | Antioxidants NAT complex (H1... | 15000874     | 80618 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 15000874(B1) | 80619 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 15000874(F2) | 80620              | 60      |
| Hepart   | Antioxidants NAT complex (H1... | 15000879     | 80621 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Antioxidants NAT complex (H1... | 15000876(B1) | 80625              | 60      |
| Hepart   | Antioxidants NAT complex (H1... | 15000876(F2) | 80626              | 60      |
| Hepart   | Rhodiola (H1064)                | 070501       | 80632 <sup>†</sup> | 20      |
| Hepart   | Rhodiola (H1064)                | 15001045     | 80672 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001669     | 80707 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001672(B2) | 80708              | 60      |
| Hepart   | Calcium (H1008)                 | 15001672(B1) | 80709 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001672(MM) | 80710              | 60      |
| Hepart   | Calcium (H1008)                 | 15001671     | 80711 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001673(MM) | 80712 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001673(B2) | 80713              | 60      |
| Hepart   | Calcium (H1008)                 | 15001673(B1) | 80714              | 60      |
| Hepart   | Calcium (H1008)                 | 15001668(B1) | 80715 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001666(B1) | 80720              | 60      |
| Hepart   | Calcium (H1008)                 | 15001666(F2) | 80721              | 60      |
| Hepart   | Calcium (H1008)                 | 15001666(MM) | 80722 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001670(B1) | 80723              | 60      |
| Hepart   | Calcium (H1008)                 | 15001665(B1) | 80724 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001670(MM) | 80725              | 60      |
| Hepart   | Calcium (H1008)                 | 15001665(F2) | 80726              | 60      |

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| Supplier | Substance                       | Batch         | Sample ID          | Spectra |
|----------|---------------------------------|---------------|--------------------|---------|
| Hepart   | Calcium (H1008)                 | 15001665 (MM) | 80727              | 60      |
| Hepart   | Calcium (H1008)                 | 15001668 (F2) | 80728              | 60      |
| Hepart   | Calcium (H1008)                 | 15001670 (B2) | 80729 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001675 (MM) | 80730              | 60      |
| Hepart   | Calcium (H1008)                 | 15001675 (B1) | 80731              | 60      |
| Hepart   | Calcium (H1008)                 | 15001675 (B2) | 80732 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001675/4    | 80733              | 60      |
| Hepart   | Calcium (H1008)                 | 15001676 (MM) | 80734 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001674 (B2) | 80741 <sup>†</sup> | 20      |
| Hepart   | Calcium (H1008)                 | 15001674 (B1) | 80742              | 60      |
| Hepart   | Calcium (H1008)                 | 15001674 (MM) | 80743              | 60      |
| Hepart   | Flavour orange (H1405)          | 16000262      | 80768 <sup>†</sup> | 20      |
| 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   | Glutathione (H1020)             | 16000938      | 80813              | 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      |
| Hepart   | Rhodiola (H1064)                | 17000278      | 80915              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17000268      | 80938              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17000269      | 80939              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17000267      | 80940              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17000266      | 80941              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17000264      | 80942              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17000263      | 80943              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17000262      | 80944              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17000261      | 80945              | 40      |
| Hepart   | Calcium (H1008)                 | 17000249MM    | 80971              | 40      |
| Hepart   | Calcium (H1008)                 | 17000250      | 80972              | 40      |
| Hepart   | Calcium (H1008)                 | 17000201MM    | 80973              | 40      |
| Hepart   | Calcium (H1008)                 | 17000202MM    | 80974              | 40      |
| Hepart   | Calcium (H1008)                 | 17000203      | 80975              | 40      |
| Hepart   | Calcium (H1008)                 | 17000204MM    | 80976              | 40      |
| Hepart   | Calcium (H1008)                 | 17000205      | 80977              | 40      |
| Hepart   | Calcium (H1008)                 | 17000206      | 80978              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17001754/0    | 80988              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17001757      | 80989              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17001758      | 81002              | 40      |
| Hepart   | Antioxidants NAT complex (H1... | 17001755      | 81021              | 40      |
| Hepart   | Orthocolon complex (H1800)      | 18000640      | 81043              | 40      |
| Hepart   | Flavour orange (H1405)          | 18000770      | 81064              | 40      |

- 25 908 spectra from a total of 569 batches from further 113 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 295 spectra from 19 *Apo-Ident* customers from 134 batches from the substance/substance group *HCK classification II*.
- These include spectra of independent samples from 119 batches, of which no spectra have been used for the generation of the database.

| Supplier          | Substance                       | Batch      | Spectra |
|-------------------|---------------------------------|------------|---------|
| Unisan            | Antioxidants NAT complex (H1... | 1851       | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 14000044   | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 67201      | 4       |
| Unisan            | Antioxidants NAT complex (H1... | 1400042    | 1       |
| UNISAN            | Antioxidants NAT complex (H1... | 14000042   | 1       |
| Hepart AG         | Antioxidants NAT complex (H1... | 67201      | 1       |
| Hepart AG         | Antioxidants NAT complex (H1... | 14000044   | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 14000963   | 2       |
| Unisan            | Antioxidants NAT complex (H1... | 14000961   | 1       |
| UNISAN            | Antioxidants NAT complex (H1... | 14000961   | 1       |
| UNISAN            | Antioxidants NAT complex (H1... | 14000963   | 3       |
| Hepart AG         | Antioxidants NAT complex (H1... | 67501      | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 14001847/0 | 2       |
| Unisan            | Antioxidants NAT complex (H1... | 14001847/1 | 1       |
| Hepart AG         | Antioxidants NAT complex (H1... | 14001848   | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 14001851/0 | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 14001848/0 | 1       |
| unisan            | Antioxidants NAT complex (H1... | 15000877   | 1       |
| Unisan 02.04.2016 | Antioxidants NAT complex (H1... | 15000874/0 | 2       |
| Unisan            | Antioxidants NAT complex (H1... | 16000968/0 | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 15000877/0 | 1       |
| Hepart AG         | Antioxidants NAT complex (H1... | 16000378   | 1       |
| Hepart AG         | Antioxidants NAT complex (H1... | 16000376   | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 15000880   | 1       |
| Hepart            | Antioxidants NAT complex (H1... | 16000970   | 1       |
| Hepart            | Antioxidants NAT complex (H1... | 17000260   | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 30901      | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 16000376   | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 19901      | 3       |
| Hepart AG         | Antioxidants NAT complex (H1... | 30901      | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 30904      | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 30902      | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 11001      | 1       |
| hepart ag         | Antioxidants NAT complex (H1... | 19901      | 1       |
| Unisan            | Antioxidants NAT complex (H1... | 51901      | 4       |

*continued on the next page*

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

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| Supplier                   | Substance                       | Batch      | Spectra |
|----------------------------|---------------------------------|------------|---------|
| Unisan                     | Antioxidants NAT complex (H1... | 30903      | 3       |
| Hedinger                   | Antioxidants NAT complex (H1... | 51901      | 1       |
| Unisan                     | Antioxidants NAT complex (H1... | 51902      | 1       |
| Hepart AG                  | Antioxidants NAT complex (H1... | 51902      | 1       |
| Hepart AG, CH-8280 Kreu... | Antioxidants NAT complex (H1... | 52101      | 1       |
| Unisan                     | Antioxidants NAT complex (H1... | 52001      | 2       |
| Hepart AG                  | Antioxidants NAT complex (H1... | 52101      | 3       |
| Hepart AG                  | Antioxidants NAT complex (H1... | 52201      | 2       |
| Unisan                     | Antioxidants NAT complex (H1... | 52101      | 1       |
| Unisan Gmbh, 78465 Kons... | Antioxidants NAT complex (H1... | 52201      | 1       |
| 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... | 67501      | 1       |
| Unisan                     | Antioxidants NAT complex (H1... | 67601      | 2       |
| Unisan                     | Antioxidants NAT complex (H1... | 68201      | 4       |
| Hepart AG, CH-8280 Kreu... | Antioxidants NAT complex (H1... | 1034019901 | 1       |
| Hepart AG                  | Antioxidants NAT complex (H1... | 1034030901 | 1       |
| Unisan                     | Antioxidants NAT complex (H1... | 1034019901 | 1       |
| Hepart AG                  | Antioxidants NAT complex (H1... | 1034030902 | 1       |
| Hepart AG                  | Antioxidants NAT complex (H1... | 1034019901 | 1       |
| Hepart AG, CH-8280 Kreu... | Antioxidants NAT complex (H1... | 1034030901 | 1       |
| Hepart AG                  | Antioxidants NAT complex (H1... | 1034030904 | 1       |
| Unisan                     | Antioxidants NAT complex (H1... | 1034030902 | 1       |
| Unisan                     | 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       |
| Unisan 2.10.2015           | Bioflavonoid complex (H1006)    | 14001675/1 | 1       |
| Hepart AG                  | Bioflavonoid complex (H1006)    | 14001675/1 | 1       |
| Unisan 02.04.2016          | Bioflavonoid complex (H1006)    | 14001675/2 | 1       |
| Unisan                     | Bioflavonoid complex (H1006)    | 42501      | 2       |
| Hepart                     | Bioflavonoid complex (H1006)    | 14001675/5 | 1       |
| hepart                     | Bioflavonoid complex (H1006)    | H100631    | 1       |
| Hepart                     | Bioflavonoid complex (H1006)    | 17000256   | 1       |
| Unisan                     | Bioflavonoid complex (H1006)    | 1281683901 | 1       |
| Unisan                     | Bioflavonoid complex (H1006)    | 19001      | 1       |
| Hepart AG                  | Bioflavonoid complex (H1006)    | 42501      | 1       |
| Hepart AG                  | Bioflavonoid complex (H1006)    | 56001      | 2       |
| Hepart AG                  | Bioflavonoid complex (H1006)    | 1284019001 | 1       |
| Unisan                     | Bioflavonoid complex (H1006)    | 1284019001 | 1       |
| Hepart AG                  | Bioflavonoid complex (H1006)    | 1284042501 | 1       |
| Unisan                     | Bioflavonoid complex (H1006)    | 1284042501 | 2       |
| Unisan                     | Bioflavonoid complex (H1006)    |            | 1       |
| Hepart AG, CH-8280 Kreu... | Bioflavonoid complex (H1006)    | 56001      | 1       |
| Unisan                     | Bioflavonoid complex (H1006)    | 1284648802 | 1       |
| Unisan                     | Calcium (H1008)                 | 8901       | 7       |
| Hepart AG                  | Calcium (H1008)                 | 8901       | 2       |
| Unisan/Hepart AG           | Calcium (H1008)                 | 8901       | 1       |
| Unisan                     | Calcium (H1008)                 | 55001      | 4       |
| Hepart AG                  | Calcium (H1008)                 | 55001      | 1       |
| unisan                     | Calcium (H1008)                 | 55001      | 1       |
| Unisan                     | Calcium (H1008)                 | 55101      | 3       |
| Unisan                     | Calcium (H1008)                 | 55301      | 1       |
| Hepart AG                  | Calcium (H1008)                 | 55401      | 4       |
| Hepart AG                  | Calcium (H1008)                 | 55301      | 2       |
| Hepart AG                  | Calcium (H1008)                 | 55201      | 1       |
| Unisan                     | Calcium (H1008)                 | 55201      | 1       |
| Unisan                     | Calcium (H1008)                 | 55401      | 2       |

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| <b>Supplier</b>            | <b>Substance</b>    | <b>Batch</b> | <b>Spectra</b> |
|----------------------------|---------------------|--------------|----------------|
| Unisan Gmbh, 78465 Kons... | Calcium (H1008)     | 55401        | 1              |
| Hepart AG                  | Calcium (H1008)     | 55501        | 5              |
| Hepart AG, CH-8280 Kreu... | Calcium (H1008)     | 55501        | 2              |
| Unisan                     | Calcium (H1008)     | 55501        | 1              |
| Unisan                     | Calcium (H1008)     | 55601        | 2              |
| Hepart AG, CH-8280 Kreu... | Calcium (H1008)     | 1104008901   | 4              |
| Hepart AG                  | Calcium (H1008)     | 1104008901   | 6              |
| Unisan                     | Calcium (H1008)     | 1104008901   | 1              |
| Unisan                     | Calcium (H1008)     | 14000106     | 1              |
| Hepart AG                  | Calcium (H1008)     | 14000108     | 1              |
| Unisan                     | Calcium (H1008)     | 1104956001   | 1              |
| Unisan                     | Calcium (H1008)     | 1105008901   | 1              |
| Hepart AG                  | Calcium (H1008)     | 14000107     | 1              |
| Unisan                     | Calcium (H1008)     | 14000108     | 1              |
| Hepart AG                  | Calcium (H1008)     | 14000110     | 1              |
| Unisan                     | Calcium (H1008)     | 14000110     | 1              |
| UNISAN                     | Calcium (H1008)     | 14000110     | 1              |
| Hepart AG                  | Calcium (H1008)     | 14001933     | 1              |
| Unisan                     | Calcium (H1008)     | 14001934/0   | 1              |
| Sanacorp                   | Calcium (H1008)     | Fehl t       | 1              |
| Hepart                     | Calcium (H1008)     | 14001934/0   | 1              |
| Unisan                     | Calcium (H1008)     | 15001666     | 1              |
| Unisan                     | Calcium (H1008)     | 14001938/0   | 1              |
| Hepart                     | Calcium (H1008)     | 15001673     | 3              |
| Unisan                     | Calcium (H1008)     | 15001666/0   | 1              |
| Hepart                     | Calcium (H1008)     | 15001671     | 1              |
| Hepart                     | Calcium (H1008)     | 15001667/0   | 1              |
| Unisan                     | Calcium (H1008)     | 15001667     | 1              |
| Unisan                     | Calcium (H1008)     | 956001       | 1              |
| hepart                     | Calcium (H1008)     | 15001674     | 3              |
| hepart                     | Calcium (H1008)     | 15001675     | 2              |
| hepart                     | Calcium (H1008)     | 15001675/4   | 1              |
| Hepart                     | Calcium (H1008)     | 15001676     | 3              |
| Hepart                     | Calcium (H1008)     | 15001677     | 1              |
| Hepart                     | Calcium (H1008)     | 15001676/4   | 1              |
| Unisan                     | Glutathione (H1020) | 25703        | 3              |
| Unisan                     | Glutathione (H1020) | 40201        | 4              |
| Hepart AG, CH-8280 Kreu... | Glutathione (H1020) | 40201        | 1              |
| Unisan                     | Glutathione (H1020) | 74901        | 3              |
| UNISAN                     | Glutathione (H1020) | 74901        | 1              |
| Hepart AG                  | Glutathione (H1020) | 40201        | 1              |
| Unisan                     | Glutathione (H1020) | 1251019703   | 2              |
| Hepart AG, CH-8280 Kreu... | Glutathione (H1020) | 1251019703   | 1              |
| Hepart AG, CH-8280 Kreu... | Glutathione (H1020) | 1251025703   | 1              |
| Hepart AG                  | Glutathione (H1020) | 1254025703   | 1              |
| Unisan                     | Glutathione (H1020) | 1254025703   | 1              |
| Purren Apotheke            | Glutathione (H1020) | 1254955501   | 1              |
| Hepart AG                  | Glutathione (H1020) | 1254040201   | 1              |
| Hepart                     | Glutathione (H1020) | 15000478     | 1              |
| Unisan                     | Isoflavones (H1025) | 25704        | 1              |
| Unisan                     | Isoflavones (H1025) | 56701        | 4              |
| Hepart AG                  | Isoflavones (H1025) | 38801        | 1              |
| Unisan/Hepart AG           | Isoflavones (H1025) | 38801        | 1              |
| Hepart AG                  | Isoflavones (H1025) | 56701        | 1              |
| Unisan                     | Isoflavones (H1025) | 1310025704   | 1              |
| Unisan                     | Isoflavones (H1025) | 1310988301   | 1              |
| Hepart AG                  | Isoflavones (H1025) | 1314025704   | 1              |
| Hepart AG                  | Isoflavones (H1025) | 1314038801   | 1              |
| Unisan 02.04.2016          | Isoflavones (H1025) | 15000205/1   | 1              |
| Purren Apotheke            | Isoflavones (H1025) | 1314955701   | 1              |

