

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) Überprüfen der Abstände zwischen den Grenzen der trennbaren Substanzen: Die Distanzmatrix enthält die *Mahalanobis-Abstände* von jeder Substanz zu jeder anderen. Die Werte hin und zurück sind jeweils unterschiedlich, weil die Streuung der Ausgangssubstanz eingeht. Ist eine Distanz kleiner als der Mindestabstand, so gelten die Substanzen als nicht sicher trennbar. Der Mindestabstand ist auf 9 festgelegt. Der Entwickler des Modells darf einen größeren Mindestabstand festlegen (ein Wert für das gesamte *chemometrische Modell*), um die Trennschärfe zu erhöhen.
- e) Überprüfung des Modells anhand der Referenzspektren. Es sind keine *falsch-positiven* Ergebnisse erlaubt.

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

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

3. Set of validation spectra (validation samples)

The following is provided for validation:

- a) *Type A*: The reference spectra = calibration spectra from which the database was generated. These also include spectra from substances which the *chemometric model* should not identify, but were also recorded during generation in order to increase selectivity. (As a result, the model “learns” to differentiate from other substances which are actually unknown to it.)
- b) *Type B*: Spectra recorded under the control of *HiperScan GmbH* and not used for the generation of the database. These also include reference spectra of other substance classes, and spectra that are not used as reference spectra. Samples are considered to be independent, if they originate from a batch, of which no spectra have been used for the generation of the database. (Up to *IdentModule 2018-01*, samples were still considered independent if the sampling was done independently, i.e. if they originate from another sales container.)
- c) *Type C*: Spectra from the field, which have not been recorded under the control of *HiperScan GmbH* and have not been used for the generation of the database. The spectra include not only substances of the substance class to be tested, but also substances from other classes.

All manufacturers’ batches from which spectra are used for the validation are listed by substance in this document: for substances included in the substance class *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 14 000 spectra not belonging to the substance are presented and no *false positive* classification is made, a hypothetical number of three *false positive* results is assumed (*Rule of Three* [10, 11]) and the *specificity* is defined with 100.0000 % (> 99.9786 %). Here, it applies that the higher the number of validation spectra which form the statistical basis, the better the *specificity* calculated via the lower *specificity* limit will be approximated.

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

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

Significance of testing with *Apo-Ident*

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

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

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

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

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

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

Conclusion

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

Explanation of terminology

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

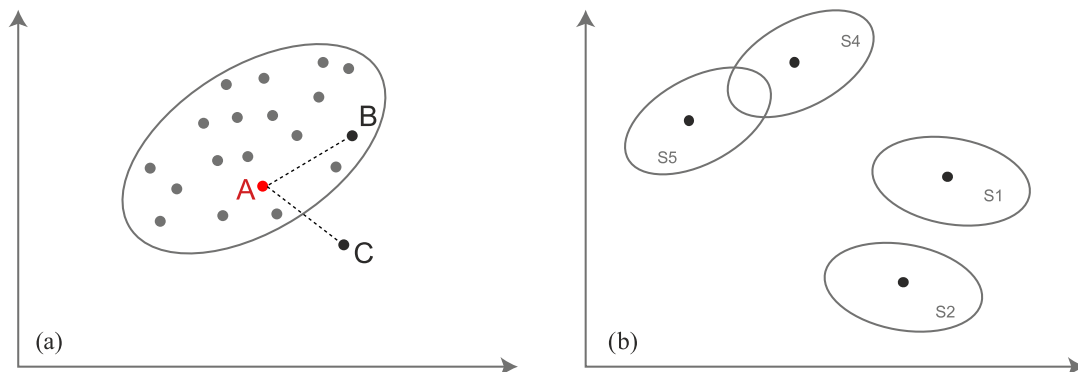


Figure 1: (a) The *Mahalanobis distance* from *A* to *B* is less than from *A* to *C*. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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

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

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

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

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

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

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

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

Summary

A total of 45 492 spectra from 1553 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:

Typ A Calibration spectra. These are the spectra used to generate the chemometric model. They were recorded by *HiperScan GmbH*. Detailed information regarding the batches or samples can be found in the following validation reports under *calibration samples* and under *Type A*. Further information is listed in [Appendix A](#).

Substance class	Substances	Batches	Spectra
HCK - nutritional supplements (Hepart)	118	442	22 851

From category *A* a total of 22 851 spectra from 442 batches for a total of 118 substances were taken into account for validation.

Typ B Spectra from independent samples which are not included in database generation. These spectra were recorded by *HiperScan GmbH*. Detailed information regarding the batches or samples can be found in the following validation reports in the section *Type B* or in [Appendix B](#).

Substance class	Substances	Batches	Spectra
HCK - nutritional supplements (Hepart)	92	447	20 754

From category *B* a total of 20 754 spectra from 447 batches for a total of 92 substances were taken into account for validation.

Typ C Spectra from independent samples which are not included in database generation. *Apo-Ident* customers carried out the measurements. Detailed information regarding the batches or samples can be found in the following validation reports in the section *Type C* or in [Appendix C](#).