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| Supplier                   | Substance              | Batch      | Spectra |
|----------------------------|------------------------|------------|---------|
| Unisan                     | Isoflavones (H1025)    | 15000205/0 | 3       |
| Unisan                     | Isoflavones (H1025)    | 15000205   | 1       |
| Unisan                     | Isoflavones (H1025)    | 15000205/3 | 1       |
| Unisan                     | OPC Grape seed (H1066) |            | 1       |
| Unisan                     | OPC Grape seed (H1066) | 70401      | 2       |
| Hepart AG                  | OPC Grape seed (H1066) | 70401      | 5       |
| UNISAN                     | OPC Grape seed (H1066) | 70401      | 1       |
| Hepart                     | OPC Grape seed (H1066) | 15000215   | 1       |
| Hepart AG                  | OPC Grape seed (H1066) | 16000637   | 1       |
| Hepart                     | OPC Grape seed (H1066) | 15000215/0 | 1       |
| Unisan                     | OPC Grape seed (H1066) | 18401      | 2       |
| Hepart                     | OPC Grape seed (H1066) | 16001439   | 1       |
| Hepart AG                  | OPC Grape seed (H1066) | 18401      | 1       |
| Unisan                     | OPC Grape seed (H1066) | 68301      | 4       |
| Hepart AG, CH-8280 Kreu... | OPC Grape seed (H1066) | 130208     | 1       |
| Hepart AG                  | OPC Grape seed (H1066) | 1504018401 | 2       |
| Hepart                     | Rhodiola (H1064)       | 15001045   | 1       |
| Unisan                     | OPC Grape seed (H1066) | 1504018401 | 1       |
| Hepart AG                  | Rhodiola (H1064)       | 70501      | 2       |
| Unisan/Hepart AG           | Vitamin B1 (H1101)     | 53301      | 1       |
| Unisan                     | Vitamin B1 (H1101)     | 30202      | 4       |
| Hepart AG                  | Vitamin B1 (H1101)     | 53301      | 2       |
| Unisan                     | Vitamin B1 (H1101)     | 53301      | 1       |
| Hepart AG, CH-8280 Kreu... | Vitamin B1 (H1101)     | 53301      | 1       |
| UNISAN                     | Vitamin B1 (H1101)     | 75001      | 1       |
| Hepart AG                  | Vitamin B1 (H1101)     | 75001      | 1       |
| Hepart AG                  | Vitamin B1 (H1101)     | 75001/3    | 2       |
| Hepart AG                  | Vitamin B1 (H1101)     | 14001112   | 1       |
| Hepart AG                  | Vitamin B1 (H1101)     | 14001112/0 | 1       |
| Unisan                     | Vitamin B1 (H1101)     | 14001112/0 | 1       |
| Unisan                     | Vitamin B1 (H1101)     | 15001620/0 | 1       |
| Unisan                     | Vitamin B1 (H1101)     | 15001622/0 | 1       |
| Hepart AG                  | Vitamin B1 (H1101)     | 15001622/0 | 1       |
| Hepart AG, Unisan GmbH     | Vitamin B1 (H1101)     | 15001622/0 | 1       |
| Hepart AG                  | Vitamin B1 (H1101)     | 16000698/0 | 1       |
| Hepart AG                  | Vitamin B1 (H1101)     | 1621030202 | 1       |
| Hepart AG                  | Vitamin B1 (H1101)     | 1622030202 | 2       |
| Unisan                     | Vitamin B1 (H1101)     | 1622977301 | 1       |
| Unisan                     | Vitamin B1 (H1101)     | 1621030202 | 1       |
| Unisan                     | Vitamin B1 (H1101)     | 977301     | 2       |

- 1494 spectra from 18 *Apo-Ident* customers from a total of 549 batches from a further 54 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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              | 3360          | 0              | 12 184        |
| Type B | 0              | 6462          | 687            | 25 707        |
| Type C | 0              | 263           | 32             | 1494          |

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 % (> 99.9240 %) | 100.0000 % (> 99.8214 %) |
| Type B | 100.0000 % (> 99.9296 %) | 90.3903 % (> 90.3483 %)  |
| Type C | 100.0000 % (> 98.8325 %) | 89.1525 % (> 88.1356 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 39.31                           |
| 80313     | 80313               | 0.00                         | 32.84                           |
| 80315     | 80315               | 0.00                         | 38.73                           |
| 80316     | 80316               | 0.00                         | 21.81                           |
| 80317     | 80317               | 0.00                         | 41.47                           |
| 80318     | 80318               | 0.00                         | 35.60                           |
| 80322     | 80322               | 0.00                         | 41.48                           |
| 80323     | 80323               | 0.00                         | 42.21                           |
| 80327     | 80327               | 0.00                         | 43.83                           |
| 80329     | 80329               | 0.00                         | 32.88                           |
| 80337     | 80337               | 0.00                         | 39.41                           |
| 80342     | 80342               | 0.00                         | 21.82                           |
| 80345     | 80345               | 0.00                         | 32.70                           |
| 80352     | 80352               | 0.00                         | 15.12                           |
| 80380     | 80380               | 0.00                         | 22.70                           |
| 80390     | 80390               | 0.00                         | 31.54                           |
| 80392     | 80392               | 0.00                         | 35.40                           |
| 80398     | 80398               | 0.00                         | 23.81                           |
| 80404     | 80404               | 0.00                         | 31.59                           |
| 80405     | 80405               | 0.00                         | 30.51                           |
| 80412     | 80412               | 0.00                         | 44.51                           |
| 80419     | 80419               | 0.00                         | 28.85                           |
| 80422     | 80422               | 0.00                         | 45.10                           |
| 80430     | 80430               | 0.00                         | 27.10                           |
| 80469     | 80469               | 0.00                         | 33.27                           |

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| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80473            | 80473                      | 0.00                                | 35.18                                  |
| 80479            | 80479                      | 0.00                                | 40.32                                  |
| 80492            | 80492                      | 0.00                                | 35.94                                  |
| 80504            | 80504                      | 0.00                                | 28.72                                  |
| 80505            | 80505                      | 0.00                                | 27.03                                  |
| 80506            | 80506                      | 0.00                                | 27.40                                  |
| 80507            | 80507                      | 0.00                                | 25.34                                  |
| 80508            | 80508                      | 0.00                                | 27.60                                  |
| 80509            | 80509                      | 0.00                                | 26.47                                  |
| 80521            | 80521                      | 0.00                                | 46.42                                  |
| 80522            | 80522                      | 0.00                                | 48.71                                  |
| 80525            | 80525                      | 0.00                                | 43.08                                  |
| 80526            | 80526                      | 0.00                                | 42.51                                  |
| 80527            | 80527                      | 0.00                                | 43.57                                  |
| 80529            | 80529                      | 0.00                                | 37.01                                  |
| 80583            | 80583                      | 0.00                                | 24.72                                  |
| 80607            | 80607                      | 0.00                                | 31.26                                  |
| 80609            | 80609                      | 0.00                                | 33.72                                  |
| 80613            | 80613                      | 0.00                                | 32.10                                  |
| 80616            | 80616                      | 0.00                                | 34.14                                  |
| 80618            | 80618                      | 0.00                                | 31.89                                  |
| 80619            | 80619                      | 0.00                                | 33.71                                  |
| 80621            | 80621                      | 0.00                                | 33.61                                  |
| 80624            | 80624                      | 0.00                                | 30.86                                  |
| 80632            | 80632                      | 0.00                                | 34.04                                  |
| 80672            | 80672                      | 0.00                                | 26.46                                  |
| 80707            | 80707                      | 0.00                                | 48.18                                  |
| 80709            | 80709                      | 0.00                                | 45.15                                  |
| 80711            | 80711                      | 0.00                                | 48.73                                  |
| 80712            | 80712                      | 0.00                                | 44.84                                  |
| 80715            | 80715                      | 0.00                                | 44.28                                  |
| 80719            | 80719                      | 0.00                                | 46.37                                  |
| 80722            | 80722                      | 0.00                                | 44.46                                  |
| 80724            | 80724                      | 0.00                                | 44.66                                  |
| 80729            | 80729                      | 0.00                                | 46.99                                  |
| 80732            | 80732                      | 0.00                                | 47.02                                  |
| 80734            | 80734                      | 0.00                                | 44.36                                  |
| 80740            | 80740                      | 0.00                                | 46.27                                  |
| 80741            | 80741                      | 0.00                                | 45.76                                  |
| 80768            | 80768                      | 0.00                                | 38.86                                  |
| 80783            | 80783                      | 0.00                                | 31.51                                  |
| 80815            | 80815                      | 0.00                                | 43.65                                  |
| 80853            | 80853                      | 0.00                                | 36.63                                  |
| 80864            | 80864                      | 0.00                                | 23.63                                  |
| 80878            | 80878                      | 0.00                                | 34.66                                  |
| 80946            | 80946                      | 0.00                                | 26.91                                  |
| 80953            | 80953                      | 0.00                                | 39.67                                  |
| 80980            | 80980                      | 0.00                                | 43.01                                  |
| 80986            | 80986                      | 0.00                                | 20.31                                  |
| 80987            | 80987                      | 0.00                                | 18.76                                  |
| 81001            | 81001                      | 0.00                                | 24.40                                  |
| 81016            | 81016                      | 0.00                                | 32.69                                  |
| 81041            | 81041                      | 0.00                                | 22.84                                  |

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| <b>Sample ID</b> | <b>Reference<br/>sample ID</b> | <b>Distance to<br/>reference sample</b> | <b>Distance to<br/>next foreign sample</b> |
|------------------|--------------------------------|-----------------------------------------|--------------------------------------------|
| 81042            | 81042                          | 0.00                                    | 22.87                                      |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Inositol hexanicotinate (H1022)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80087-2018-07-18  
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 |

## Validation samples

A total of 50 390 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 *Inositol hexanicotinate* (H1022). These samples are listed above in the section [calibration samples](#). The reference samples originate from 3 different batches.
- 15 404 spectra from a total of 340 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 190 spectra from 5 reference samples of the substance/substance group *Inositol hexanicotinate* (H1022).
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                       | Batch       | Sample ID          | Spectra |
|----------|---------------------------------|-------------|--------------------|---------|
| Hepart   | Inositol hexanicotinate (H10... | zu erfassen | 80042              | 40      |
| Hepart   | Inositol hexanicotinate (H10... | 652206      | 80087              | 40      |
| Hepart   | Inositol hexanicotinate (H10... | 0979201     | 80106              | 50      |
| Hepart   | Inositol hexanicotinate (H10... | 15000013    | 80554 <sup>†</sup> | 20      |
| Hepart   | Inositol hexanicotinate (H10... | 16000750    | 80814              | 40      |

- 32 867 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 12 spectra from 4 *Apo-Ident* customers from 8 batches from the substance/substance group *Inositol hexanicotinate (H1022)*.
- These include spectra of independent samples from 6 batches, of which no spectra have been used for the generation of the database.

| Supplier         | Substance                       | Batch      | Spectra |
|------------------|---------------------------------|------------|---------|
| Unisan           | Inositol hexanicotinate (H10... | 46001      | 1       |
| unisan           | Inositol hexanicotinate (H10... | 15000013   | 1       |
| Hepart AG        | Inositol hexanicotinate (H10... | 15000013   | 1       |
| Unisan           | Inositol hexanicotinate (H10... | 14000920   | 1       |
| Hepart AG        | Inositol hexanicotinate (H10... | 16000750/4 | 1       |
| Unisan/Hepart AG | Inositol hexanicotinate (H10... | 46001      | 1       |
| Unisan           | Inositol hexanicotinate (H10... | 1810046001 | 1       |
| Fagron           | Inositol hexanicotinate (H10... | 1811046001 | 1       |
| Unisan           | Inositol hexanicotinate (H10... | 1810979201 | 1       |
| Hepart AG        | Inositol hexanicotinate (H10... | 1811979201 | 2       |
| Purren Apotheke  | Inositol hexanicotinate (H10... | 1811979201 | 1       |

- 1777 spectra from 20 *Apo-Ident* customers from a total of 674 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 15 404        |
| <b>Type B</b> | 0              | 107           | 83             | 32 867        |
| <b>Type C</b> | 0              | 8             | 4              | 1777          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9252 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 56.3158 % (> 54.7368 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8547 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 85.41                           |
| 80465     | 80465               | 0.00                         | 90.69                           |
| 80554     | 80554               | 0.00                         | 91.67                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Iron (H1015) / Copper (H1032)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80341-2018-07-18  
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 |

## Validation samples

A total of 50 390 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 *Iron (H1015) / Copper (H1032)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 7 different batches.
- 15 184 spectra from a total of 336 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 930 spectra from 26 reference samples of the substance/substance group *Iron (H1015) / Copper (H1032)*.
- These include spectra of independent samples from 11 batches, of which no spectra have been used for the generation of the database.

| 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)   | 0928101 | 80162     | 50      |
| Hepart   | Iron (H1015)   | 998701  | 80183     | 40      |
| Hepart   | Copper (H1032) | 007901  | 80200     | 20      |
| Hepart   | Iron (H1015)   | 603206  | 80213     | 30      |
| Hepart   | Iron (H1015)   | 040901  | 80276     | 40      |

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| Supplier | Substance      | Batch        | Sample ID          | Spectra |
|----------|----------------|--------------|--------------------|---------|
| Hepart   | Copper (H1032) | 007901       | 80277              | 40      |
| Hepart   | Copper (H1032) | 046401       | 80305              | 40      |
| Hepart   | Copper (H1032) | 046401       | 80306              | 40      |
| Hepart   | Iron (H1015)   | 14000285     | 80413              | 40      |
| Hepart   | Iron (H1015)   | 14000285     | 80510 <sup>†</sup> | 20      |
| Hepart   | Iron (H1015)   | 040901       | 80511 <sup>†</sup> | 20      |
| Hepart   | Copper (H1032) | 15000211     | 80536 <sup>†</sup> | 20      |
| Hepart   | Iron (H1015)   | 040901       | 80568 <sup>†</sup> | 20      |
| Hepart   | Iron (H1015)   | 14000285     | 80569 <sup>†</sup> | 20      |
| Hepart   | Iron (H1015)   | 15001259(F2) | 80649              | 60      |
| Hepart   | Iron (H1015)   | 15001258     | 80650 <sup>†</sup> | 20      |
| Hepart   | Iron (H1015)   | 15001259(B1) | 80651 <sup>†</sup> | 20      |
| Hepart   | Iron (H1015)   | 15001258(F2) | 80652              | 60      |
| Hepart   | Iron (H1015)   | 15001259     | 80653 <sup>†</sup> | 20      |
| Hepart   | Iron (H1015)   | 15001258(B1) | 80654              | 60      |
| Hepart   | Copper (H1032) | 15000211/5   | 80875              | 40      |
| Hepart   | Iron (H1015)   | 17000279     | 80917              | 40      |

- 32 127 spectra from a total of 719 batches from further 121 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 78 spectra from 15 *Apo-Ident* customers from 24 batches from the substance/substance group *Iron (H1015) / Copper (H1032)*.
- These include spectra of independent samples from 21 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance    | Batch      | Spectra |
|----------------------------|--------------|------------|---------|
| Unisan                     | Iron (H1015) | 40901      | 16      |
| Hepart AG                  | Iron (H1015) | 40901      | 3       |
| Unisan/Hepart AG           | Iron (H1015) | 40901      | 1       |
| Hepart AG                  | Iron (H1015) | 1114040901 | 2       |
| Unisan                     | Iron (H1015) | 1114040901 | 2       |
| Unisan                     | Iron (H1015) | 1114603206 | 1       |
| Unisan                     | Iron (H1015) | 1114998701 | 5       |
| Hepart AG, CH-8280 Kreu... | Iron (H1015) | 1114998701 | 1       |
| Hepart AG                  | Iron (H1015) | 1114998701 | 1       |
| Hepart AG                  | Iron (H1015) | 14000285   | 2       |
| Unisan                     | Iron (H1015) | 14000285   | 1       |
| UNISAN                     | Iron (H1015) | 14000285   | 1       |
| Unisan                     | Iron (H1015) | 14000285/2 | 1       |
| Unisan                     | Iron (H1015) | 14000285/1 | 2       |

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

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| Supplier          | Substance      | Batch      | Spectra |
|-------------------|----------------|------------|---------|
| Unisan 11.08.2105 | Iron (H1015)   | 14000285/2 | 1       |
| Unisan 2.10.2015  | Iron (H1015)   | 14000285/3 | 2       |
| Unisan            | Iron (H1015)   | 14000285/5 | 1       |
| Hepart AG         | Iron (H1015)   | 14000285/4 | 1       |
| Unisan            | Iron (H1015)   | 998701     | 6       |
| Unisan            | Iron (H1015)   | 15001258/0 | 1       |
| Unisan 02.04.2016 | Iron (H1015)   | 15001258/0 | 1       |
| Hepart            | Iron (H1015)   | 15001258   | 1       |
| Unisan            | Iron (H1015)   | 15001258/2 | 2       |
| Unisan            | Iron (H1015)   | 15001259   | 1       |
| Unisan            | Copper (H1032) | 7901       | 1       |
| Unisan            | Copper (H1032) | 46401      | 2       |
| Unisan/Hepart AG  | Copper (H1032) | 13041501   | 3       |
| Unisan            | Copper (H1032) | 933901     | 1       |
| Hepart AG         | Copper (H1032) | 46401      | 1       |
| UNISAN            | Copper (H1032) | 13041501   | 5       |
| Hepart AG         | Copper (H1032) | 13041501   | 1       |
| Hepart AG         | Copper (H1032) | 130415-K1  | 1       |
| Unisan            | Copper (H1032) | 15000211/0 | 1       |
| hepart            | Copper (H1032) | 15000211/0 | 1       |
| Unisan            | Copper (H1032) | 1542933901 | 1       |
| Unisan            | Copper (H1032) | 1542933901 | 1       |
| Hepart AG         | Copper (H1032) | 1544007901 | 1       |
| Caelo             | Copper (H1032) | 933901     | 1       |
| Hepart AG         | Copper (H1032) | 1544046401 | 1       |

- 1711 spectra from 20 *Apo-Ident* customers from a total of 658 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 360           | 0              | 15 184        |
| <b>Type B</b> | 0              | 725           | 205            | 32 127        |
| <b>Type C</b> | 0              | 71            | 7              | 1711          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9244 %) | 100.0000 % (> 98.3333 %) |
| <b>Type B</b> | 100.0000 % (> 99.9242 %) | 77.9570 % (> 77.6344 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8351 %) | 91.0256 % (> 87.1795 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 40.29                           |
| 80510     | 80510               | 0.00                         | 18.06                           |
| 80511     | 80511               | 0.00                         | 17.36                           |
| 80536     | 80536               | 0.00                         | 36.93                           |
| 80568     | 80568               | 0.00                         | 15.76                           |
| 80569     | 80569               | 0.00                         | 20.23                           |
| 80650     | 80650               | 0.00                         | 11.75                           |
| 80651     | 80651               | 0.00                         | 12.26                           |
| 80653     | 80653               | 0.00                         | 12.11                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Isoleucine (L-) (H1045)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80134-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 384 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 260 spectra from 8 reference samples of the substance/substance group *Isoleucine (L-) (H1045)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance               | Batch       | Sample ID          | Spectra |
|----------|-------------------------|-------------|--------------------|---------|
| Hepart   | Isoleucine (L-) (H1045) | zu erfassen | 80051              | 40      |
| Hepart   | Isoleucine (L-) (H1045) | 0968701     | 80134              | 50      |
| Hepart   | Isoleucine (L-) (H1045) | 942901      | 80222              | 30      |
| Hepart   | Isoleucine (L-) (H1045) | 027701      | 80249              | 40      |
| Hepart   | Isoleucine (L-) (H1045) | 14001772    | 80498 <sup>†</sup> | 20      |
| Hepart   | Isoleucine (L-) (H1045) | 15001641    | 80678 <sup>†</sup> | 20      |
| Hepart   | Isoleucine (L-) (H1045) | 15001640    | 80679 <sup>†</sup> | 20      |
| Hepart   | Isoleucine (L-) (H1045) | 17000900    | 80909              | 40      |

- 32 797 spectra from a total of 729 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 15 spectra from 7 *Apo-Ident* customers from 7 batches from the substance/substance group *Isoleucine (L-) (H1045)*.
- These include spectra of independent samples from 7 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance               | Batch      | Spectra |
|----------------------------|-------------------------|------------|---------|
| Hepart AG                  | Isoleucine (L-) (H1045) | 66301      | 1       |
| Hepart AG                  | Isoleucine (L-) (H1045) | 15001640/2 | 1       |
| Unisan                     | Isoleucine (L-) (H1045) | 66301      | 2       |
| Fritz Schiele              | Isoleucine (L-) (H1045) | 1805027701 | 1       |
| Unisan                     | Isoleucine (L-) (H1045) | 27701      | 2       |
| Hepart AG, CH-8280 Kreu... | Isoleucine (L-) (H1045) | 66301      | 1       |
| Unisan                     | Isoleucine (L-) (H1045) | 1804027701 | 2       |
| Hepart AG, CH-8280 Kreu... | Isoleucine (L-) (H1045) | 1804968701 | 1       |
| Hepart AG                  | Isoleucine (L-) (H1045) | 1805027701 | 2       |
| Unisan                     | Isoleucine (L-) (H1045) | 1805027701 | 1       |
| Unisan                     | Isoleucine (L-) (H1045) | 1805968701 | 1       |

- 1774 spectra from 20 *Apo-Ident* customers from a total of 675 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 138           | 122            | 32 797        |
| <b>Type C</b> | 0              | 5             | 10             | 1774          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 53.0769 % (> 51.9231 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8500 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 40.71                           |
| 80498     | 80498               | 0.00                         | 36.85                           |
| 80678     | 80678               | 0.00                         | 39.65                           |
| 80679     | 80679               | 0.00                         | 43.95                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **L-5-HTP (H1035)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80111-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 130 spectra from 3 reference samples of the substance/substance group L-5-HTP (H1035).
- These include spectra of independent samples from 3 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance       | Batch       | Sample ID | Spectra |
|----------|-----------------|-------------|-----------|---------|
| Hepart   | L-5-HTP (H1035) | zu erfassen | 80047     | 40      |
| Hepart   | L-5-HTP (H1035) | 968801      | 80111     | 50      |
| Hepart   | L-5-HTP (H1035) | 0999801     | 80148     | 40      |

- 32 927 spectra from a total of 734 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 10 spectra from 5 *Apo-Ident* customers from 7 batches from the substance/substance group L-5-HTP (H1035).
- These include spectra of independent samples from 6 batches, of which no spectra have been used for the generation of the database.

| Supplier  | Substance       | Batch      | Spectra |
|-----------|-----------------|------------|---------|
| Unisan    | L-5-HTP (H1035) | 25006      | 3       |
| Unisan    | L-5-HTP (H1035) | 26102      | 1       |
| Unisan    | L-5-HTP (H1035) | 1836025006 | 1       |
| Hepart AG | L-5-HTP (H1035) | 1837025006 | 1       |
| Hepart AG | L-5-HTP (H1035) | 1837999801 | 2       |
| Hepart AG | L-5-HTP (H1035) | 15001503   | 1       |
| Hepart AG | L-5-HTP (H1035) | 16000441/0 | 1       |

- 1779 spectra from 20 *Apo-Ident* customers from a total of 675 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 0             | 130            | 32 927        |
| <b>Type C</b> | 0              | 1             | 9              | 1779          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9245 %) | 0.0000 % (≥ 0.0000 %)    |
| <b>Type C</b> | 100.0000 % (> 98.8593 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 32.81                           |
| 80851     | 80851               | 0.00                         | 29.64                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Leucine (L-) (H1046)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80150-2018-07-18  
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 |

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

### Type A All calibration spectra.

- 100 spectra of 2 reference samples from the substance/substance group *Leucine (L-) (H1046)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 444 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 180 spectra from 4 reference samples of the substance/substance group *Leucine (L-) (H1046)*.
- These include spectra of independent samples from 3 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance            | Batch       | Sample ID | Spectra |
|----------|----------------------|-------------|-----------|---------|
| Hepart   | Leucine (L-) (H1046) | zu erfassen | 80052     | 40      |
| Hepart   | Leucine (L-) (H1046) | 965101      | 80150     | 50      |
| Hepart   | Leucine (L-) (H1046) | 994101      | 80203     | 30      |
| Hepart   | Leucine (L-) (H1046) | 15000283    | 80570     | 60      |

- 32 877 spectra from a total of 733 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 11 spectra from 7 *Apo-Ident* customers from 6 batches from the substance/substance group *Leucine (L-) (H1046)*.
- These include spectra of independent samples from 6 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance            | Batch      | Spectra |
|----------------------------|----------------------|------------|---------|
| Unisan                     | Leucine (L-) (H1046) | 25706      | 1       |
| Hepart AG, CH-8280 Kreu... | Leucine (L-) (H1046) | 52601      | 2       |
| Unisan/Hepart AG           | Leucine (L-) (H1046) | 52601      | 1       |
| Hepart AG                  | Leucine (L-) (H1046) | 15000283/1 | 1       |
| Unisan                     | Leucine (L-) (H1046) | 52601      | 1       |
| Hepart AG                  | Leucine (L-) (H1046) | 1809994101 | 2       |
| Purren Apotheke            | Leucine (L-) (H1046) | 1809965101 | 1       |
| Unisan                     | Leucine (L-) (H1046) | 1809965101 | 1       |
| Unisan                     | Leucine (L-) (H1046) | 994101     | 1       |

- 1778 spectra from 20 *Apo-Ident* customers from a total of 676 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 100           | 0              | 15 444        |
| <b>Type B</b> | 0              | 176           | 4              | 32 877        |
| <b>Type C</b> | 0              | 7             | 4              | 1778          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9257 %) | 100.0000 % (> 94.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 97.7778 % (> 96.1111 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8568 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 40.59                           |
| 80410     | 80410               | 0.00                         | 45.61                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Lipoic acid (a-) (H1000)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80022-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 5 different batches.
- 15 325 spectra from a total of 338 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 541 spectra from 14 reference samples of the substance/substance group *Lipoic acid (a-) (H1000)*.
- These include spectra of independent samples from 8 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                | Batch          | Sample ID          | Spectra |
|----------|--------------------------|----------------|--------------------|---------|
| Hepart   | Lipoic acid (a-) (H1000) | 0954001        | 80022              | 40      |
| Hepart   | Lipoic acid (a-) (H1000) | 0954001        | 80178              | 40      |
| Hepart   | Lipoic acid (a-) (H1000) | 0993101        | 80185              | 40      |
| Hepart   | Lipoic acid (a-) (H1000) | 054301         | 80321 <sup>†</sup> | 1       |
| Hepart   | Lipoic acid (a-) (H1000) | 066601         | 80369              | 60      |
| Hepart   | Lipoic acid (a-) (H1000) | 14001420       | 80482 <sup>†</sup> | 20      |
| Hepart   | Lipoic acid (a-) (H1000) | 14001726       | 80491 <sup>†</sup> | 20      |
| Hepart   | Lipoic acid (a-) (H1000) | 15001526(B1.1) | 80680              | 60      |
| Hepart   | Lipoic acid (a-) (H1000) | 15001526(B1.2) | 80681 <sup>†</sup> | 20      |
| Hepart   | Lipoic acid (a-) (H1000) | 14000497       | 80682 <sup>†</sup> | 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      |
| Hepart   | Lipoic acid (a-) (H1000) | 18000250       | 81017              | 40      |

- 32 516 spectra from a total of 723 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 28 spectra from 10 *Apo-Ident* customers from 9 batches from the substance/substance group *Lipoic acid (a-) (H1000)*.
- These include spectra of independent samples from 7 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance                | Batch      | Spectra |
|----------------------------|--------------------------|------------|---------|
| Unisan                     | Lipoic acid (a-) (H1000) | 66601      | 1       |
| Unisan                     | Lipoic acid (a-) (H1000) | 14000497   | 1       |
| Hepart AG                  | Lipoic acid (a-) (H1000) | 66601      | 2       |
| Hepart AG                  | Lipoic acid (a-) (H1000) | 14001726   | 1       |
| UNISAN                     | Lipoic acid (a-) (H1000) | 14001726   | 2       |
| Unisan                     | Lipoic acid (a-) (H1000) | 25701      | 7       |
| Unisan                     | Lipoic acid (a-) (H1000) | 993101     | 2       |
| Unisan/Hepart AG           | Lipoic acid (a-) (H1000) | 25701      | 1       |
| Hepart AG                  | Lipoic acid (a-) (H1000) | H100031    | 2       |
| 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       |
| Unisan                     | Lipoic acid (a-) (H1000) | 1312993101 | 2       |
| Hepart AG                  | Lipoic acid (a-) (H1000) | 54301      | 1       |
| Hepart AG                  | Lipoic acid (a-) (H1000) | 1313025701 | 2       |

- 1761 spectra from 20 *Apo-Ident* customers from a total of 673 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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*).

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

|        | False positive | True positive | False negative | True negative |
|--------|----------------|---------------|----------------|---------------|
| Type A | 0              | 219           | 0              | 15 325        |
| Type B | 0              | 499           | 42             | 32 516        |
| Type C | 0              | 26            | 2              | 1761          |

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 % (> 99.9247 %) | 100.0000 % (> 97.2603 %) |
| Type B | 100.0000 % (> 99.9242 %) | 92.2366 % (> 91.6821 %)  |
| Type C | 100.0000 % (> 98.8414 %) | 92.8571 % (> 82.1429 %)  |

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

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

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

### Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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                         | 55.02                           |
| 80482     | 80482               | 0.00                         | 77.52                           |
| 80491     | 80491               | 0.00                         | 56.42                           |
| 80681     | 80681               | 0.00                         | 57.48                           |
| 80682     | 80682               | 0.00                         | 57.13                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Lysine (L-) (H1047)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80151-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 5 different batches.
- 15 264 spectra from a total of 338 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 270 spectra from 7 reference samples of the substance/substance group *Lysine (L-) (H1047)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance           | Batch       | Sample ID          | Spectra |
|----------|---------------------|-------------|--------------------|---------|
| Hepart   | Lysine (L-) (H1047) | zu erfassen | 80053              | 40      |
| Hepart   | Lysine (L-) (H1047) | 017302      | 80151              | 50      |
| Hepart   | Lysine (L-) (H1047) | 955002      | 80152              | 50      |
| Hepart   | Lysine (L-) (H1047) | 941501      | 80221              | 30      |
| Hepart   | Lysine (L-) (H1047) | 028801      | 80295              | 40      |
| Hepart   | Lysine (L-) (H1047) | 15000372    | 80562 <sup>†</sup> | 20      |
| Hepart   | Lysine (L-) (H1047) | 16001503/0  | 80848              | 40      |

- 32 787 spectra from a total of 730 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 15 spectra from 9 *Apo-Ident* customers from 9 batches from the substance/substance group *Lysine (L-) (H1047)*.
- These include spectra of independent samples from 8 batches, of which no spectra have been used for the generation of the database.

| 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) | 14000944   | 1       |
| Hepart AG                  | Lysine (L-) (H1047) | 14000944   | 1       |
| Unisan                     | Lysine (L-) (H1047) | 1800017302 | 3       |
| Hepart AG                  | Lysine (L-) (H1047) | 1800017302 | 1       |
| Hepart AG, CH-8280 Kreu... | Lysine (L-) (H1047) | 1800955002 | 1       |
| Hepart AG                  | Lysine (L-) (H1047) | 15000372/2 | 1       |
| Unisan                     | Lysine (L-) (H1047) | 15000372/0 | 1       |
| Unisan                     | Lysine (L-) (H1047) | 28801      | 2       |
| Unisan                     | Lysine (L-) (H1047) | 1801028801 | 1       |

- 1774 spectra from 20 *Apo-Ident* customers from a total of 673 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 280           | 0              | 15 264        |
| <b>Type B</b> | 0              | 95            | 175            | 32 787        |
| <b>Type C</b> | 0              | 11            | 4              | 1774          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9246 %) | 100.0000 % (> 97.8571 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 35.1852 % (> 34.0741 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8500 %) | n/a (n/a)                |

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

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

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80343            | 80343                      | 0.00                                | 51.52                                  |
| 80360            | 80360                      | 0.00                                | 60.41                                  |
| 80453            | 80453                      | 0.00                                | 52.78                                  |
| 80458            | 80458                      | 0.00                                | 63.65                                  |
| 80468            | 80468                      | 0.00                                | 62.73                                  |
| 80562            | 80562                      | 0.00                                | 59.33                                  |
| 80847            | 80847                      | 0.00                                | 70.42                                  |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Magnesium (H1060)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80061-2018-07-18  
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 |
| Hepart   | Magnesium (H1060) | 18000949 | 81058     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Magnesium (H1060)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 6 different batches.
- 15 294 spectra from a total of 337 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 1540 spectra from 35 reference samples of the substance/substance group *Magnesium (H1060)*.
- These include spectra of independent samples from 30 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance         | Batch       | Sample ID          | Spectra |
|----------|-------------------|-------------|--------------------|---------|
| Hepart   | Magnesium (H1060) | zu erfassen | 80012              | 40      |
| Hepart   | Magnesium (H1060) | zu erfassen | 80019              | 40      |
| Hepart   | Magnesium (H1060) | 973501      | 80061              | 30      |
| Hepart   | Magnesium (H1060) | 941701      | 80120              | 50      |
| Hepart   | Magnesium (H1060) | 0973501     | 80130              | 50      |
| Hepart   | Magnesium (H1060) | 043501      | 80283              | 40      |
| Hepart   | Magnesium (H1060) | 043601      | 80351              | 40      |
| Hepart   | Magnesium (H1060) | 069601      | 80378 <sup>†</sup> | 10      |
| Hepart   | Magnesium (H1060) | 070001      | 80423              | 40      |
| Hepart   | Magnesium (H1060) | 069801      | 80427              | 40      |
| Hepart   | Magnesium (H1060) | 069901      | 80429              | 40      |
| Hepart   | Magnesium (H1060) | 069701      | 80437              | 40      |
| Hepart   | Magnesium (H1060) | 14001893    | 80515 <sup>†</sup> | 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      |

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| Supplier | Substance         | Batch    | Sample ID          | Spectra |
|----------|-------------------|----------|--------------------|---------|
| Hepart   | Magnesium (H1060) | 16000264 | 80767 <sup>†</sup> | 20      |
| Hepart   | Magnesium (H1060) | 16000270 | 80769              | 60      |
| Hepart   | Magnesium (H1060) | 16000269 | 80770 <sup>†</sup> | 20      |
| Hepart   | Magnesium (H1060) | 16000267 | 80771              | 60      |
| Hepart   | Magnesium (H1060) | 16000271 | 80772              | 60      |
| Hepart   | Magnesium (H1060) | 16000268 | 80773              | 60      |
| Hepart   | Magnesium (H1060) | 16000265 | 80774              | 60      |
| Hepart   | Magnesium (H1060) | 16000272 | 80775              | 60      |
| Hepart   | Magnesium (H1060) | 16000266 | 80776              | 60      |
| Hepart   | Magnesium (H1060) | 16001703 | 80857              | 40      |
| Hepart   | Magnesium (H1060) | 16001704 | 80858              | 40      |
| Hepart   | Magnesium (H1060) | 16001705 | 80859              | 40      |
| Hepart   | Magnesium (H1060) | 16001706 | 80860              | 40      |
| Hepart   | Magnesium (H1060) | 18000420 | 81057              | 40      |
| Hepart   | Magnesium (H1060) | 18000950 | 81059              | 40      |
| Hepart   | Magnesium (H1060) | 18000951 | 81060              | 40      |
| Hepart   | Magnesium (H1060) | 18000952 | 81061              | 40      |
| Hepart   | Magnesium (H1060) | 18000953 | 81062              | 40      |

- 31 517 spectra from a total of 703 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 72 spectra from 15 *Apo-Ident* customers from 22 batches from the substance/substance group *Magnesium (H1060)*.
- These include spectra of independent samples from 19 batches, of which no spectra have been used for the generation of the database.

| Supplier  | Substance         | Batch      | Spectra |
|-----------|-------------------|------------|---------|
| Unisan    | Magnesium (H1060) | 14001893   | 1       |
| Unisan    | Magnesium (H1060) | 14001895   | 4       |
| Hepart AG | Magnesium (H1060) | 14001895/2 | 1       |
| Unisan    | Magnesium (H1060) | 43501      | 2       |
| Hepart    | Magnesium (H1060) | 16000269   | 1       |
| Unisan    | Magnesium (H1060) | 16000265/1 | 1       |
| Unisan    | Magnesium (H1060) | 16000265/0 | 1       |
| unbekannt | Magnesium (H1060) | 16000264   | 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       |