Substance class	Substances	Batches	Spectra
HCK - nutritional supplements (Hepart)	63	866	1887

From category *C* a total of 1887 spectra from 866 batches for a total of 63 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	22 833	18	1 850 931
Type B	0	19 778	596	1 681 356
Type C	0	1535	343	152 855

All substances/substance groups in the substance class *HCK - nutritional supplements (Hepat)* can be clearly distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Typ A	100.000 00 % (> 99.999 16 %)	99.995 38 % (> 99.961 50 %)
Typ B	100.000 00 % (> 99.998 56 %)	92.085 95 % (> 92.024 40 %)
Typ C	100.000 00 % (> 99.984 79 %)	73.240 36 % (> 72.807 22 %)

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

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

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **a-Lipoic acid (H1000)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80022-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

a-Lipoic acid (H1000)

Special notes

When selecting the *a-Lipoic acid (H1000)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
a-Lipoic acid (H1000)	5	6	13

Second-stage model

For differentiation of the substance/substance group *a-Lipoic acid (H1000)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *a-Lipoic acid (H1000)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	a-Lipoic acid (H...	054301	80321	58	from supplier
Hepart	a-Lipoic acid (H...	14001420	80482	60	from supplier
Hepart	a-Lipoic acid (H...	14001726	80491	60	from supplier
Hepart	a-Lipoic acid (H...	15001526 (B1.2)	80681	60	from supplier
Hepart	a-Lipoic acid (H...	14000497	80682	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 298 spectra of 5 reference samples from the substance/substance group *a-Lipoic acid (H1000)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 22 553 spectra from a total of 435 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 320 spectra of 6 reference samples from the substance/substance group *a-Lipoic acid (H1000)*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	a-Lipoic acid (H1000)	066601	80369	40
Hepart	a-Lipoic acid (H1000)	15001526(B1.1)	80680	60
Hepart	a-Lipoic acid (H1000)	14000497(F1)	80683	60
Hepart	a-Lipoic acid (H1000)	14000497(F2)	80684	60
Hepart	a-Lipoic acid (H1000)	15001526(MM)	80685	60
Hepart	a-Lipoic acid (H1000)	18000250	81017	40

- 20 434 spectra from a total of 441 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 33 spectra from 12 *Apo-Ident* customers from 15 batches from the substance/substance group *a-Lipoic acid (H1000)*.
- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	a-Lipoic acid (H1000)	66601	2
Hepart	a-Lipoic acid (H1000)	18000250	1
Hepart / Unisan	a-Lipoic acid (H1000)	150015262	1
Hepart AG	a-Lipoic acid (H1000)	1313025701	2
Hepart AG	a-Lipoic acid (H1000)	25701	1
Hepart AG	a-Lipoic acid (H1000)	54301	1
Hepart AG	a-Lipoic acid (H1000)	14000497/1	1
Hepart AG	a-Lipoic acid (H1000)	15001526/2	3
Hepart AG	a-Lipoic acid (H1000)	150001526/2	1
Th. Geyer	a-Lipoic acid (H1000)	15001526/0	1
unisan	a-Lipoic acid (H1000)	H100031	1
unisan	a-Lipoic acid (H1000)	66601	1
Unisan	a-Lipoic acid (H1000)	993101	2
Unisan	a-Lipoic acid (H1000)	25701	6
Unisan	a-Lipoic acid (H1000)	1312993101	1
Unisan	a-Lipoic acid (H1000)	66601	1
Unisan	a-Lipoic acid (H1000)	14001726	2
Unisan	a-Lipoic acid (H1000)	14000497	1
Unisan GmbH, 78465 Kons...	a-Lipoic acid (H1000)	25701	2
Unisan/Hepart AG	a-Lipoic acid (H1000)	25701	1
Unisan/Hepart AG	a-Lipoic acid (H1000)	54301	1

- 1854 spectra from 19 *Apo-Ident* customers from a total of 844 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 *a-Lipoic acid (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 *a-Lipoic acid (H1000)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	298	0	22 553
Type B	0	312	8	20 434
Type C	0	31	2	1854

The substance/substance group *a-Lipoic acid (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 % (> 99.9309 %)	100.0000 % (> 97.9866 %)
Type B	100.0000 % (> 99.8804 %)	97.5000 % (> 96.5625 %)
Type C	100.0000 % (> 98.7242 %)	93.9394 % (> 84.8485 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *a-Lipoic acid (H1000)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	61.93	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *a-Lipoic acid (H1000)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80482	80482	0.00	81.46
80682	80682	0.00	63.39
80321	80321	0.00	61.93
80491	80491	0.00	62.06
80681	80681	0.00	63.53

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Aminomix NAC (H1002)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80003-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Aminomix NAC (H1002)	9	15	19

Second-stage model

For differentiation of the substance/substance group *Aminomix NAC (H1002)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Aminomix NAC (H1002)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Aminomix NAC (H1...	041401	80312	40	from supplier
Hepart	Aminomix NAC (H1...	041402	80314	60	from supplier
Hepart	Aminomix NAC (H1...	14000258	80407	40	from supplier
Hepart	Aminomix NAC (H1...	14000258	80444	40	from supplier
Hepart	Aminomix NAC (H1...	14000259	80447	40	from supplier
Hepart	Aminomix NAC (H1...	15000295 (B1)	80538	60	from supplier
Hepart	Aminomix NAC (H1...	15000297 (F2)	80544	60	from supplier
Hepart	Aminomix NAC (H1...	15000320	80545	60	from supplier
Hepart	Aminomix NAC (H1...	15000321	80546	60	from supplier
Hepart	Aminomix NAC (H1...	15000319 (F2)	80549	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 520 spectra of 10 reference samples from the substance/substance group *Aminomix NAC (H1002)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 22 331 spectra from a total of 431 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 840 spectra of 17 reference samples from the substance/substance group *Aminomix NAC (H1002)*.