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

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| Supplier                   | Substance         | Batch      | Spectra |
|----------------------------|-------------------|------------|---------|
| Unisan/Hepart AG           | Magnesium (H1060) | 43601      | 1       |
| Hepart AG                  | Magnesium (H1060) | 43701      | 1       |
| Hepart AG, CH-8280 Kreu... | Magnesium (H1060) | 43602      | 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      | 4       |
| Unisan                     | Magnesium (H1060) | 69601      | 1       |
| Unisan                     | Magnesium (H1060) | 69801      | 4       |
| UNISAN                     | Magnesium (H1060) | 69701      | 3       |
| Hepart AG                  | Magnesium (H1060) | 69801      | 3       |
| Unisan                     | Magnesium (H1060) | 69801/2    | 1       |
| Hepart AG                  | Magnesium (H1060) | 69901      | 4       |
| Hepart AG, CH-8280 Kreu... | Magnesium (H1060) | 1134043601 | 1       |
| Unisan/Hepart AG           | Magnesium (H1060) | 973501     | 1       |
| Unisan                     | Magnesium (H1060) | 973501     | 3       |
| Hepart AG, CH-8280 Kreu... | Magnesium (H1060) | 1134973501 | 2       |
| Unisan                     | Magnesium (H1060) | 1134973501 | 4       |
| Hepart AG                  | Magnesium (H1060) | 1134973501 | 5       |
| unisan                     | Magnesium (H1060) | 14001895   | 1       |
| Hepart AG                  | Magnesium (H1060) | 14001895   | 1       |
| Hepart AG                  | Magnesium (H1060) | 14001895/1 | 1       |
| Unisan                     | Magnesium (H1060) | H106021    | 1       |

- 1717 spectra from 20 *Apo-Ident* customers from a total of 660 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 250           | 0              | 15 294        |
| <b>Type B</b> | 0              | 1250          | 290            | 31 517        |
| <b>Type C</b> | 0              | 32            | 40             | 1717          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9246 %) | 100.0000 % (> 97.6000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9241 %) | 81.1688 % (> 80.9740 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8354 %) | 44.4444 % (> 40.2778 %)  |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 31.53                           |
| 80515     | 80515               | 0.00                         | 40.88                           |
| 80767     | 80767               | 0.00                         | 32.03                           |
| 80770     | 80770               | 0.00                         | 31.62                           |
| 80856     | 80856               | 0.00                         | 25.83                           |
| 81058     | 81058               | 0.00                         | 29.27                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Methylsulfonylmethane (MSM) (H1062)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80102-2018-07-18  
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... | 17001247 | 80957     | 40      | from supplier |

## Validation samples

A total of 50 390 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 section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 324 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 210 spectra from 5 reference samples of the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                       | Batch       | Sample ID          | Spectra |
|----------|---------------------------------|-------------|--------------------|---------|
| Hepart   | Methylsulfonylmethane (MSM) ... | zu erfassen | 80062              | 30      |
| Hepart   | Methylsulfonylmethane (MSM) ... | 979401      | 80102              | 50      |
| Hepart   | Methylsulfonylmethane (MSM) ... | 0964001     | 80115              | 50      |
| Hepart   | Methylsulfonylmethane (MSM) ... | 15001371    | 80703 <sup>†</sup> | 40      |
| Hepart   | Methylsulfonylmethane (MSM) ... | 16000449/0  | 80782              | 40      |

- 32 847 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B*

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

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 14 spectra from 6 *Apo-Ident* customers from 10 batches from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*.
- These include spectra of independent samples from 9 batches, of which no spectra have been used for the generation of the database.

| Supplier         | Substance                       | Batch       | Spectra |
|------------------|---------------------------------|-------------|---------|
| Hepart AG        | Methylsulfonylmethane (MSM) ... | 140000921/1 | 1       |
| Hepart AG        | Methylsulfonylmethane (MSM) ... | 56201       | 1       |
| HCK              | Methylsulfonylmethane (MSM) ... | 1400921/1   | 1       |
| Unisan           | Methylsulfonylmethane (MSM) ... | 56201       | 2       |
| Unisan           | Methylsulfonylmethane (MSM) ... | 15001371    | 1       |
| Unisan           | Methylsulfonylmethane (MSM) ... | 979401      | 1       |
| Unisan           | Methylsulfonylmethane (MSM) ... | 25013       | 2       |
| Unisan           | Methylsulfonylmethane (MSM) ... | 26101       | 1       |
| Hepart AG        | Methylsulfonylmethane (MSM) ... | 15001371    | 1       |
| Unisan           | Methylsulfonylmethane (MSM) ... | 1818025013  | 1       |
| Unisan/Hepart AG | Methylsulfonylmethane (MSM) ... | 1819025013  | 1       |
| Hepart AG        | Methylsulfonylmethane (MSM) ... | 1819026101  | 1       |

- 1775 spectra from 20 *Apo-Ident* customers from a total of 672 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 220           | 0              | 15 324        |
| <b>Type B</b> | 0              | 173           | 37             | 32 847        |
| <b>Type C</b> | 0              | 9             | 5              | 1775          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9247 %) | 100.0000 % (> 97.2727 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 82.3810 % (> 80.9524 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8514 %) | n/a (n/a)                |

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

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

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80332            | 80332                      | 0.00                                | 79.53                                  |
| 80467            | 80467                      | 0.00                                | 89.48                                  |
| 80703            | 80703                      | 0.00                                | 84.15                                  |
| 80957            | 80957                      | 0.00                                | 68.54                                  |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Ornithine (L-) (H1048)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80175-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 384 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 270 spectra from 8 reference samples of the substance/substance group *Ornithine (L-) (H1048)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance              | Batch        | Sample ID          | Spectra |
|----------|------------------------|--------------|--------------------|---------|
| Hepart   | Ornithine (L-) (H1048) | zu erfassen  | 80054              | 40      |
| Hepart   | Ornithine (L-) (H1048) | 979301       | 80175              | 40      |
| Hepart   | Ornithine (L-) (H1048) | 646703       | 80195              | 40      |
| Hepart   | Ornithine (L-) (H1048) | 001202       | 80206              | 30      |
| Hepart   | Ornithine (L-) (H1048) | 15000004     | 80629 <sup>†</sup> | 20      |
| Hepart   | Ornithine (L-) (H1048) | 15001364     | 80667 <sup>†</sup> | 20      |
| Hepart   | Ornithine (L-) (H1048) | 15001364(F2) | 80668              | 60      |
| Hepart   | Ornithine (L-) (H1048) | 15001364(F1) | 80669 <sup>†</sup> | 20      |

- 32 787 spectra from a total of 729 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 16 spectra from 7 *Apo-Ident* customers from 8 batches from the substance/substance group *Ornithine (L-) (H1048)*.
- These include spectra of independent samples from 8 batches, of which no spectra have been used for the generation of the database.

| Supplier               | Substance              | Batch      | Spectra |
|------------------------|------------------------|------------|---------|
| Unisan/Hepart AG       | Ornithine (L-) (H1048) | 27001      | 3       |
| Hepart AG, Unisan GmbH | Ornithine (L-) (H1048) | 27001      | 3       |
| Hepart AG              | Ornithine (L-) (H1048) | 27001/5    | 1       |
| Hepart AG              | Ornithine (L-) (H1048) | 1817025008 | 1       |
| Unisan                 | Ornithine (L-) (H1048) | 1816979301 | 2       |
| Unisan                 | Ornithine (L-) (H1048) | 979301     | 2       |
| Purren Apotheke        | Ornithine (L-) (H1048) | 1817979301 | 1       |
| Hepart AG              | Ornithine (L-) (H1048) | 27001/8    | 1       |
| Hepart                 | Ornithine (L-) (H1048) | 16000935/0 | 2       |

- 1773 spectra from 20 *Apo-Ident* customers from a total of 674 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 192           | 78             | 32 787        |
| <b>Type C</b> | 0              | 5             | 11             | 1773          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 71.1111 % (> 70.0000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8489 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 77.41                           |
| 80667     | 80667               | 0.00                         | 76.95                           |
| 80669     | 80669               | 0.00                         | 80.89                           |
| 80811     | 80811               | 0.00                         | 67.06                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Orthovimin Neutral Complex (H1403)</b>                       |
| Substance class                     | HCK - nutritional supplements (Hepart)                          |
| Report date                         | 18/07/2018                                                      |
| Report number                       | 80744-2018-07-18                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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 | <i>European Pharmacopoeia 8th Edition, Basic Version 2014</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]          |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>        |
| Anhang F          | <a href="#">Zusatz zu den Modellen der zweiten Stufe</a>          |

### Validation method

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

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

Finally, 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 |
| Hepart   | Orthovimin Neutr... | 17001152 | 81020     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Orthovimin Neutral Complex (H1403)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 60 spectra from 2 reference samples of the substance/substance group *Orthovimin Neutral Complex (H1403)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                        | Batch    | Sample ID          | Spectra |
|----------|----------------------------------|----------|--------------------|---------|
| Hepart   | Orthovimin Neutral Complex (...) | 15001850 | 80744 <sup>†</sup> | 20      |
| Hepart   | Orthovimin Neutral Complex (...) | 17001625 | 80983              | 40      |

- 32 997 spectra from a total of 734 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details

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

provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Orthovimin Neutral Complex (H1403)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

## 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 58            | 2              | 32 852        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9259 %) | 96.6667 % (> 91.6667 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 26.19                           |
| 81020     | 81020               | 0.00                         | 26.21                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **PET basis (H1503)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80566-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 1 different batches.
- 15 464 spectra from a total of 342 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 40 spectra from 2 reference samples of the substance/substance group *PET basis (H1503)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance         | Batch    | Sample ID          | Spectra |
|----------|-------------------|----------|--------------------|---------|
| Hepart   | PET basis (H1503) | 15000402 | 80566 <sup>†</sup> | 20      |
| Hepart   | PET basis (H1503) | 15000402 | 80636 <sup>†</sup> | 20      |

- 33 017 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET basis (H1503)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 40            | 0              | 32 977        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9268 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 28.80                           |
| 80636     | 80636               | 0.00                         | 25.45                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **PET coenzyme Q10 (H0022)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80561-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 1 different batches.
- 15 464 spectra from a total of 343 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 40 spectra from 2 reference samples of the substance/substance group *PET coenzyme Q10 (H0022)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                | Batch    | Sample ID          | Spectra |
|----------|--------------------------|----------|--------------------|---------|
| Hepart   | PET coenzyme Q10 (H0022) | 15000401 | 80561 <sup>†</sup> | 20      |
| Hepart   | PET coenzyme Q10 (H0022) | 15000401 | 80635 <sup>†</sup> | 20      |

- 33 017 spectra from a total of 736 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details

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

provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET coenzyme Q10 (H0022)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 40            | 0              | 33 017        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9255 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 21.66                           |
| 80635     | 80635               | 0.00                         | 23.16                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **PET immune system (H1502)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80564-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 1 different batches.
- 15 464 spectra from a total of 342 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 40 spectra from 2 reference samples of the substance/substance group *PET immune system (H1502)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                 | Batch    | Sample ID          | Spectra |
|----------|---------------------------|----------|--------------------|---------|
| Hepart   | PET immune system (H1502) | 15000405 | 80564 <sup>†</sup> | 20      |
| Hepart   | PET immune system (H1502) | 15000405 | 80634 <sup>†</sup> | 20      |

- 33 017 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details

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

provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET immune system (H1502)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 40            | 0              | 32 977        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9268 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 29.75                           |
| 80634     | 80634               | 0.00                         | 28.68                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **PET joints (H1501)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80567-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 1 different batches.
- 15 464 spectra from a total of 342 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 40 spectra from 2 reference samples of the substance/substance group *PET joints (H1501)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance          | Batch    | Sample ID          | Spectra |
|----------|--------------------|----------|--------------------|---------|
| Hepart   | PET joints (H1501) | 15000404 | 80567 <sup>†</sup> | 20      |
| Hepart   | PET joints (H1501) | 15000404 | 80630 <sup>†</sup> | 20      |

- 33 017 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET joints (H1501)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 40            | 0              | 32 977        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9268 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 19.41                           |
| 80630     | 80630               | 0.00                         | 20.93                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **PET skin and hair (H1504)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80565-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 1 different batches.
- 15 464 spectra from a total of 342 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 40 spectra from 2 reference samples of the substance/substance group *PET skin and hair (H1504)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                 | Batch    | Sample ID          | Spectra |
|----------|---------------------------|----------|--------------------|---------|
| Hepart   | PET skin and hair (H1504) | 15000403 | 80565 <sup>†</sup> | 20      |
| Hepart   | PET skin and hair (H1504) | 15000403 | 80633 <sup>†</sup> | 20      |

- 33 017 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details

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

provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET skin and hair (H1504)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 40            | 0              | 32 977        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9268 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 47.51                           |
| 80633     | 80633               | 0.00                         | 46.08                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **PET well-aging (H1500)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80563-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 342 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 40 spectra from 2 reference samples of the substance/substance group *PET well-aging (H1500)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance              | Batch    | Sample ID          | Spectra |
|----------|------------------------|----------|--------------------|---------|
| Hepart   | PET well-aging (H1500) | 15000401 | 80563 <sup>†</sup> | 20      |
| Hepart   | PET well-aging (H1500) | 15000406 | 80631 <sup>†</sup> | 20      |

- 33 017 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET well-aging (H1500)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 40            | 0              | 33 017        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9255 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 14.26                           |
| 80631     | 80631               | 0.00                         | 13.58                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Phenylalanine (L-) (H1049)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80090-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 215 spectra from 5 reference samples of the substance/substance group *Phenylalanine (L-)* (H1049).
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                  | Batch       | Sample ID | Spectra |
|----------|----------------------------|-------------|-----------|---------|
| Hepart   | Phenylalanine (L-) (H1049) | zu erfassen | 80055     | 30      |
| Hepart   | Phenylalanine (L-) (H1049) | 964401      | 80090     | 55      |
| Hepart   | Phenylalanine (L-) (H1049) | 001201      | 80198     | 60      |
| Hepart   | Phenylalanine (L-) (H1049) | 019707      | 80202     | 30      |
| Hepart   | Phenylalanine (L-) (H1049) | 17000876    | 80916     | 40      |

- 32 842 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details

provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 14 spectra from 7 *Apo-Ident* customers from 5 batches from the substance/substance group *Phenylalanine (L-) (H1049)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier         | Substance                  | Batch      | Spectra |
|------------------|----------------------------|------------|---------|
| Unisan           | Phenylalanine (L-) (H1049) | 25009      | 6       |
| Hepart AG        | Phenylalanine (L-) (H1049) | 25009      | 3       |
| Hepart AG        | Phenylalanine (L-) (H1049) | 74401/1    | 1       |
| Unisan           | Phenylalanine (L-) (H1049) | 74401/0    | 1       |
| Unisan           | Phenylalanine (L-) (H1049) | 1828019707 | 1       |
| Hepart AG        | Phenylalanine (L-) (H1049) | 1828025009 | 1       |
| Unisan/Hepart AG | Phenylalanine (L-) (H1049) | 1828025009 | 1       |

- 1775 spectra from 20 *Apo-Ident* customers from a total of 677 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 40            | 175            | 32 842        |
| <b>Type C</b> | 0              | 1             | 13             | 1775          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 18.6047 % (> 17.2093 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8514 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 48.14                           |
| 80852     | 80852               | 0.00                         | 48.67                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Potassium (H1030)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80043-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 6 different batches.
- 15 294 spectra from a total of 337 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 759 spectra from 19 reference samples of the substance/substance group *Potassium (H1030)*.
- These include spectra of independent samples from 12 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance         | Batch        | Sample ID          | Spectra |
|----------|-------------------|--------------|--------------------|---------|
| Hepart   | Potassium (H1030) | 0944201      | 80043              | 40      |
| Hepart   | Potassium (H1030) | 0944201      | 80156              | 50      |
| Hepart   | Potassium (H1030) | 931901       | 80224              | 30      |
| Hepart   | Potassium (H1030) | 028901       | 80264              | 39      |
| Hepart   | Potassium (H1030) | 028901       | 80267              | 40      |
| Hepart   | Potassium (H1030) | 130328001    | 80347              | 40      |
| Hepart   | Potassium (H1030) | 039302       | 80372 <sup>†</sup> | 10      |
| Hepart   | Potassium (H1030) | 069201       | 80376              | 50      |
| Hepart   | Potassium (H1030) | 15000597     | 80571 <sup>†</sup> | 20      |
| Hepart   | Potassium (H1030) | 15000597(B1) | 80572              | 60      |
| Hepart   | Potassium (H1030) | 15000598     | 80573              | 60      |
| Hepart   | Potassium (H1030) | 15000598(B1) | 80574 <sup>†</sup> | 20      |
| Hepart   | Potassium (H1030) | 15000598(F2) | 80575              | 60      |
| Hepart   | Potassium (H1030) | 15000599     | 80576 <sup>†</sup> | 20      |
| Hepart   | Potassium (H1030) | 15000599(F2) | 80577              | 60      |
| Hepart   | Potassium (H1030) | 15000600     | 80578 <sup>†</sup> | 20      |
| Hepart   | Potassium (H1030) | 15000600(B1) | 80579              | 60      |

*continued on the next page*

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| Supplier | Substance         | Batch    | Sample ID | Spectra |
|----------|-------------------|----------|-----------|---------|
| Hepart   | Potassium (H1030) | 16001646 | 80869     | 40      |
| Hepart   | Potassium (H1030) | 16001647 | 80870     | 40      |

- 32 298 spectra from a total of 719 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 43 spectra from 11 *Apo-Ident* customers from 15 batches from the substance/substance group *Potassium (H1030)*.
- These include spectra of independent samples from 14 batches, of which no spectra have been used for the generation of the database.

| 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       |
| Fagron           | Potassium (H1030) | 39301      | 1       |
| Hepart AG        | Potassium (H1030) | 39301      | 1       |
| Unisan/Hepart AG | Potassium (H1030) | 39302      | 1       |
| Hepart AG        | Potassium (H1030) | 39302      | 1       |
| Unisan           | Potassium (H1030) | 69201      | 5       |
| Unisan           | Potassium (H1030) | 69301      | 3       |
| UNISAN           | Potassium (H1030) | 69201      | 1       |
| Unisan           | Potassium (H1030) | 39302      | 1       |
| Hepart AG        | Potassium (H1030) | 69301/1    | 1       |
| Hepart AG        | Potassium (H1030) | 69301      | 1       |
| Hepart AG        | Potassium (H1030) | 1124028903 | 1       |
| Unisan           | Potassium (H1030) | 944201     | 4       |
| Unisan           | Potassium (H1030) | 69401      | 1       |
| Unisan           | Potassium (H1030) | 1124028903 | 1       |
| Unisan           | Potassium (H1030) | 69401/0    | 1       |
| Unisan           | Potassium (H1030) | 130328001  | 3       |
| Hepart AG        | Potassium (H1030) | 1124944201 | 1       |
| Unisan           | Potassium (H1030) | 1124944201 | 1       |
| hepart           | Potassium (H1030) | 15000597/0 | 1       |
| Unisan           | Potassium (H1030) | 15000597/0 | 1       |
| Unisan           | Potassium (H1030) | 15000599   | 1       |

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

- 1746 spectra from 20 *Apo-Ident* customers from a total of 667 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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              | 15 294        |
| Type B | 0              | 691           | 68             | 32 298        |
| Type C | 0              | 36            | 7              | 1746          |

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 % (> 99.9246 %) | 100.0000 % (> 97.6000 %) |
| Type B | 100.0000 % (> 99.9242 %) | 91.0408 % (> 90.6456 %)  |
| Type C | 100.0000 % (> 98.8380 %) | 83.7209 % (> 76.7442 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 35.57                           |
| 80571     | 80571               | 0.00                         | 48.71                           |
| 80574     | 80574               | 0.00                         | 49.64                           |
| 80576     | 80576               | 0.00                         | 49.91                           |
| 80578     | 80578               | 0.00                         | 49.87                           |
| 80868     | 80868               | 0.00                         | 49.96                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Proline (-L) NF (H1050)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80905-2018-07-18  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Proline (-L) NF (H1050); L-proline NF (H1050)

### Special notes

When selecting the *Proline (-L) NF (H1050)* 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 *Proline (-L) NF (H1050)*:

| Supplier | Substance           | Batch    | Sample ID | Spectra | Certificate   |
|----------|---------------------|----------|-----------|---------|---------------|
| Hepart   | Proline (-L) NF ... | 17000952 | 80935     | 40      | from supplier |
| Hepart   | Proline (-L) NF ... | 18000403 | 81023     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Proline (-L) NF (H1050)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 80 spectra from 2 reference samples of the substance/substance group *Proline (-L) NF (H1050)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance               | Batch    | Sample ID | Spectra |
|----------|-------------------------|----------|-----------|---------|
| Hepart   | Proline (-L) NF (H1050) | 16000951 | 80905     | 40      |
| Hepart   | Proline (-L) NF (H1050) | 16000951 | 80936     | 40      |

- 32 977 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Proline (-L) NF (H1050)*.

- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

## Validation results

The validation runs checked whether the substance/substance group *Proline (-L) NF (H1050)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Proline (-L) NF (H1050)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 0             | 80             | 32 977        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

The substance/substance group *Proline (-L) NF (H1050)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9248 %) | 0.0000 % (≥ 0.0000 %)    |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 80935     | 80935               | 0.00                         | 29.22                           |
| 81023     | 81023               | 0.00                         | 31.95                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Silicium (H1070)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80906-2018-07-18  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Silicium (H1070)

### Special notes

When selecting the *Silicium (H1070)* 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 *Silicium (H1070)*:

| Supplier | Substance        | Batch    | Sample ID | Spectra | Certificate   |
|----------|------------------|----------|-----------|---------|---------------|
| Hepart   | Silicium (H1070) | 17000326 | 80906     | 40      | from supplier |
| Hepart   | Silicium (H1070) | 17000817 | 80914     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Silicium (H1070)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 40 spectra from 1 reference samples of the substance/substance group *Silicium (H1070)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance        | Batch    | Sample ID | Spectra |
|----------|------------------|----------|-----------|---------|
| Hepart   | Silicium (H1070) | 18000448 | 81022     | 40      |

- 33 017 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Silicium (H1070)*.

- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

## Validation results

The validation runs checked whether the substance/substance group *Silicium (H1070)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Silicium (H1070)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 0             | 40             | 33 017        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

The substance/substance group *Silicium (H1070)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9255 %) | 0.0000 % (≥ 0.0000 %)    |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 80906     | 80906               | 0.00                         | 33.79                           |
| 80914     | 80914               | 0.00                         | 30.16                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Silymarin (H1071)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80068-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 230 spectra from 6 reference samples of the substance/substance group *Silymarin (H1071)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| 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) | 029901   | 80265              | 40      |
| Hepart   | Silymarin (H1071) | 067701   | 80375              | 60      |
| Hepart   | Silymarin (H1071) | 15001046 | 80671 <sup>†</sup> | 20      |

- 32 827 spectra from a total of 731 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 24 spectra from 11 *Apo-Ident* customers from 11 batches from the substance/substance group *Silymarin (H1071)*.
- These include spectra of independent samples from 10 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance         | Batch      | Spectra |
|----------------------------|-------------------|------------|---------|
| Hepart AG, CH-8280 Kreu... | Silymarin (H1071) | 29901      | 2       |
| Unisan                     | Silymarin (H1071) | 67701/7    | 1       |
| unisan                     | Silymarin (H1071) | 67701      | 2       |
| Unisan                     | Silymarin (H1071) | 29901      | 3       |
| Hepart                     | Silymarin (H1071) | 15001046   | 1       |
| Unisan                     | Silymarin (H1071) | 46101      | 1       |
| Unisan/Hepart AG           | Silymarin (H1071) | 29901      | 1       |
| Hepart AG                  | Silymarin (H1071) | 67701      | 3       |
| Unisan                     | Silymarin (H1071) | 46101/0    | 1       |
| UNISAN                     | Silymarin (H1071) | 67701      | 1       |
| Hepart AG, CH-8280 Kreu... | Silymarin (H1071) | 1241046101 | 1       |
| Unisan                     | Silymarin (H1071) | 950401     | 2       |
| Hepart AG, CH-8280 Kreu... | Silymarin (H1071) | 1241950401 | 1       |
| Unisan                     | Silymarin (H1071) | 1241950401 | 2       |
| Hepart AG                  | Silymarin (H1071) | 1244029901 | 1       |
| hepart ag                  | Silymarin (H1071) | 1244950401 | 1       |

- 1765 spectra from 20 *Apo-Ident* customers from a total of 671 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 81            | 149            | 32 827        |
| <b>Type C</b> | 0              | 1             | 23             | 1765          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 35.2174 % (> 33.9130 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8431 %) | 4.1667 % (≥ 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                         | 33.19                           |
| 80861     | 80861               | 0.00                         | 26.88                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Stomach complex (H1120)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80666-2018-07-18  
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 |

## Validation samples

A total of 50 390 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 *Stomach complex (H1120)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 60 spectra from 2 reference samples of the substance/substance group *Stomach complex (H1120)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance               | Batch    | Sample ID          | Spectra |
|----------|-------------------------|----------|--------------------|---------|
| Hepart   | Stomach complex (H1120) | 15001350 | 80666 <sup>†</sup> | 20      |
| Hepart   | Stomach complex (H1120) | 16001139 | 80889              | 40      |

- 32 997 spectra from a total of 734 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Stomach complex (H1120)*.
- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

## 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 60            | 0              | 32 997        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 90.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 30.45                           |
| 80888     | 80888               | 0.00                         | 38.36                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Taurine (H1084)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80071-2018-07-18  
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 |
| Hepart   | Taurine (H1084) | 18000419 | 81063     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Taurine (H1084)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 3 different batches.
- 15 384 spectra from a total of 340 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 260 spectra from 7 reference samples of the substance/substance group *Taurine (H1084)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance       | Batch    | Sample ID          | Spectra |
|----------|-----------------|----------|--------------------|---------|
| Hepart   | Taurine (H1084) | 960201   | 80071              | 30      |
| Hepart   | Taurine (H1084) | 960201   | 80088              | 50      |
| Hepart   | Taurine (H1084) | 017301   | 80142              | 50      |
| Hepart   | Taurine (H1084) | 600402   | 80216              | 30      |
| Hepart   | Taurine (H1084) | 028001   | 80250              | 40      |
| Hepart   | Taurine (H1084) | 14001767 | 80497 <sup>†</sup> | 20      |
| Hepart   | Taurine (H1084) | 16000947 | 80810              | 40      |

- 32 797 spectra from a total of 730 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 24 spectra from 10 *Apo-Ident* customers from 8 batches from the substance/substance group *Taurine (H1084)*.
- These include spectra of independent samples from 6 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance       | Batch      | Spectra |
|----------------------------|-----------------|------------|---------|
| Hepart AG, CH-8280 Kreu... | Taurine (H1084) | 25710      | 3       |
| Unisan                     | Taurine (H1084) | 25710      | 1       |
| Unisan                     | Taurine (H1084) | 28001      | 8       |
| Unisan/Hepart AG           | Taurine (H1084) | 28001      | 2       |
| Hepart AG                  | Taurine (H1084) | 28001      | 2       |
| Unisan                     | Taurine (H1084) | 1294960201 | 2       |
| Unisan                     | Taurine (H1084) | 1294028001 | 1       |
| Hepart AG                  | Taurine (H1084) | 1294028001 | 1       |
| Unisan                     | Taurine (H1084) | 14001767/0 | 1       |
| hepart                     | Taurine (H1084) | 14001767/1 | 1       |
| unisan                     | Taurine (H1084) | 14001767   | 1       |
| Hepart                     | Taurine (H1084) | 16000946   | 1       |

- 1765 spectra from 20 *Apo-Ident* customers from a total of 674 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 169           | 91             | 32 797        |
| <b>Type C</b> | 0              | 8             | 16             | 1765          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 65.0000 % (> 63.8462 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8431 %) | 33.3333 % (> 20.8333 %)  |

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

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

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

### Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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                         | 67.71                           |
| 80809     | 80809               | 0.00                         | 69.73                           |
| 80887     | 80887               | 0.00                         | 68.89                           |
| 81063     | 81063               | 0.00                         | 67.11                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Threonine (L-) (H1052)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80107-2018-07-18  
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 |
| Hepart   | Threonine (L-) (...) | 14001718 | 81018     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Threonine (L-) (H1052)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 1 different batches.
- 15 464 spectra from a total of 342 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 190 spectra from 5 reference samples of the substance/substance group *Threonine (L-) (H1052)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance              | Batch       | Sample ID          | Spectra |
|----------|------------------------|-------------|--------------------|---------|
| Hepart   | Threonine (L-) (H1052) | zu erfassen | 80057              | 30      |
| Hepart   | Threonine (L-) (H1052) | 638802      | 80107              | 50      |
| Hepart   | Threonine (L-) (H1052) | 014901      | 80122              | 50      |
| Hepart   | Threonine (L-) (H1052) | 14001718    | 80496 <sup>†</sup> | 20      |
| Hepart   | Threonine (L-) (H1052) | 17000875    | 80920              | 40      |

- 32 867 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 12 spectra from 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Threonine (L-) (H1052)*.
- These include spectra of independent samples from 4 batches, of which no spectra have been used for the generation of the database.

| Supplier        | Substance              | Batch      | Spectra |
|-----------------|------------------------|------------|---------|
| unisan          | Threonine (L-) (H1052) | 25708      | 1       |
| Hepart AG       | Threonine (L-) (H1052) | 25708      | 3       |
| Unisan          | Threonine (L-) (H1052) | 25708      | 2       |
| UNISAN          | Threonine (L-) (H1052) | 25708      | 1       |
| Unisan          | Threonine (L-) (H1052) | 14001718   | 1       |
| Hepart AG       | Threonine (L-) (H1052) | 1832014901 | 1       |
| Purren Apotheke | Threonine (L-) (H1052) | 1833014901 | 1       |
| Unisan          | Threonine (L-) (H1052) | 14001718/1 | 1       |
| Unisan          | Threonine (L-) (H1052) | 1832014901 | 1       |

- 1777 spectra from 20 *Apo-Ident* customers from a total of 677 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 60            | 130            | 32 867        |
| <b>Type C</b> | 0              | 2             | 10             | 1777          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 31.5789 % (> 30.0000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8547 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 48.32                           |
| 81018     | 81018               | 0.00                         | 54.46                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | Trace elements BAG (H1078)                                      |
| Substance class                     | HCK - nutritional supplements (Hepart)                          |
| Report date                         | 18/07/2018                                                      |
| Report number                       | 80205-2018-07-18                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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 | <i>European Pharmacopoeia 8th Edition, Basic Version 2014</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]          |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>        |
| Anhang F          | <a href="#">Zusatz zu den Modellen der zweiten Stufe</a>          |

### Validation method

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

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

Finally, 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 50 390 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 section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 40 spectra from 1 reference samples of the substance/substance group *Trace elements BAG (H1078)*.
- These include spectra of independent samples from 1 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                  | Batch    | Sample ID | Spectra |
|----------|----------------------------|----------|-----------|---------|
| Hepart   | Trace elements BAG (H1078) | 16000797 | 80801     | 40      |

- 33 017 spectra from a total of 735 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

### Type C Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Trace elements BAG (H1078)*.

- These include spectra of independent samples from 0 batches, of which no spectra have been used for the generation of the database.
- 1789 spectra from 20 *Apo-Ident* customers from a total of 682 batches from a further 62 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 40            | 0              | 33 017        |
| <b>Type C</b> | 0              | 0             | 0              | 1789          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9255 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8315 %) | n/a (n/a)                |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower 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                         | 15.36                           |
| 80800     | 80800               | 0.00                         | 15.19                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Trace elements JK (H1080)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80069-2018-07-18  
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 |
| Hepart   | Trace elements J... | 18000455 | 81029     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Trace elements JK (H1080)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 5 different batches.
- 15 304 spectra from a total of 338 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 490 spectra from 13 reference samples of the substance/substance group *Trace elements JK (H1080)*.
- These include spectra of independent samples from 10 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                 | Batch    | Sample ID          | Spectra |
|----------|---------------------------|----------|--------------------|---------|
| Hepart   | Trace elements JK (H1080) | 0956901  | 80069              | 30      |
| Hepart   | Trace elements JK (H1080) | 0956901  | 80137              | 50      |
| Hepart   | Trace elements JK (H1080) | 919701   | 80223              | 30      |
| Hepart   | Trace elements JK (H1080) | 011701   | 80235              | 40      |
| Hepart   | Trace elements JK (H1080) | 15000525 | 80673              | 60      |
| Hepart   | Trace elements JK (H1080) | 072901   | 80701 <sup>†</sup> | 20      |
| Hepart   | Trace elements JK (H1080) | 15000526 | 80766 <sup>†</sup> | 20      |
| Hepart   | Trace elements JK (H1080) | 17000870 | 80932              | 40      |
| Hepart   | Trace elements JK (H1080) | 17000871 | 80933              | 40      |
| Hepart   | Trace elements JK (H1080) | 17000869 | 80934              | 40      |
| Hepart   | Trace elements JK (H1080) | 18000456 | 81030              | 40      |
| Hepart   | Trace elements JK (H1080) | 18000457 | 81031              | 40      |
| Hepart   | Trace elements JK (H1080) | 18000484 | 81032              | 40      |

<sup>†</sup>These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*).