- Among them are spectra of independent samples from 15 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Aminomix NAC (H1002)	15000295	80537	60
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)	15000321 (B1)	80547	60
Hepart	Aminomix NAC (H1002)	15000319	80548	60
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
Hepart	Aminomix NAC (H1002)	19002356	81214	40
Hepart	Aminomix NAC (H1002)	14000259	80408	40
Hepart	Aminomix NAC (H1002)	041401	80457	40

- 19914 spectra from a total of 430 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 45 spectra from 10 *Apo-Ident* customers from 23 batches from the substance/substance group *Aminomix NAC (H1002)*.
- Among them are spectra of independent samples from 19 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Aminomix NAC (H1002)	16001017/0	1
HCK	Aminomix NAC (H1002)	16001453	1
Hepart	Aminomix NAC (H1002)	17000766	1
Hepart	Aminomix NAC (H1002)	17000766/0	1
Hepart	Aminomix NAC (H1002)	18001998/0	1
Hepart	Aminomix NAC (H1002)	16001453/0	1
Hepart AG	Aminomix NAC (H1002)	1054019101	2
Hepart AG	Aminomix NAC (H1002)	41402	2
Hepart AG	Aminomix NAC (H1002)	41401	2
Hepart AG	Aminomix NAC (H1002)	15000320	1
Hepart AG	Aminomix NAC (H1002)	16001452	1
Hepart AG	Aminomix NAC (H1002)	16001552/0	1
Hepart AG	Aminomix NAC (H1002)	17000766/0	1
Hepart AG, CH-8280 Kreu...	Aminomix NAC (H1002)	1054019101	1
unisan	Aminomix NAC (H1002)	15000297	1
Unisan	Aminomix NAC (H1002)	971701	1

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Supplier	Substance	Batch	Spectra
Unisan	Aminomix NAC (H1002)	19101	1
Unisan	Aminomix NAC (H1002)	41401	1
Unisan	Aminomix NAC (H1002)	41402	4
Unisan	Aminomix NAC (H1002)	14000258	3
Unisan	Aminomix NAC (H1002)	140000259	1
Unisan	Aminomix NAC (H1002)	14000259	1
Unisan	Aminomix NAC (H1002)	15000295/0	3
Unisan	Aminomix NAC (H1002)	15000320	1
Unisan	Aminomix NAC (H1002)	15000320/0	2
Unisan	Aminomix NAC (H1002)	15000298/0	1
Unisan	Aminomix NAC (H1002)	165001017/0	1
Unisan	Aminomix NAC (H1002)	16001017/0	1
Unisan	Aminomix NAC (H1002)	16001453/0	1
Unisan	Aminomix NAC (H1002)	17000766	2
Unisan 02.04.2016	Aminomix NAC (H1002)	15000320/0	1
Unisan/Hepart AG	Aminomix NAC (H1002)	41402	1
unisan	Aminomix NAC (H1002)		1

- 1842 spectra from 19 *Apo-Ident* customers from a total of 838 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 *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
Type A	0	520	0	22 331
Type B	0	825	15	19 914
Type C	0	32	13	1842

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9307 %)	100.0000 % (> 98.8462 %)
Type B	100.0000 % (> 99.8801 %)	98.2143 % (> 97.8571 %)
Type C	100.0000 % (> 98.7218 %)	71.1111 % (> 64.4444 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Aminomix NAC (H1002)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	17.59	—
Pumpkin protein (H1429)	23.02	—
Lupin protein complex (H1427)	24.04	—
Coenzyme Q10 (H1013)	27.05	—
Antibiosis forte complex (H1115)	32.03	—
Glutamine (L-) (H1043)	32.85	—
Isoflavones (H1025)	35.55	—
PET skin and hair (H1504)	37.37	—
Hemp protein (H1406)	39.44	—
Amino V complex (H1400)	40.64	—
Vitamin E NAT (H1107)	41.47	—
PET basis (H1503)	43.42	—
Calcium (H1008)	45.89	—
Vitamin B1 (H1101)	48.61	—
Carnitine (L-) (H1038)	49.15	—
Yeast organic (H1007)	54.81	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Aminomix NAC (H1002)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80312	80312	0.00	35.55
80314	80314	0.00	33.90
80407	80407	0.00	33.90
80544	80544	0.00	35.65
80545	80545	0.00	29.77
80546	80546	0.00	34.47
80538	80538	0.00	32.93
80549	80549	0.00	32.43
80444	80444	0.00	25.76
80447	80447	0.00	23.66