- 32 567 spectra from a total of 724 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 39 spectra from 12 *Apo-Ident* customers from 11 batches from the substance/substance group *Trace elements JK (H1080)*.
- These include spectra of independent samples from 10 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance                 | Batch      | Spectra |
|----------------------------|---------------------------|------------|---------|
| Unisan                     | Trace elements JK (H1080) | 11701      | 9       |
| Hepart AG                  | Trace elements JK (H1080) | 72701      | 2       |
| Hepart AG                  | Trace elements JK (H1080) | 72901      | 2       |
| UNISAN                     | Trace elements JK (H1080) | 72701      | 1       |
| Hepart AG                  | Trace elements JK (H1080) | 15000525   | 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       |
| Hepart AG                  | Trace elements JK (H1080) | 11701      | 8       |
| Unisan/Hepart AG           | Trace elements JK (H1080) | 11701      | 3       |
| Unisan                     | Trace elements JK (H1080) | 72701      | 1       |
| Unisan                     | Trace elements JK (H1080) | 1026011701 | 2       |
| Hepart AG                  | Trace elements JK (H1080) | 1026011701 | 2       |
| Unisan GmbH, 78465 Kons... | Trace elements JK (H1080) | 1026011701 | 1       |
| Unisan                     | Trace elements JK (H1080) | 1026919701 | 1       |
| Unisan GmbH, 78465 Kons... | Trace elements JK (H1080) | 1026956901 | 1       |
| Unisan                     | Trace elements JK (H1080) | 1026956901 | 1       |
| Unisan                     | Trace elements JK (H1080) | 1028956901 | 1       |

- 1750 spectra from 20 *Apo-Ident* customers from a total of 671 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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

Hence, these spectra are not independent and are not of *Type B*.

incorrect. The following table breaks down the numbers of correct and incorrect results according to 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              | 15 304        |
| Type B | 0              | 340           | 150            | 32 567        |
| Type C | 0              | 10            | 29             | 1750          |

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 % (> 99.9247 %) | 100.0000 % (> 97.5000 %) |
| Type B | 100.0000 % (> 99.9242 %) | 69.3878 % (> 68.7755 %)  |
| Type C | 100.0000 % (> 98.8387 %) | 25.6410 % (> 17.9487 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 29.05                           |
| 80388     | 80388               | 0.00                         | 27.93                           |
| 80389     | 80389               | 0.00                         | 29.29                           |
| 80701     | 80701               | 0.00                         | 25.26                           |
| 80766     | 80766               | 0.00                         | 22.23                           |
| 81029     | 81029               | 0.00                         | 25.54                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Trace elements SE (H1082)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80070-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 8 different batches.
- 15 184 spectra from a total of 335 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 1300 spectra from 29 reference samples of the substance/substance group *Trace elements SE (H1082)*.
- These include spectra of independent samples from 19 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance                 | Batch       | Sample ID | Spectra |
|----------|---------------------------|-------------|-----------|---------|
| Hepart   | Trace elements SE (H1082) | zu erfassen | 80007     | 40      |
| Hepart   | Trace elements SE (H1082) | 0937201     | 80070     | 30      |
| Hepart   | Trace elements SE (H1082) | 0937201     | 80092     | 50      |
| Hepart   | Trace elements SE (H1082) | 012401      | 80141     | 50      |
| Hepart   | Trace elements SE (H1082) | 929202      | 80172     | 40      |
| Hepart   | Trace elements SE (H1082) | 031301      | 80263     | 40      |
| Hepart   | Trace elements SE (H1082) | 042301      | 80278     | 55      |
| Hepart   | Trace elements SE (H1082) | 042301      | 80290     | 55      |
| Hepart   | Trace elements SE (H1082) | 14000722    | 80462     | 40      |

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| Supplier | Substance                 | Batch        | Sample ID          | Spectra |
|----------|---------------------------|--------------|--------------------|---------|
| Hepart   | Trace elements SE (H1082) | 14000720     | 80463              | 40      |
| Hepart   | Trace elements SE (H1082) | 15000555     | 80588 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Trace elements SE (H1082) | 15000556(F2) | 80593              | 60      |
| Hepart   | Trace elements SE (H1082) | 15000557     | 80594 <sup>†</sup> | 20      |
| Hepart   | Trace elements SE (H1082) | 15000557(B1) | 80595              | 60      |
| Hepart   | Trace elements SE (H1082) | 15000557(F2) | 80596              | 60      |
| Hepart   | Trace elements SE (H1082) | 15000558     | 80597 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Trace elements SE (H1082) | 15000553(F2) | 80602              | 60      |
| Hepart   | Trace elements SE (H1082) | 17000886     | 80960              | 40      |
| Hepart   | Trace elements SE (H1082) | 17000888     | 80961              | 40      |
| Hepart   | Trace elements SE (H1082) | 17000887     | 80962              | 40      |
| Hepart   | Trace elements SE (H1082) | 15000558     | 80979              | 40      |

- 31 757 spectra from a total of 711 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 35 spectra from 12 *Apo-Ident* customers from 15 batches from the substance/substance group *Trace elements SE (H1082)*.
- These include spectra of independent samples from 12 batches, of which no spectra have been used for the generation of the database.

| Supplier  | Substance                 | Batch      | Spectra |
|-----------|---------------------------|------------|---------|
| Hepart AG | Trace elements SE (H1082) | 41401      | 1       |
| 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) | 14000721   | 1       |
| Unisan    | Trace elements SE (H1082) | 14000721/0 | 1       |
| Unisan    | Trace elements SE (H1082) | 14000722   | 1       |
| Unisan    | Trace elements SE (H1082) | 15000553   | 1       |
| Hepart AG | Trace elements SE (H1082) | 15000556   | 1       |
| Unisan    | Trace elements SE (H1082) | 15000556/0 | 1       |

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

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| Supplier                   | Substance                 | Batch      | Spectra |
|----------------------------|---------------------------|------------|---------|
| 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) | 1024012401 | 2       |
| Unisan                     | Trace elements SE (H1082) | 1024042301 | 1       |
| Hepart AG                  | Trace elements SE (H1082) | 937201     | 4       |
| Unisan                     | Trace elements SE (H1082) | 1024929202 | 1       |
| Hepart AG, CH-8280 Kreu... | Trace elements SE (H1082) | 937201     | 1       |
| Unisan                     | Trace elements SE (H1082) | 937201     | 2       |

- 1754 spectra from 20 *Apo-Ident* customers from a total of 668 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 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              | 15 184        |
| Type B | 0              | 940           | 360            | 31 757        |
| Type C | 0              | 10            | 25             | 1754          |

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 % (> 99.9244 %) | 100.0000 % (> 98.3333 %) |
| Type B | 100.0000 % (> 99.9241 %) | 72.3077 % (> 72.0769 %)  |
| Type C | 100.0000 % (> 98.8395 %) | 28.5714 % (> 20.0000 %)  |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 80459     | 80459               | 0.00                         | 30.45                           |
| 80460     | 80460               | 0.00                         | 32.42                           |
| 80461     | 80461               | 0.00                         | 31.37                           |
| 80464     | 80464               | 0.00                         | 31.97                           |
| 80588     | 80588               | 0.00                         | 60.27                           |
| 80592     | 80592               | 0.00                         | 53.10                           |
| 80594     | 80594               | 0.00                         | 56.19                           |
| 80597     | 80597               | 0.00                         | 66.18                           |
| 80601     | 80601               | 0.00                         | 60.58                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Tryptophan (L-) (H1053)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80127-2018-07-18  
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-) ... | 16001394 | 80845     | 40      | from supplier |
| Hepart   | Tryptophan (L-) ... | 16001404 | 80846     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Tryptophan (L-) (H1053)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 4 different batches.
- 15 384 spectra from a total of 339 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 250 spectra from 6 reference samples of the substance/substance group *Tryptophan (L-) (H1053)*.
- These include spectra of independent samples from 5 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance               | Batch       | Sample ID          | Spectra |
|----------|-------------------------|-------------|--------------------|---------|
| Hepart   | Tryptophan (L-) (H1053) | zu erfassen | 80058              | 30      |
| Hepart   | Tryptophan (L-) (H1053) | 0950001     | 80127              | 50      |
| Hepart   | Tryptophan (L-) (H1053) | 0978501     | 80135              | 50      |
| Hepart   | Tryptophan (L-) (H1053) | 027901      | 80251              | 40      |
| Hepart   | Tryptophan (L-) (H1053) | 15000441    | 80581 <sup>†</sup> | 20      |
| Hepart   | Tryptophan (L-) (H1053) | 15000443    | 80582              | 60      |

- 32 807 spectra from a total of 731 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B*

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

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

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 29 spectra from 9 *Apo-Ident* customers from 14 batches from the substance/substance group *Tryptophan (L-) (H1053)*.
- These include spectra of independent samples from 14 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance               | Batch      | Spectra |
|----------------------------|-------------------------|------------|---------|
| Hepart AG                  | Tryptophan (L-) (H1053) | 74501      | 2       |
| unisan                     | Tryptophan (L-) (H1053) |            | 1       |
| Unisan                     | Tryptophan (L-) (H1053) | 74501      | 2       |
| Unisan                     | Tryptophan (L-) (H1053) | 74501/4    | 1       |
| Unisan                     | Tryptophan (L-) (H1053) | 150000441  | 1       |
| Unisan                     | Tryptophan (L-) (H1053) | 27901      | 2       |
| Unisan                     | Tryptophan (L-) (H1053) | 25011      | 1       |
| Caelo                      | Tryptophan (L-) (H1053) | 15000443/0 | 1       |
| 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) | 1824025011 | 1       |
| Unisan                     | Tryptophan (L-) (H1053) | 1824950001 | 2       |
| Fagron                     | Tryptophan (L-) (H1053) | 1824027901 | 2       |
| Purren Apotheke            | Tryptophan (L-) (H1053) | 1825950001 | 1       |
| Hepart AG                  | Tryptophan (L-) (H1053) | 27902      | 1       |
| Unisan                     | Tryptophan (L-) (H1053) | 950001     | 1       |
| Purren Apotheke            | Tryptophan (L-) (H1053) | 978501     | 1       |

- 1760 spectra from 20 *Apo-Ident* customers from a total of 669 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 80            | 170            | 32 807        |
| <b>Type C</b> | 0              | 7             | 22             | 1760          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 32.0000 % (> 30.8000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8411 %) | 24.1379 % (> 13.7931 %)  |

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

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

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80401            | 80401                      | 0.00                                | 61.30                                  |
| 80581            | 80581                      | 0.00                                | 70.51                                  |
| 80845            | 80845                      | 0.00                                | 59.59                                  |
| 80846            | 80846                      | 0.00                                | 67.98                                  |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Tyrosine (L-) (H1054)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80121-2018-07-18  
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 |
| Hepart   | Tyrosine (L-) (H... | 18000412 | 81050     | 40      | from supplier |

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

### Type A All calibration spectra.

- 160 spectra of 3 reference samples from the substance/substance group *Tyrosine (L-) (H1054)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 3 different batches.
- 15 384 spectra from a total of 340 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 200 spectra from 6 reference samples of the substance/substance group *Tyrosine (L-) (H1054)*.
- These include spectra of independent samples from 3 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance             | Batch       | Sample ID          | Spectra |
|----------|-----------------------|-------------|--------------------|---------|
| Hepart   | Tyrosine (L-) (H1054) | zu erfassen | 80059              | 30      |
| Hepart   | Tyrosine (L-) (H1054) | 979102      | 80121              | 50      |
| Hepart   | Tyrosine (L-) (H1054) | 029502      | 80244              | 40      |
| Hepart   | Tyrosine (L-) (H1054) | 029502      | 80248              | 40      |
| Hepart   | Tyrosine (L-) (H1054) | 074601      | 80386 <sup>†</sup> | 20      |
| Hepart   | Tyrosine (L-) (H1054) | 15001380    | 80704 <sup>†</sup> | 20      |

- 32 857 spectra from a total of 732 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 21 spectra from 7 *Apo-Ident* customers from 7 batches from the substance/substance group *Tyrosine (L-) (H1054)*.
- These include spectra of independent samples from 7 batches, of which no spectra have been used for the generation of the database.

| Supplier  | Substance             | Batch      | Spectra |
|-----------|-----------------------|------------|---------|
| Unisan    | Tyrosine (L-) (H1054) | 29501      | 4       |
| Hepart AG | Tyrosine (L-) (H1054) | 29502      | 1       |
| Unisan    | Tyrosine (L-) (H1054) | 29502      | 5       |
| UNISAN    | Tyrosine (L-) (H1054) | 74601      | 1       |
| Hepart AG | Tyrosine (L-) (H1054) | 74601      | 2       |
| Unisan    | Tyrosine (L-) (H1054) | 74601/3    | 1       |
| Hepart AG | Tyrosine (L-) (H1054) | 74601/3    | 2       |
| Unisan    | Tyrosine (L-) (H1054) | 1826029501 | 2       |
| Unisan    | Tyrosine (L-) (H1054) | 979102     | 2       |
| Hepart AG | Tyrosine (L-) (H1054) | 1827029501 | 1       |

- 1768 spectra from 20 *Apo-Ident* customers from a total of 675 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 43            | 157            | 32 857        |
| <b>Type C</b> | 0              | 6             | 15             | 1768          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 21.5000 % (> 20.0000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8448 %) | 28.5714 % (> 14.2857 %)  |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 80386     | 80386               | 0.00                         | 88.89                           |
| 80704     | 80704               | 0.00                         | 92.75                           |
| 81050     | 81050               | 0.00                         | 89.71                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Valine (L-) (H1056)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80145-2018-07-18  
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... | 16001380/0 | 80844     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Valine (L-) (H1056)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 2 different batches.
- 15 464 spectra from a total of 341 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 270 spectra from 7 reference samples of the substance/substance group *Valine (L-) (H1056)*.
- These include spectra of independent samples from 6 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance           | Batch       | Sample ID          | Spectra |
|----------|---------------------|-------------|--------------------|---------|
| Hepart   | Valine (L-) (H1056) | zu erfassen | 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) | 025012      | 80291              | 40      |
| Hepart   | Valine (L-) (H1056) | 14001947    | 80520 <sup>†</sup> | 20      |
| Hepart   | Valine (L-) (H1056) | 15001436    | 80670              | 60      |

- 32 787 spectra from a total of 730 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 10 spectra from 6 *Apo-Ident* customers from 7 batches from the substance/substance group *Valine (L-) (H1056)*.
- These include spectra of independent samples from 6 batches, of which no spectra have been used for the generation of the database.

| Supplier        | Substance           | Batch      | Spectra |
|-----------------|---------------------|------------|---------|
| Unisan          | Valine (L-) (H1056) | 25012      | 2       |
| Unisan          | Valine (L-) (H1056) | 1806025012 | 2       |
| Unisan          | Valine (L-) (H1056) | 15001436   | 1       |
| Hepart          | Valine (L-) (H1056) | 14001947   | 1       |
| Hepart AG       | Valine (L-) (H1056) | 1807025012 | 1       |
| Purren Apotheke | Valine (L-) (H1056) | 1807936701 | 1       |
| Unisan          | Valine (L-) (H1056) | 1807961101 | 1       |
| Hepart AG       | Valine (L-) (H1056) | 15001436   | 1       |

- 1779 spectra from 20 *Apo-Ident* customers from a total of 675 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 15 464        |
| <b>Type B</b> | 0              | 144           | 126            | 32 787        |
| <b>Type C</b> | 0              | 4             | 6              | 1779          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9261 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9243 %) | 53.3333 % (> 52.2222 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8593 %) | n/a (n/a)                |

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 71.60                           |
| 80844     | 80844               | 0.00                         | 66.41                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Vitamin B6 (H1103)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80074-2018-07-18  
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 |
| Hepart   | Vitamin B6 (H1103) | 16001239 | 80919     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Vitamin B6 (H1103)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 3 different batches.
- 15 384 spectra from a total of 340 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 200 spectra from 5 reference samples of the substance/substance group *Vitamin B6 (H1103)*.
- These include spectra of independent samples from 2 batches, of which no spectra have been used for the generation of the database.

| 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 <sup>†</sup> | 20      |
| Hepart   | Vitamin B6 (H1103) | 15000279 | 80781              | 60      |

- 32 857 spectra from a total of 733 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

**Type C** Spectra from the field, which were not recorded under the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 23 spectra from 10 *Apo-Ident* customers from 14 batches from the substance/substance group *Vitamin B6 (H1103)*.
- These include spectra of independent samples from 13 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance          | Batch      | Spectra |
|----------------------------|--------------------|------------|---------|
| Hepart AG, CH-8280 Kreu... | Vitamin B6 (H1103) | 25711      | 1       |
| Unisan                     | Vitamin B6 (H1103) | 20101      | 1       |
| Unisan                     | Vitamin B6 (H1103) | 25711      | 7       |
| Hepart AG                  | Vitamin B6 (H1103) | 25711      | 1       |
| Unisan                     | Vitamin B6 (H1103) | 14001576   | 1       |
| Unisan                     | Vitamin B6 (H1103) | 14001576/2 | 1       |
| Hepart AG                  | Vitamin B6 (H1103) | 1400576    | 1       |
| Unisan                     | Vitamin B6 (H1103) | 15000279/2 | 1       |
| Hepart AG, Unisan GmbH     | Vitamin B6 (H1103) | 15000279/0 | 1       |
| Unisan                     | Vitamin B6 (H1103) | 1552020101 | 1       |
| Hepart AG                  | Vitamin B6 (H1103) | 1552025711 | 1       |
| Euro OTC                   | Vitamin B6 (H1103) | 15000279/1 | 1       |
| Hepart AG, CH-8280 Kreu... | Vitamin B6 (H1103) | 1552025711 | 1       |
| Hepart AG                  | Vitamin B6 (H1103) | 1554020101 | 1       |
| Hepart                     | Vitamin B6 (H1103) | 15000879   | 1       |
| Unisan                     | Vitamin B6 (H1103) | 1554025711 | 1       |
| Purren Apotheke            | Vitamin B6 (H1103) | 1554938001 | 1       |

- 1766 spectra from 20 *Apo-Ident* customers from a total of 668 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 15 384        |
| <b>Type B</b> | 0              | 72            | 128            | 32 857        |
| <b>Type C</b> | 0              | 12            | 11             | 1766          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9250 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9244 %) | 36.0000 % (> 34.5000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8436 %) | 52.1739 % (> 39.1304 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 67.37                           |
| 80798     | 80798               | 0.00                         | 62.84                           |
| 80886     | 80886               | 0.00                         | 68.27                           |
| 80919     | 80919               | 0.00                         | 69.33                           |

# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Vitamin C (H1104)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80009-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 14 different batches.
- 14 944 spectra from a total of 329 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 1099 spectra from 28 reference samples of the substance/substance group *Vitamin C (H1104)*.
- These include spectra of independent samples from 18 batches, of which no spectra have been used for the generation of the database.

| 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      |

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| Supplier | Substance         | Batch    | Sample ID          | Spectra |
|----------|-------------------|----------|--------------------|---------|
| Hepart   | Vitamin C (H1104) | 013201   | 80161              | 50      |
| Hepart   | Vitamin C (H1104) | 013202   | 80229              | 40      |
| Hepart   | Vitamin C (H1104) | 044501   | 80296              | 40      |
| Hepart   | Vitamin C (H1104) | 025020   | 80304              | 40      |
| Hepart   | Vitamin C (H1104) | 14001780 | 80499 <sup>†</sup> | 20      |
| Hepart   | Vitamin C (H1104) | 14001788 | 80500 <sup>†</sup> | 20      |
| Hepart   | Vitamin C (H1104) | 14001794 | 80501 <sup>†</sup> | 20      |
| Hepart   | Vitamin C (H1104) | 14001797 | 80502 <sup>†</sup> | 20      |
| Hepart   | Vitamin C (H1104) | 16000200 | 80751 <sup>†</sup> | 20      |
| Hepart   | Vitamin C (H1104) | 16000197 | 80752              | 60      |
| Hepart   | Vitamin C (H1104) | 16000198 | 80753 <sup>†</sup> | 20      |
| Hepart   | Vitamin C (H1104) | 16000199 | 80754              | 60      |
| Hepart   | Vitamin C (H1104) | 16000201 | 80755              | 60      |
| Hepart   | Vitamin C (H1104) | 16000229 | 80756 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Vitamin C (H1104) | 17000915 | 80963              | 40      |
| Hepart   | Vitamin C (H1104) | 17000916 | 80964              | 40      |
| Hepart   | Vitamin C (H1104) | 17000917 | 80965              | 40      |
| Hepart   | Vitamin C (H1104) | 17000918 | 80966              | 40      |
| Hepart   | Vitamin C (H1104) | 17000919 | 80967              | 40      |
| Hepart   | Vitamin C (H1104) | 17000920 | 80968              | 40      |

- 31 958 spectra from a total of 710 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 70 spectra from 12 *Apo-Ident* customers from 26 batches from the substance/substance group *Vitamin C (H1104)*.
- These include spectra of independent samples from 19 batches, of which no spectra have been used for the generation of the database.

| Supplier  | Substance         | Batch    | Spectra |
|-----------|-------------------|----------|---------|
| unisan    | Vitamin C (H1104) | 14001794 | 1       |
| Unisan    | Vitamin C (H1104) | 14001797 | 1       |
| Hepart AG | Vitamin C (H1104) | 16000198 | 1       |
| unbekannt | Vitamin C (H1104) | 16000200 | 1       |
| unbekannt | Vitamin C (H1104) | 16000198 | 1       |
| unbekannt | Vitamin C (H1104) | 16000197 | 1       |
| Unisan    | Vitamin C (H1104) | 16000198 | 1       |

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

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| Supplier                   | Substance         | Batch      | Spectra |
|----------------------------|-------------------|------------|---------|
| unbekannt                  | Vitamin C (H1104) | 16000199   | 1       |
| unbekannt                  | Vitamin C (H1104) | 16000229   | 1       |
| unbekannt                  | Vitamin C (H1104) | 16000230   | 1       |
| unbekannt                  | Vitamin C (H1104) | 16000201   | 1       |
| unbekannt                  | Vitamin C (H1104) | 16000202   | 1       |
| unbekannt                  | Vitamin C (H1104) | 16000203   | 1       |
| Unisan                     | Vitamin C (H1104) | 44501      | 7       |
| unbekannt                  | Vitamin C (H1104) | 16000231   | 1       |
| Unisan                     | Vitamin C (H1104) | 25020      | 2       |
| Unisan GmbH, 78465 Kons... | Vitamin C (H1104) | 25020      | 1       |
| Hepart AG                  | Vitamin C (H1104) | 44501      | 3       |
| Unisan/Hepart AG           | Vitamin C (H1104) | 44501      | 1       |
| Unisan                     | Vitamin C (H1104) | 44502      | 4       |
| Hepart AG                  | Vitamin C (H1104) | 44502      | 3       |
| Unisan                     | Vitamin C (H1104) | 44601      | 1       |
| Fagron                     | Vitamin C (H1104) | 44502      | 1       |
| Hepart AG                  | Vitamin C (H1104) | 44601      | 2       |
| Unisan/Hepart AG           | Vitamin C (H1104) | 44602      | 2       |
| Falcento                   | Vitamin C (H1104) | 44602      | 1       |
| Unisan                     | Vitamin C (H1104) | 73901      | 3       |
| Hepart AG                  | Vitamin C (H1104) | 73901      | 4       |
| UNISAN                     | Vitamin C (H1104) | 74001      | 1       |
| Hepart AG                  | Vitamin C (H1104) | 74101      | 1       |
| Unisan                     | Vitamin C (H1104) | 74001      | 2       |
| Unisan                     | Vitamin C (H1104) | 74101      | 1       |
| Hepart AG                  | Vitamin C (H1104) | 74201      | 2       |
| Hepart AG                  | Vitamin C (H1104) | 1084025020 | 3       |
| Unisan                     | Vitamin C (H1104) | 1084025020 | 1       |
| Unisan                     | Vitamin C (H1104) | 1085025020 | 5       |
| Hepart AG                  | Vitamin C (H1104) | 1085025020 | 2       |
| Hepart AG, CH-8280 Kreu... | Vitamin C (H1104) | 1084025019 | 1       |
| Unisan                     | Vitamin C (H1104) | 14001780/0 | 1       |
| Unisan                     | Vitamin C (H1104) | 14001788   | 1       |

- 1719 spectra from 20 *Apo-Ident* customers from a total of 658 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 600           | 0              | 14 944        |
| <b>Type B</b> | 0              | 1027          | 72             | 31 958        |
| <b>Type C</b> | 0              | 56            | 14             | 1719          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9242 %) | 100.0000 % (> 99.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9241 %) | 93.4486 % (> 93.1756 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8355 %) | 80.0000 % (> 75.7143 %)  |

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

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

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

### Identity according to identity test using NIR spectroscopy

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

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 80363            | 80363                      | 0.00                                | 54.42                                  |
| 80394            | 80394                      | 0.00                                | 32.47                                  |
| 80395            | 80395                      | 0.00                                | 30.49                                  |
| 80396            | 80396                      | 0.00                                | 46.26                                  |
| 80397            | 80397                      | 0.00                                | 29.46                                  |
| 80418            | 80418                      | 0.00                                | 45.99                                  |
| 80438            | 80438                      | 0.00                                | 55.89                                  |
| 80499            | 80499                      | 0.00                                | 31.03                                  |
| 80500            | 80500                      | 0.00                                | 32.70                                  |
| 80501            | 80501                      | 0.00                                | 34.85                                  |
| 80502            | 80502                      | 0.00                                | 50.53                                  |
| 80751            | 80751                      | 0.00                                | 51.42                                  |
| 80753            | 80753                      | 0.00                                | 55.27                                  |
| 80756            | 80756                      | 0.00                                | 52.30                                  |
| 80760            | 80760                      | 0.00                                | 51.49                                  |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Vitamin complex (H1100)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80073-2018-07-18  
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 |
| Hepart   | Vitamin complex ... | 17001751/0   | 80990     | 40      | from supplier |

## Validation samples

A total of 50 390 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

**Type A** All calibration spectra.

- 680 spectra of 17 reference samples from the substance/substance group *Vitamin complex (H1100)*. These samples are listed above in the section [calibration samples](#). The reference samples originate from 17 different batches.
- 14 864 spectra from a total of 326 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 1205 spectra from 34 reference samples of the substance/substance group *Vitamin complex (H1100)*.
- These include spectra of independent samples from 21 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance               | Batch       | Sample ID | Spectra |
|----------|-------------------------|-------------|-----------|---------|
| Hepart   | Vitamin complex (H1100) | zu erfassen | 80004     | 40      |

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| Supplier | Substance               | Batch        | Sample ID          | Spectra |
|----------|-------------------------|--------------|--------------------|---------|
| Hepart   | Vitamin complex (H1100) | 009901       | 80073              | 30      |
| Hepart   | Vitamin complex (H1100) | 009901       | 80091              | 40      |
| Hepart   | Vitamin complex (H1100) | 0966901      | 80109              | 40      |
| Hepart   | Vitamin complex (H1100) | 923902       | 80214              | 35      |
| Hepart   | Vitamin complex (H1100) | 023401       | 80231              | 40      |
| Hepart   | Vitamin complex (H1100) | 0966901      | 80237              | 40      |
| Hepart   | Vitamin complex (H1100) | 025301       | 80292              | 40      |
| Hepart   | Vitamin complex (H1100) | 025101       | 80293              | 40      |
| Hepart   | Vitamin complex (H1100) | 14001590     | 80485 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 14001589     | 80486 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 14001591     | 80487 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 15001276(B1) | 80637 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 15001277(F2) | 80638 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 15001275(B1) | 80639              | 60      |
| Hepart   | Vitamin complex (H1100) | 15001274(B1) | 80640 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 15001277(B1) | 80641              | 60      |
| Hepart   | Vitamin complex (H1100) | 15001275(F2) | 80642 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 15001277     | 80643 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 15001274(F2) | 80644              | 60      |
| Hepart   | Vitamin complex (H1100) | 15001276     | 80645              | 60      |
| Hepart   | Vitamin complex (H1100) | 15001276(F2) | 80646 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 15001274     | 80647 <sup>†</sup> | 20      |
| Hepart   | Vitamin complex (H1100) | 15001275     | 80648 <sup>†</sup> | 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      |
| Hepart   | Vitamin complex (H1100) | 17001654     | 80984              | 40      |
| Hepart   | Vitamin complex (H1100) | 17001752/0   | 80991              | 40      |
| Hepart   | Vitamin complex (H1100) | 17000880/0   | 80992              | 40      |
| Hepart   | Vitamin complex (H1100) | 17001753/0   | 80993              | 40      |
| Hepart   | Vitamin complex (H1100) | 17001750/0   | 80994              | 40      |

- 31 852 spectra from a total of 705 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 75 spectra from 13 *Apo-Ident* customers from 30 batches from the substance/substance group *Vitamin complex (H1100)*.
- These include spectra of independent samples from 28 batches, of which no spectra have been used for the generation of the database.

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

| Supplier                   | Substance               | Batch       | Spectra |
|----------------------------|-------------------------|-------------|---------|
| Unisan/Hepart AG           | Vitamin complex (H1100) | 48301       | 1       |
| Hepart AG                  | Vitamin complex (H1100) | 77101       | 1       |
| Unisan                     | Vitamin complex (H1100) | 74101       | 1       |
| Unisan                     | Vitamin complex (H1100) | 77001       | 1       |
| Hepart AG                  | Vitamin complex (H1100) | 77201       | 3       |
| Unisan                     | Vitamin complex (H1100) | 77201       | 3       |
| Hepart AG                  | Vitamin complex (H1100) | 14001589    | 3       |
| Unisan                     | Vitamin complex (H1100) | 14001590/0  | 1       |
| Unisan                     | Vitamin complex (H1100) | 1400159/0   | 1       |
| Unisan                     | Vitamin complex (H1100) | 14001589    | 1       |
| Unisan                     | Vitamin complex (H1100) | 15001275/0  | 1       |
| Unisan                     | Vitamin complex (H1100) | 14001590/1  | 1       |
| Hepart AG                  | Vitamin complex (H1100) | 15001277    | 1       |
| Unisan                     | Vitamin complex (H1100) | 15001276/0  | 1       |
| Unisan                     | Vitamin complex (H1100) | 25101       | 1       |
| Unisan                     | Vitamin complex (H1100) | 15001277/0  | 1       |
| Hepart                     | Vitamin complex (H1100) | 16000958    | 1       |
| Unisan                     | Vitamin complex (H1100) | 16000958/0  | 1       |
| Unisan                     | Vitamin complex (H1100) | 25201       | 1       |
| Hepart AG                  | Vitamin complex (H1100) | 49201       | 4       |
| Unisan/Hepart AG           | Vitamin complex (H1100) | 49201       | 1       |
| Unisan                     | Vitamin complex (H1100) | 49201       | 2       |
| Hepart AG                  | Vitamin complex (H1100) | 49202       | 5       |
| Unisan                     | Vitamin complex (H1100) | 49202       | 2       |
| Hepart AG, CH-8280 Kreu... | Vitamin complex (H1100) | 49301       | 5       |
| 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       |
| Unisan                     | Vitamin complex (H1100) | 1014009901  | 1       |
| Hepart AG                  | Vitamin complex (H1100) | 1014025101  | 1       |
| Hepart AG                  | Vitamin complex (H1100) | 1014025301  | 1       |
| Hepart AG, CH-8280 Kreu... | Vitamin complex (H1100) | 1014025101  | 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) | 904006      | 1       |
| Unisan                     | Vitamin complex (H1100) | 4966901     | 1       |
| Unisan                     | Vitamin complex (H1100) | H110031     | 2       |

- 1714 spectra from 20 *Apo-Ident* customers from a total of 653 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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              | 680           | 0              | 14 864        |
| Type B | 0              | 1141          | 64             | 31 852        |
| Type C | 0              | 68            | 7              | 1714          |

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 % (> 99.9242 %) | 100.0000 % (> 99.1176 %) |
| Type B | 100.0000 % (> 99.9241 %) | 94.6888 % (> 94.4398 %)  |
| Type C | 100.0000 % (> 98.8352 %) | 90.6667 % (> 86.6667 %)  |

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

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

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

### Identity according to identity test using NIR spectroscopy

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

| Sample ID | Reference sample ID | Distance to reference sample | Distance to next foreign sample |
|-----------|---------------------|------------------------------|---------------------------------|
| 80349     | 80349               | 0.00                         | 46.01                           |
| 80411     | 80411               | 0.00                         | 48.81                           |
| 80431     | 80431               | 0.00                         | 47.56                           |
| 80432     | 80432               | 0.00                         | 47.04                           |
| 80485     | 80485               | 0.00                         | 45.98                           |
| 80486     | 80486               | 0.00                         | 49.40                           |
| 80487     | 80487               | 0.00                         | 47.93                           |
| 80637     | 80637               | 0.00                         | 48.31                           |
| 80638     | 80638               | 0.00                         | 49.40                           |
| 80640     | 80640               | 0.00                         | 49.54                           |
| 80642     | 80642               | 0.00                         | 48.12                           |
| 80643     | 80643               | 0.00                         | 47.97                           |
| 80646     | 80646               | 0.00                         | 48.12                           |
| 80647     | 80647               | 0.00                         | 49.60                           |
| 80648     | 80648               | 0.00                         | 48.03                           |
| 80827     | 80827               | 0.00                         | 49.39                           |
| 80990     | 80990               | 0.00                         | 46.78                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Vitamin E NAT (H1107)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80010-2018-07-18  
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 50 390 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 section [calibration samples](#). The reference samples originate from 11 different batches.
- 15 109 spectra from a total of 332 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a †. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 1440 spectra from 33 reference samples of the substance/substance group *Vitamin E NAT (H1107)*.
- These include spectra of independent samples from 21 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance             | Batch   | Sample ID | Spectra |
|----------|-----------------------|---------|-----------|---------|
| Hepart   | Vitamin E NAT (H1107) | 945901  | 80010     | 40      |
| Hepart   | Vitamin E NAT (H1107) | 0961301 | 80077     | 30      |
| Hepart   | Vitamin E NAT (H1107) | 0961301 | 80098     | 50      |
| Hepart   | Vitamin E NAT (H1107) | 017901  | 80117     | 50      |
| Hepart   | Vitamin E NAT (H1107) | 919301  | 80219     | 30      |
| Hepart   | Vitamin E NAT (H1107) | 017701  | 80230     | 40      |
| Hepart   | Vitamin E NAT (H1107) | 961301  | 80238     | 40      |

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| Supplier | Substance             | Batch        | Sample ID          | Spectra |
|----------|-----------------------|--------------|--------------------|---------|
| Hepart   | Vitamin E NAT (H1107) | 065001       | 80350              | 40      |
| Hepart   | Vitamin E NAT (H1107) | 071501       | 80381              | 60      |
| Hepart   | Vitamin E NAT (H1107) | 071501       | 80382              | 60      |
| Hepart   | Vitamin E NAT (H1107) | 071501       | 80383              | 60      |
| Hepart   | Vitamin E NAT (H1107) | 071501       | 80384              | 60      |
| Hepart   | Vitamin E NAT (H1107) | 14001815     | 80512 <sup>†</sup> | 20      |
| Hepart   | Vitamin E NAT (H1107) | 14001821     | 80513 <sup>†</sup> | 20      |
| Hepart   | Vitamin E NAT (H1107) | 14001822     | 80514 <sup>†</sup> | 20      |
| Hepart   | Vitamin E NAT (H1107) | 15001557(B1) | 80686              | 60      |
| Hepart   | Vitamin E NAT (H1107) | 15001558(F2) | 80687              | 60      |
| Hepart   | Vitamin E NAT (H1107) | 15001558     | 80688 <sup>†</sup> | 20      |
| Hepart   | Vitamin E NAT (H1107) | 15001561(B1) | 80689              | 60      |
| Hepart   | Vitamin E NAT (H1107) | 15001559(F2) | 80690 <sup>†</sup> | 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 <sup>†</sup> | 20      |
| Hepart   | Vitamin E NAT (H1107) | 15001560(B1) | 80694 <sup>†</sup> | 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 <sup>†</sup> | 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      |
| Hepart   | Vitamin E NAT (H1107) | 17000890     | 80958              | 40      |
| Hepart   | Vitamin E NAT (H1107) | 17000891     | 80969              | 40      |
| Hepart   | Vitamin E NAT (H1107) | 17000892     | 80970              | 40      |

- 31 617 spectra from a total of 707 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 53 spectra from 14 *Apo-Ident* customers from 22 batches from the substance/substance group *Vitamin E NAT (H1107)*.
- These include spectra of independent samples from 18 batches, of which no spectra have been used for the generation of the database.