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

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Antibiosis forte complex (H1115) / Antibiose mite complex (H1113)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80675-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803);
Antibiosis forte complex (H1115); Antibiosis mite complex (H1113); Pathogene complex (H1803)

Special notes

When selecting the *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Antibiosis forte complex (H1115)	2	2	0
Antibiosis mite complex (H1113)	2	4	0
Pathogene complex (H1803)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antibiosis forte...	15001169	80675	60	from supplier
Hepart	Antibiosis forte...	17001137	80912	40	from supplier
Hepart	Antibiosis mite ...	16001074	80900	40	from supplier
Hepart	Antibiosis mite ...	16001073	80903	40	from supplier
Hepart	Pathogene comple...	18000637	81038	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 22 631 spectra from a total of 435 batches from further 115 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Antibiosis forte complex (H1...	17001151	81019	40
Hepart	Antibiosis forte complex (H1...	19000078	81152	40
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

- 20 514 spectra from a total of 441 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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) / Antibiose mite complex (H1113) / Pathogene complex (H1803)* can clearly be 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) / Antibiose mite complex (H1113) / Pathogene complex (H1803)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	22 631
Type B	0	200	40	20 514
Type C	0	0	0	1887

The substance/substance group *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)* can be clearly distinguished from all other substances. In order 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 % (> 99.9310 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.8805 %)	83.3333 % (> 82.0833 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Walnut leaf (H1114)	18.61	—
Garcinia cambogia (H1017)	19.78	—
Antioxidants NAT complex (H1004)	23.26	—
Seabuckthorn organic (H1412)	23.46	—
Histamine block complex (H1117)	24.61	—
Copper (H1032)	24.79	—
Ginkgo (H1024)	29.80	—
Calcium (H1008)	32.16	—
Iron (H1015)	33.75	—
PET basis (H1503)	36.86	—
Flavour orange (H1405)	43.56	—
Rhodiola (H1064)	44.94	—
Potassium (H1030)	45.83	—
Camu camu (H1411)	46.55	—
PET joints (H1501)	46.80	—
Vitamin C (H1104)	48.67	—
Argentum (H1116)	52.38	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Antibiosis forte complex (H1115) / Antibiose mite complex (H1113) / Pathogene complex (H1803)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80912	80912	0.00	96.55
80900	80900	0.00	18.61
81038	81038	0.00	23.46
80903	80903	0.00	29.64
80675	80675	0.00	133.91

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Argentum (H1116)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80674-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Argentum (H1116)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Argentum (H1116)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Argentum (H1116)	15001151	80674	60	from supplier
Hepart	Argentum (H1116)	16001077	80890	40	from supplier

Validation samples

A total of 45 492 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 *Argentum (H1116)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 751 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Argentum (H1116)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Argentum (H1116)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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
Type A	0	100	0	22 751
Type B	0	0	0	20 754
Type C	0	0	0	1887

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9315 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Argentum (H1116)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Iron (H1015)	11.88	—
Garcinia cambogia (H1017)	63.41	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Argentum (H1116)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80674	80674	0.00	12.04
80890	80890	0.00	15.71

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Arginine (L-) (H1036)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80026-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Arginine (L-) (H1036)	4	8	17

Second-stage model

For differentiation of the substance/substance group *Arginine (L-) (H1036)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Arginine (L-) (H...	066501	80373	40	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
Hepart	Arginine (L-) (H...	18001388	81113	40	from supplier

Validation samples

A total of 45 492 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 *Arginine (L-) (H1036)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 651 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 360 spectra of 9 reference samples from the substance/substance group *Arginine (L-) (H1036)*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Arginine (L-) (H1036)	052401	80330	60
Hepart	Arginine (L-) (H1036)	14000563	80446	20
Hepart	Arginine (L-) (H1036)	14000564	80448	40
Hepart	Arginine (L-) (H1036)	17000878	80928	40
Hepart	Arginine (L-) (H1036)	17000877	80929	40
Hepart	Arginine (L-) (H1036)	18001443	81114	40
Hepart	Arginine (L-) (H1036)	19000626	81188	40
Hepart	Arginine (L-) (H1036)	19000689	81189	40
Hepart	Arginine (L-) (H1036)	16000950	80808	40

- 20394 spectra from a total of 438 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 43 spectra from 12 *Apo-Ident* customers from 17 batches from the substance/substance group *Arginine (L-) (H1036)*.
- Among them are spectra of independent samples from 17 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Arginine (L-) (H1036)	1324044301	1
HCK	Arginine (L-) (H1036)	14000564	1
Hepart	Arginine (L-) (H1036)	17000877/0	1
Hepart	Arginine (L-) (H1036)	17000878	4
Hepart	Arginine (L-) (H1036)	17000878/1	2
Hepart AG	Arginine (L-) (H1036)	66501	1
Hepart AG	Arginine (L-) (H1036)	14000563/2	1
Hepart AG	Arginine (L-) (H1036)	17000877/0	1
Hepart AG	Arginine (L-) (H1036)	17000878/0	9
unisan	Arginine (L-) (H1036)	52401	1
Unisan	Arginine (L-) (H1036)	44301	2
Unisan	Arginine (L-) (H1036)	27802	1
Unisan	Arginine (L-) (H1036)	1324950601	1
Unisan	Arginine (L-) (H1036)	52401	1
Unisan	Arginine (L-) (H1036)	66501	5
Unisan	Arginine (L-) (H1036)	14000563	1
Unisan	Arginine (L-) (H1036)	14000564/0	1
Unisan	Arginine (L-) (H1036)	14000564/2	1
Unisan	Arginine (L-) (H1036)	16000949/0	1
Unisan	Arginine (L-) (H1036)	17000877	3
UNISAN	Arginine (L-) (H1036)	66501	1
Unisan GmbH, 78465 Kons...	Arginine (L-) (H1036)	52401	2
Unisan/Hepart AG	Arginine (L-) (H1036)	1324044301	1

- 1844 spectra from 19 *Apo-Ident* customers from a total of 842 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 *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	200	0	22 651
Type B	0	300	60	20 394
Type C	0	29	14	1844

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 % (> 99.9310 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8803 %)	83.3333 % (> 82.5000 %)
Type C	100.0000 % (> 98.7221 %)	67.4419 % (> 60.4651 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Arginine (L-) (H1036)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Iron (H1015)	32.72	—
Antioxidants NAT complex (H1004)	37.14	—
Psyllium husks (H1432)	38.29	—
Calcium (H1008)	40.28	—
Vitamin B1 (H1101)	44.92	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Arginine (L-) (H1036)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80876	80876	0.00	42.05
81113	81113	0.00	40.95
80373	80373	0.00	38.29
80867	80867	0.00	40.02
80807	80807	0.00	44.00

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Artichoke extract (H1440)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81088-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Artichoke extract (H1440)

Special notes

When selecting the *Artichoke extract (H1440)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Artichoke extract (H1440)	1	1	0

Second-stage model

For differentiation of the substance/substance group *Artichoke extract (H1440)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Artichoke extract (H1440)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Artichoke extrac...	18001094	81088	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Artichoke extract (H1440)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Artichoke extract (H1440)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Artichoke extract (H1440)	20000368	81234	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were

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

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Artichoke extract (H1440)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Artichoke extract (H1440)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Artichoke extract (H1440)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Artichoke extract (H1440)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Artichoke extract (H1440)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Juniper (H1112)	17.55	—
Marshmallow extract (H1439)	21.37	—
Detox complex (H1118)	21.52	—
Gentian extract (H1438)	22.87	—
Garcinia cambogia (H1017)	26.61	—
Antioxidants NAT complex (H1004)	26.73	—
Orthovimin Neutral Complex (H1403)	27.29	—
Ginseng (H1018)	29.66	—
Saffron style (H1434)	32.46	—
Calcium (H1008)	32.69	—
Psyllium husks (H1432)	37.51	—
Saffron flowers (H1435)	38.31	—
Baobab (H1410)	38.52	—
Lycopene (H1058)	39.92	—
Enzyme complex (H1118)	43.82	—
Iron (H1015)	43.85	—
Silicium (H1070)	44.63	—
Flavour orange (H1405)	46.08	—
Vitamin B1 (H1101)	46.60	—
Vitamin K2 (75µg Mono) (H1108)	53.49	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Artichoke extract (H1440)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81088	81088	0.00	17.55

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Baobab (H1410)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80921-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Baobab (H1410)

Special notes

When selecting the *Baobab (H1410)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Baobab (H1410)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Baobab (H1410)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Baobab (H1410)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Baobab (H1410)	16001158	80921	40	from supplier
Hepart	Baobab (H1410)	18000501/0	81158	40	from supplier

Validation samples

A total of 45 492 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 *Baobab (H1410)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Baobab (H1410)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Baobab (H1410)	17001785/0	81003	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Baobab (H1410)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Baobab (H1410)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Baobab (H1410)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Baobab (H1410)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Baobab (H1410)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Detox complex (H1118)	14.30	—
Antioxidants NAT complex (H1004)	17.27	—
Ginseng (H1018)	20.31	—
Juniper (H1112)	20.46	—
Silicium (H1070)	20.50	—
Calcium (H1008)	21.62	—
Glutathione (H1020)	24.62	—
Boron (H1005)	25.53	—
Vitamin B1 (H1101)	28.24	—
Saffron style (H1434)	28.34	—
Orthovimin Neutral Complex (H1403)	30.34	—
Cabbage extract (H1121)	31.72	—
Marshmallow extract (H1439)	32.17	—
Orthocolon complex (H1800)	32.98	—
Vitamin K2 (75µg Mono) (H1108)	34.54	—
Zinc (H1110)	36.08	—
Flavour orange (H1405)	36.58	—
Garcinia cambogia (H1017)	37.02	—
PET coenzyme Q10 (H0022)	38.18	—
Lycopene (H1058)	38.38	—
Vitamin E NAT (H1107)	39.40	—
Broccoli (H1415)	41.13	—
Folic acid (H1016)	41.13	—
Enzyme complex (H1118)	41.64	—
Seabuckthorn organic (H1412)	41.64	—
Selenium yeast (H1068)	42.75	—
Gentian extract (H1438)	43.26	—
Coenzyme Q10 (H1013)	44.46	—
Leaky gut complex (H1802)	44.76	—
Psyllium husks (H1432)	45.15	—
Artichoke extract (H1440)	46.37	—
Isoflavones (H1025)	48.27	—
Camu camu (H1411)	49.53	—
Ginger extract (H1437)	50.85	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Baobab (H1410)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80921	80921	0.00	20.72
81158	81158	0.00	14.30