| Supplier  | Substance             | Batch    | Spectra |
|-----------|-----------------------|----------|---------|
| Unisan    | Vitamin E NAT (H1107) | 71501    | 5       |
| Unisan    | Vitamin E NAT (H1107) | 65001    | 3       |
| Hepart AG | Vitamin E NAT (H1107) | 71501    | 2       |
| UNISAN    | Vitamin E NAT (H1107) | 71701    | 1       |
| Hepart AG | Vitamin E NAT (H1107) | 14001815 | 2       |

continued on the next page

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

continued from previous page

| Supplier                   | Substance             | Batch      | Spectra |
|----------------------------|-----------------------|------------|---------|
| Unisan                     | Vitamin E NAT (H1107) | 71701      | 2       |
| Unisan                     | Vitamin E NAT (H1107) | 14001821   | 1       |
| Unisan 2.10.2015           | Vitamin E NAT (H1107) | 14001821/0 | 1       |
| HCK                        | Vitamin E NAT (H1107) | 14001822/0 | 1       |
| Hepart AG                  | Vitamin E NAT (H1107) | 15001557   | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 14001821/0 | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 15001558   | 1       |
| Unisan 02.04.2016          | Vitamin E NAT (H1107) | 15001558/0 | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 17901      | 1       |
| Hepart                     | Vitamin E NAT (H1107) | 16000591/0 | 1       |
| Purren Apotheke            | Vitamin E NAT (H1107) | 945901     | 1       |
| Hepart                     | Vitamin E NAT (H1107) | 160005910  | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 15001659/0 | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 25021      | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 25022      | 8       |
|                            | Vitamin E NAT (H1107) | 25022      | 2       |
| Hepart AG                  | Vitamin E NAT (H1107) | 25022      | 2       |
| Hepart AG, Unisan GmbH     | Vitamin E NAT (H1107) | 65001      | 2       |
| Hepart AG                  | Vitamin E NAT (H1107) | 65101      | 3       |
| Hepart AG, CH-8280 Kreu... | Vitamin E NAT (H1107) | 65001      | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 1094017701 | 1       |
| Hepart AG, CH-8280 Kreu... | Vitamin E NAT (H1107) | 1094017701 | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 1094025021 | 2       |
| Hepart AG                  | Vitamin E NAT (H1107) | 1094025021 | 1       |
| Hepart AG                  | Vitamin E NAT (H1107) | 1094025022 | 1       |
| Unisan                     | Vitamin E NAT (H1107) | 1095961301 | 1       |

- 1736 spectra from 20 *Apo-Ident* customers from a total of 660 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 435           | 0              | 15 109        |
| <b>Type B</b> | 0              | 1438          | 2              | 31 617        |
| <b>Type C</b> | 0              | 52            | 1              | 1736          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9243 %) | 100.0000 % (> 98.6207 %) |
| <b>Type B</b> | 100.0000 % (> 99.9241 %) | 99.8611 % (> 99.6528 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8368 %) | 98.1132 % (> 92.4528 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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                         | 18.91                           |
| 80426     | 80426               | 0.00                         | 19.69                           |
| 80512     | 80512               | 0.00                         | 21.65                           |
| 80513     | 80513               | 0.00                         | 22.38                           |
| 80514     | 80514               | 0.00                         | 20.08                           |
| 80688     | 80688               | 0.00                         | 25.76                           |
| 80690     | 80690               | 0.00                         | 24.52                           |
| 80693     | 80693               | 0.00                         | 26.27                           |
| 80694     | 80694               | 0.00                         | 24.56                           |
| 80697     | 80697               | 0.00                         | 26.61                           |
| 80826     | 80826               | 0.00                         | 19.44                           |



# VALIDATION REPORT

## IdentModul 1.3-2018-04

Validated substance/substance group **Zinc (H1110)**  
Substance class HCK - nutritional supplements (Hepart)  
Report date 18/07/2018  
Report number 80011-2018-07-18  
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 |
| Hepart   | Zinc (H1110) | 18001012 | 81068     | 40      | from supplier |
| Hepart   | Zinc (H1110) | 18000559 | 81069     | 40      | from supplier |

## Validation samples

A total of 50 390 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 *Zinc (H1110)*. These samples are listed above in the section *calibration samples*. The reference samples originate from 5 different batches.
- 15 344 spectra from a total of 338 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 recorded under the control of *HiperScan GmbH* and not used for the generation of the database.

Samples from batches, from which no spectra have been used for the generation of the database are considered as independent samples. The number of batches from which independent samples have delivered *Type B* spectra for the validation is given below and thus represents the number of independent *Type B* samples. Samples from which a number of the spectra has been used for the generation of the database and other spectra have been incorporated into the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: There was at least one other sample from the same batch (other sales containers, other sample ID), of which reference spectra (*Type A*) were used for the generation of the database.

- 430 spectra from 11 reference samples of the substance/substance group *Zinc (H1110)*.
- These include spectra of independent samples from 8 batches, of which no spectra have been used for the generation of the database.

| Supplier | Substance    | Batch       | Sample ID          | Spectra |
|----------|--------------|-------------|--------------------|---------|
| Hepart   | Zinc (H1110) | 949701      | 80011              | 40      |
| Hepart   | Zinc (H1110) | zu erfassen | 80018              | 40      |
| Hepart   | Zinc (H1110) | 0991001     | 80100              | 50      |
| Hepart   | Zinc (H1110) | 0949701     | 80143              | 50      |
| Hepart   | Zinc (H1110) | 593403      | 80227              | 30      |
| Hepart   | Zinc (H1110) | 041501      | 80287              | 40      |
| Hepart   | Zinc (H1110) | 0991001     | 80294              | 40      |
| Hepart   | Zinc (H1110) | 14001753    | 80489              | 60      |
| Hepart   | Zinc (H1110) | 14001803    | 80503 <sup>†</sup> | 20      |
| Hepart   | Zinc (H1110) | 16000196    | 80761 <sup>†</sup> | 20      |
| Hepart   | Zinc (H1110) | 16000519    | 80790              | 40      |

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

- 32627 spectra from a total of 727 batches from further 122 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra from the field, which were not recorded under of the control of *Hiperscan GmbH* and have not been used for the generation of the database. *Hiperscan GmbH* accepts the details provided by the customer regarding the manufacturer and batch number mainly unchecked.

- 59 spectra from 14 *Apo-Ident* customers from 12 batches from the substance/substance group *Zinc (H1110)*.
- These include spectra of independent samples from 10 batches, of which no spectra have been used for the generation of the database.

| Supplier                   | Substance    | Batch      | Spectra |
|----------------------------|--------------|------------|---------|
| Unisan                     | Zinc (H1110) | 410501     | 1       |
| Hepart AG                  | Zinc (H1110) | 41501      | 7       |
| Unisan                     | Zinc (H1110) | 41501      | 10      |
| Unisan                     | Zinc (H1110) | 44502      | 1       |
| Unisan                     | Zinc (H1110) | 991001     | 15      |
| Unisan                     | Zinc (H1110) | 99101      | 2       |
| Unisan                     | Zinc (H1110) | 1164949701 | 1       |
| Hepart AG                  | Zinc (H1110) | 1164991001 | 4       |
| Unisan                     | Zinc (H1110) | 1164991001 | 3       |
| Unisan                     | Zinc (H1110) | 14001753   | 1       |
| Hepart AG, CH-8280 Kreu... | Zinc (H1110) | 1164991001 | 1       |
| Unisan                     | Zinc (H1110) | 14001753/0 | 1       |
| Unisan                     | Zinc (H1110) | 14001803   | 3       |
| Hepart AG                  | Zinc (H1110) | 14001803   | 1       |
| Unisan                     | Zinc (H1110) | 14001803/1 | 1       |
| Hepart AG                  | Zinc (H1110) | 991001     | 3       |
| Unisan GmbH, 78465 Kons... | Zinc (H1110) | 991001     | 1       |
| Unisan                     | Zinc (H1110) | 16000196   | 1       |
| unbekannt                  | Zinc (H1110) | 16000196   | 1       |
| Hepart                     | Zinc (H1110) | 16000196   | 1       |

- 1730 spectra from 20 *Apo-Ident* customers from a total of 671 batches from a further 61 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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              | 200           | 0              | 15 344        |
| Type B | 0              | 395           | 35             | 32 625        |
| Type C | 0              | 57            | 2              | 1730          |

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 % (> 99.9248 %) | 100.0000 % (> 97.0000 %) |
| Type B | 100.0000 % (> 99.9246 %) | 91.8605 % (> 91.1628 %)  |
| Type C | 100.0000 % (> 98.8362 %) | 96.6102 % (> 91.5254 %)  |

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

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

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

### Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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                         | 13.56                           |
| 80761     | 80761               | 0.00                         | 11.63                           |
| 80789     | 80789               | 0.00                         | 13.87                           |
| 81068     | 81068               | 0.00                         | 11.40                           |
| 81069     | 81069               | 0.00                         | 12.07                           |

## *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 83 batches. From these 3480 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   | Acacia gum (H1001)   | 639701     | 40      | from supplier |
| Hepart   | Acacia gum (H1001)   | 639701     | 40      | from supplier |
| Hepart   | Acacia gum (H1001)   | 16000363/2 | 40      | from supplier |
| Hepart   | Acacia gum (H1001)   | 706310     | 40      | from supplier |
| Hepart   | Acacia gum (H1001)   | 728201     | 40      | from supplier |
| Hepart   | Acerola (H1413)      | 18000568/5 | 40      | from supplier |
| Hepart   | Amino H drink        | 683401     | 30      | from supplier |
| Hepart   | Baobab (H1410)       | 16001158   | 40      | from supplier |
| Hepart   | Baobab (H1410)       | 17001785/0 | 40      | from supplier |
| Hepart   | Beetroot (H1414)     | 18000857   | 40      | from supplier |
| Hepart   | Betaine hydrochl...  | 17000829   | 40      | from supplier |
| Hepart   | Camu camu (H1411)    | 18000789/0 | 40      | from supplier |
| Hepart   | Chia protein (H1...  | 17001729   | 40      | from supplier |
| Hepart   | Cocoa (H1424)        | 17000625   | 40      | from supplier |
| Hepart   | Cranberry (H1408)    | 18000790/0 | 40      | from supplier |
| Hepart   | Enzyme complex (...) | 15001134   | 60      | from supplier |
| Hepart   | Green coffee ext...  | 18000368   | 40      | from supplier |
| Hepart   | Guar (H1023)         | 048501     | 40      | from supplier |
| Hepart   | Guar (H1023)         | 048402     | 40      | from supplier |
| Hepart   | Guar (H1023)         | 048001     | 40      | from supplier |
| Hepart   | Guar (H1023)         | 048502     | 40      | from supplier |
| Hepart   | Guar (H1023)         | 048401     | 40      | from supplier |
| Hepart   | Guar (H1023)         | 970001     | 30      | from supplier |
| Hepart   | Guar (H1023)         | 699304     | 50      | from supplier |
| Hepart   | Guar (H1023)         | 703603     | 50      | from supplier |
| Hepart   | Guar (H1023)         | 701401     | 50      | from supplier |
| Hepart   | Histamine block ...  | 16001078   | 39      | from supplier |
| Hepart   | Histamine block ...  | 16001079   | 40      | from supplier |
| Hepart   | Konjac (H1426)       | 17000846   | 40      | from supplier |
| Hepart   | Konjac (H1426)       | 17000837   | 40      | from supplier |
| Hepart   | Leaky gut comple...  | 18000639   | 40      | from supplier |
| Hepart   | Leaky gut comple...  | 18000638   | 40      | from supplier |
| Hepart   | Liver kidney com...  | 18000635   | 40      | from supplier |
| Hepart   | Lupin protein co...  | 17001732   | 40      | from supplier |
| Hepart   | Lupin protein co...  | 18000948   | 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         | 0692701    | 30      | from supplier |
| Hepart   | Orthovimin B         | 735701     | 31      | from supplier |
| Hepart   | Orthovimin B         | 735701     | 40      | from supplier |
| Hepart   | Orthovimin B w. ...  | 700208     | 50      | from supplier |
| Hepart   | Orthovimin B w. ...  | 706303     | 50      | from supplier |
| Hepart   | Orthovimin B w. ...  | 699308     | 50      | from supplier |
| Hepart   | Pathogene comple...  | 18000637   | 40      | from supplier |
| Hepart   | Pea protein comp...  | 17001707   | 40      | from supplier |
| Hepart   | Pea protein comp...  | 17001708   | 40      | from supplier |
| Hepart   | Pomegranate (H14...  | 18000566/0 | 40      | from supplier |

*continued on the next page*

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| <b>Supplier</b> | <b>Substance</b>     | <b>Batch</b> | <b>Spectra</b> | <b>Certificate</b> |
|-----------------|----------------------|--------------|----------------|--------------------|
| Hepart          | Probiotic capcon     | 12-01        | 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) (H1...  | 025707       | 40             | from supplier      |
| Hepart          | Proline (-L) (H1...  | zu erfassen  | 30             | from supplier      |
| Hepart          | Proline (-L) (H1...  | 066401       | 60             | from supplier      |
| Hepart          | Psyllium husks (...) | 17001728     | 40             | from supplier      |
| Hepart          | Pumpkin protein ...  | 17001731     | 40             | from supplier      |
| Hepart          | Q10 capsules         | 0609140101   | 30             | from supplier      |
| Hepart          | Saffron flowers ...  | 18000806     | 40             | 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          | Seabuckthorn org...  | 16001154     | 40             | from supplier      |
| Hepart          | Seabuckthorn org...  | 16001709     | 40             | from supplier      |
| Hepart          | Selenium yeast (...) | 009001       | 30             | from supplier      |
| Hepart          | Selenium yeast (...) | 009001       | 50             | from supplier      |
| Hepart          | Selenium yeast (...) | 997601       | 40             | from supplier      |
| Hepart          | Selenium yeast (...) | 16001450/1   | 40             | from supplier      |
| Hepart          | Sunflower protei...  | 17001730     | 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      |
| Hepart          | Vitamin K2-Ca-Mn...  | 16000403     | 60             | from supplier      |
| Hepart          | Vitamin K2-Ca-Mn...  | 15000836     | 60             | from supplier      |
| Hepart          | Vitamin K2-Ca-Mn...  | 15000836     | 60             | from supplier      |
| Hepart          | Vitamins BAG (H1...  | 952201       | 30             | from supplier      |
| Hepart          | Walnut leaf (H11...  | 15001009     | 40             | from supplier      |
| Hepart          | Walnut leaf (H11...  | 16001149     | 40             | from supplier      |
| Hepart          | Walnut leaf (H11...  | 16001149     | 40             | from supplier      |
| Hepart          | Wild berry (H1417)   | 18000975/0   | 40             | from supplier      |
| Hepart          | Yeast organic (H...  | 16001157     | 40             | from supplier      |
| Hepart          | Yeast organic (H...  | 17001784/0   | 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 15 batches. From these, 29 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                | Acacia gum (H1001)       | 1211728201 | 4       |
| Hepart AG                | Acacia gum (H1001)       | 728201     | 2       |
| Hepart AG                | Proline (-L) (H1051)     | 25707      | 3       |
| Hepart AG                | Proline (-L) (H1051)     | 707801     | 2       |
| Hepart AG                | Vitamin K2-Ca-Mn comp... | 69001      | 3       |
| Hepart AG                | Vitamin K2-Ca-Mn comp... | 10226515   | 1       |
| Hepart AG                | Vitamin K2-Ca-Mn-Si c... | 15000836/6 | 1       |
| Hepart AG, CH-8280 Kr... | Acacia gum (H1001)       | 1211622002 | 2       |
| Unisan                   | Acacia gum (H1001)       | 1211706310 | 2       |
| Unisan                   | Acacia gum (H1001)       | 706310     | 1       |
| Unisan                   | Proline (-L) (H1051)     | 66401      | 2       |
| Unisan                   | Proline (-L) (H1051)     | 1834707801 | 1       |
| Unisan                   | Selenium yeast (H1068)   | 9001       | 1       |
| Unisan                   | Selenium yeast (H1068)   | 25709      | 1       |
| Unisan                   | Selenium yeast (H1068)   | 1151009001 | 3       |



## 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).

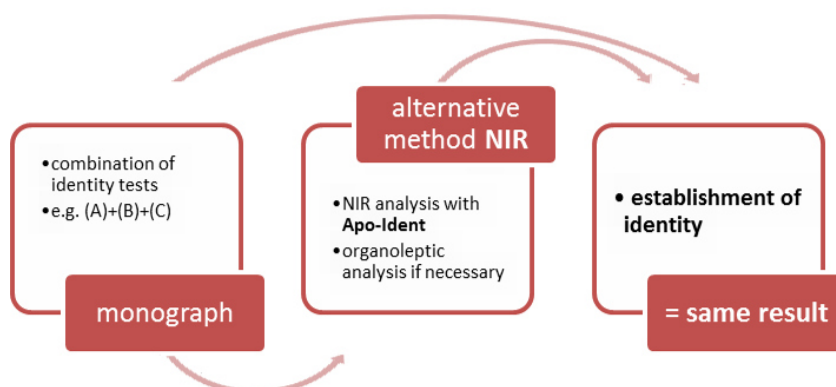


**Figure 2:** The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

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].

## ***Appendix F: Addition to the two-stage models***

As described in the general part of the *Apo-Ident* validation documentation, in the section [Model creation procedure and validation runs](#), under 2. *Generating the chemometric models (calibration) in f)*, it is possible to create a further chemometric model for certain substances (second-stage model) and to undertake the assessment in several steps.

### **Substances in stage-two models**

In the *Apo-Ident Update 2018-04*, a distinction is made between the following substances in the listed stage-two models:

#### ***Submodel 1***

Bacitracin  
Betamethasone, micronized  
Betamethasone valerate  
Budesonide, micronized  
Capsaicin, natural  
Dexamethasone  
Erythromycin  
Hydrocortisone butyrate  
Norethisterone acetate  
Prednicarbate, micronized  
Prednisolone, micronized  
Triamcinolone acetonide

#### ***Submodel 2***

Beclometasone dipropionate, anhydrous  
Betamethasone dipropionate, micronized  
Clobetasol propionate  
Diphenylcyclopropenone  
Gentamicin sulfate  
Sodium benzoate  
Sodium citrate  
Oxybutynin hydrochloride

#### ***Submodel 3***

Alfatradiol  
Estriol  
Pregnenolone  
Progesterone, micronized  
Quinine hydrochloride  
Quinine sulfate dihydrate  
Spironolactone  
Testosterone propionate

#### ***Liquid submodel***

2-ethylhexyl laurate  
Base cream DAC  
Lanette® ointment (conserved)  
Non-ionic hydrophil ointment

Squalane

Wool alcohol cream DAB/SR

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