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Beetroot (H1414)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81055-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Beetroot (H1414)

Special notes

When selecting the *Beetroot (H1414)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Beetroot (H1414)	3	0	0

Second-stage model

For differentiation of the substance/substance group *Beetroot (H1414)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Beetroot (H1414)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Beetroot (H1414)	18000857	81055	40	from supplier
Hepart	Beetroot (H1414)	18001315	81137	40	from supplier
Hepart	Beetroot (H1414)	20000105	81225	40	from supplier

Validation samples

A total of 45 492 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 *Beetroot (H1414)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 731 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Beetroot (H1414)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Beetroot (H1414)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Beetroot (H1414)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Beetroot (H1414)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	22 731
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Beetroot (H1414)* can be clearly distinguished from all other substances. In order 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 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Beetroot (H1414)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	16.43	—
Broccoli (H1415)	17.39	—

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Substanz	Distance in main model	Distance in second-stage model
Flavour orange (H1405)	20.22	—
Carrot (H1416)	25.39	—
Calcium (H1008)	25.68	—
Seabuckthorn organic (H1412)	27.11	—
Vitamin B1 (H1101)	27.65	—
PET basis (H1503)	28.54	—
Pathogene complex (H1803)	33.08	—
Acerola (H1413)	36.19	—
Iron (H1015)	36.35	—
Glutathione (H1020)	36.35	—
Cabbage extract (H1121)	37.92	—
Ginkgo (H1024)	39.09	—
Copper (H1032)	41.96	—
Antibiosis mite complex (H1113)	42.38	—
Juniper (H1112)	42.49	—
Rhodiola (H1064)	43.24	—
Detox complex (H1118)	43.48	—
Wild berry (H1417)	44.90	—
Vitamin B6 (H1103)	45.21	—
Cranberry (H1408)	46.20	—
Vitamin C (H1104)	46.82	—
Silymarin (H1071)	48.81	—
Orthocolon complex (H1800)	49.38	—
Saffron flowers (H1435)	49.44	—
Vitamins BAG (H1090)	49.70	—
PET well-aging (H1500)	50.02	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Beetroot (H1414)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81055	81055	0.00	25.39
81137	81137	0.00	26.14
81225	81225	0.00	28.54

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Betaine hydrochloride (H1119)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80926-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Betaine hydrochloride (H1119)

Special notes

When selecting the *Betaine hydrochloride (H1119)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Betaine hydrochloride (H1119)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Betaine hydrochloride (H1119)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Betaine hydrochloride (H1119)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Betaine hydrochl...	17000829	80926	40	from supplier
Hepart	Betaine hydrochl...	19000533	81169	40	from supplier

Validation samples

A total of 45 492 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 *Betaine hydrochloride (H1119)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Betaine hydrochloride (H1119)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Betaine hydrochloride (H1119)	19001723	81203	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Betaine hydrochloride (H1119)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Betaine hydrochloride (H1119)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Betaine hydrochloride (H1119)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	40	0	20 714
Type C	0	0	0	1887

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Betaine hydrochloride (H1119)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	29.62	—
Ginkgo (H1024)	30.27	—
Carnitine (L-) (H1038)	33.29	—
Silymarin (H1071)	33.67	—
Calcium (H1008)	38.88	—
Coenzyme Q10 (H1013)	39.98	—
Rhodiola (H1064)	50.03	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Betaine hydrochloride (H1119)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80926	80926	0.00	51.45
81169	81169	0.00	37.82

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Boron (H1005)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81119-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Boron (H1005)

Special notes

When selecting the *Boron (H1005)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Boron (H1005)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Boron (H1005)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Boron (H1005)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Boron (H1005)	17000827/1	81119	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Boron (H1005)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Boron (H1005)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Boron (H1005)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Boron (H1005)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Boron (H1005)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Boron (H1005)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Boron (H1005)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Silicium (H1070)	12.79	—
Marshmallow extract (H1439)	18.46	—

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Substanz	Distance in main model	Distance in second-stage model
Baobab (H1410)	21.11	—
Zinc (H1110)	24.39	—
Folic acid (H1016)	24.50	—
Orthovimin Neutral Complex (H1403)	24.94	—
Calcium (H1008)	26.29	—
Detox complex (H1118)	28.14	—
Ginger extract (H1437)	28.72	—
Ginseng (H1018)	28.94	—
Saffron style (H1434)	29.12	—
Antioxidants NAT complex (H1004)	30.78	—
Vitamin B1 (H1101)	34.56	—
Gentian extract (H1438)	35.44	—
Selenium yeast (H1068)	35.85	—
Konjac (H1426)	36.90	—
PET coenzyme Q10 (H0022)	38.78	—
Vitamin K2 (75µg Mono) (H1108)	39.81	—
Acacia gum (H1001)	41.75	—
Psyllium husks (H1432)	44.00	—
Juniper (H1112)	44.04	—
Lycopene (H1058)	44.64	—
Vitamin E NAT (H1107)	45.77	—
Biotin (H1007)	46.61	—
Coenzyme Q10 (H1013)	46.62	—
Selenium (H1067)	48.94	—
Vitamin B12 (H1102)	49.37	—
Glutathione (H1020)	49.79	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Boron (H1005)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81119	81119	0.00	11.83

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Caffeine guarana extract (H1425)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 10002191-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Caffeine guarana extract (H1425)

Special notes

When selecting the *Caffeine guarana extract (H1425)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Caffeine guarana extract (H1425)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Caffeine guarana extract (H1425)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Caffeine guarana extract (H1425)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Caffeine guarana...	19000247/0	81212	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Caffeine guarana extract (H1425)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Caffeine guarana extract (H1425)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Caffeine guarana extract (H1425)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Caffeine guarana extract (H1425)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Caffeine guarana extract (H1425)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Caffeine guarana extract (H1425)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Caffeine guarana extract (H1425)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Carnitine (L-) (H1038)	19.23	—
Calcium (H1008)	24.11	—

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Substanz	Distance in main model	Distance in second-stage model
Vitamin complex (H1100)	29.26	—
Silymarin (H1071)	30.32	—
OPC Grape seed (H1066)	32.94	—
Antioxidants NAT complex (H1004)	35.26	—
Coenzyme Q10 (H1013)	48.91	—
L-5-HTP (H1035)	50.69	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Caffeine guarana extract (H1425)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81212	81212	0.00	28.32

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Carnitine (L-) (H1038)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80013-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Carnitine (L-) (H1038)	7	7	27

Second-stage model

For differentiation of the substance/substance group *Carnitine (L-) (H1038)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Carnitine (L-) (...)	026010	80344	40	from supplier
Hepart	Carnitine (L-) (...)	130605300	80371	40	from supplier
Hepart	Carnitine (L-) (...)	130605302	80483	60	from supplier
Hepart	Carnitine (L-) (...)	15000052	80557	60	from supplier
Hepart	Carnitine (L-) (...)	15000054	80559	60	from supplier
Hepart	Carnitine (L-) (...)	16000453	80787	40	from supplier
Hepart	Carnitine (L-) (...)	18000538	81045	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 7 reference samples from the substance/substance group *Carnitine (L-) (H1038)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 22 511 spectra from a total of 433 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 320 spectra of 7 reference samples from the substance/substance group *Carnitine (L-) (H1038)*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Carnitine (L-) (H1038)	15000053	80558	60
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

- 20 434 spectra from a total of 440 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 69 spectra from 12 *Apo-Ident* customers from 33 batches from the substance/substance group *Carnitine (L-) (H1038)*.
- Among them are spectra of independent samples from 27 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Carnitine (L-) (H1038)	15000054/1	2
Hepart	Carnitine (L-) (H1038)	16000451/0	1
Hepart	Carnitine (L-) (H1038)	16000453/0	1
Hepart	Carnitine (L-) (H1038)	160004531	3
Hepart	Carnitine (L-) (H1038)	160000453	1
Hepart	Carnitine (L-) (H1038)	16000454/0	2
Hepart	Carnitine (L-) (H1038)	16000454	1
Hepart AG	Carnitine (L-) (H1038)	16000453/1	2
Hepart AG	Carnitine (L-) (H1038)	16000454/0	5
Hepart AG	Carnitine (L-) (H1038)	1184026001	1
Hepart AG	Carnitine (L-) (H1038)	26001	1
Hepart AG	Carnitine (L-) (H1038)	26010	3
Hepart AG	Carnitine (L-) (H1038)	480g	1
Hepart AG	Carnitine (L-) (H1038)	130605300	1
Hepart AG	Carnitine (L-) (H1038)	130605301	2
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	1184965901	1
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	26020	2
Hepart AG, CH-8280 Kreu...	Carnitine (L-) (H1038)	26010	1
unisan	Carnitine (L-) (H1038)	26010	1
Unisan	Carnitine (L-) (H1038)	130605302	2
Unisan	Carnitine (L-) (H1038)	130605300/3	1
Unisan	Carnitine (L-) (H1038)	15000052	1
Unisan	Carnitine (L-) (H1038)	15000053/0	2
Unisan	Carnitine (L-) (H1038)	15000053	1
Unisan	Carnitine (L-) (H1038)	15000054	1
Unisan	Carnitine (L-) (H1038)	15000053/3	1
Unisan	Carnitine (L-) (H1038)	150000540	1
Unisan	Carnitine (L-) (H1038)	15000054/0	1
Unisan	Carnitine (L-) (H1038)	16000450	1
Unisan	Carnitine (L-) (H1038)	16000451	2
Unisan	Carnitine (L-) (H1038)	965901	1

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Supplier	Substance	Batch	Spectra
Unisan	Carnitine (L-) (H1038)	130326002	1
Unisan	Carnitine (L-) (H1038)	26010	2
Unisan	Carnitine (L-) (H1038)	1184026020	3
Unisan	Carnitine (L-) (H1038)	130605300	4
Unisan	Carnitine (L-) (H1038)	130605301	1
UNISAN	Carnitine (L-) (H1038)	130605300	3
UNISAN	Carnitine (L-) (H1038)	130605302	1
Unisan	Carnitine (L-) (H1038)	1184965901	1
Unisan 2.10.2015	Carnitine (L-) (H1038)	15000052/0	2
Unsan	Carnitine (L-) (H1038)	16000450	1
Hepart	Carnitine (L-) (H1038)	16000453	1
Unisan	Carnitine (L-) (H1038)		2

- 1818 spectra from 19 *Apo-Ident* customers from a total of 827 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 *Carnitine (L-) (H1038)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Carnitine (L-) (H1038)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	22 511
Type B	0	320	0	20 434
Type C	0	63	6	1818

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9308 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.8804 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 98.7195 %)	91.3043 % (> 86.9565 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Carnitine (L-) (H1038)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Caffeine guarana extract (H1425)	24.41	—
Coenzyme Q10 (H1013)	26.82	—
Silymarin (H1071)	29.24	—
Antioxidants NAT complex (H1004)	30.69	—
Calcium (H1008)	31.13	—
Antibiosis forte complex (H1115)	34.81	—
Vitamin complex (H1100)	35.09	—
Ginkgo (H1024)	39.11	—
Yeast organic (H1007)	42.89	—
Betaine hydrochloride (H1119)	43.09	—
OPC Grape seed (H1066)	47.48	—
PET immune system (H1502)	47.98	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Carnitine (L-) (H1038)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80344	80344	0.00	24.41
80371	80371	0.00	34.43
80483	80483	0.00	30.93
80787	80787	0.00	35.22
80559	80559	0.00	35.46
80557	80557	0.00	35.21
81045	81045	0.00	34.81

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Carnosine (L-) (H1014)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80153-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Carnosine (L-) (H1014)	2	1	6

Second-stage model

For differentiation of the substance/substance group *Carnosine (L-) (H1014)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier

Validation samples

A total of 45 492 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 *Carnosine (L-) (H1014)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 711 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Carnosine (L-) (H1014)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Carnosine (L-) (H1014)	18001109	81071	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 9 spectra from 6 *Apo-Ident* customers from 6 batches from the substance/substance group *Carnosine (L-) (H1014)*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Carnosine (L-) (H1014)	1813979202	1
Hepart	Carnosine (L-) (H1014)	18001109/0	1
Hepart AG	Carnosine (L-) (H1014)	1812045901	1
Hepart AG	Carnosine (L-) (H1014)	45901	1
Hepart AG	Carnosine (L-) (H1014)	1812979202	1
Hepart AG, CH-8280 Kreu...	Carnosine (L-) (H1014)	1812045901	1
Purren Apotheke	Carnosine (L-) (H1014)	1813979202	1
UNISAN	Carnosine (L-) (H1014)	74801	1
Unisan/Hepart AG	Carnosine (L-) (H1014)	45901	1

- 1878 spectra from 19 *Apo-Ident* customers from a total of 853 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 *Carnosine (L-) (H1014)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Carnosine (L-) (H1014)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	22 711
Type B	0	40	0	20 714
Type C	0	9	0	1878

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9312 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7481 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Carnosine (L-) (H1014)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine (H1021)	62.58	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Carnosine (L-) (H1014)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80393	80393	0.00	84.87
80655	80655	0.00	82.48
80452	80452	0.00	82.41

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Carrot (H1416)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81087-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Carrot (H1416)

Special notes

When selecting the *Carrot (H1416)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Carrot (H1416)	1	1	0

Second-stage model

For differentiation of the substance/substance group *Carrot (H1416)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Carrot (H1416)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Carrot (H1416)	18001309	81087	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Carrot (H1416)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Carrot (H1416)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Carrot (H1416)	18001335/0	81093	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were

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

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Carrot (H1416)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Carrot (H1416)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Carrot (H1416)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	12	28	20 714
Type C	0	0	0	1887

The substance/substance group *Carrot (H1416)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8834 %)	30.0000 % (> 22.5000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Carrot (H1416)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cabbage extract (H1121)	18.39	—
Flavour orange (H1405)	20.45	—
Antioxidants NAT complex (H1004)	23.83	—
Broccoli (H1415)	24.45	—
Calcium (H1008)	26.42	—
Seabuckthorn organic (H1412)	29.18	—
Vitamin B1 (H1101)	29.63	—
Glutathione (H1020)	31.91	—
Wild berry (H1417)	32.24	—
Orthoclon complex (H1800)	37.00	—
Acerola (H1413)	42.83	—
Ginseng (H1018)	44.02	—
Beetroot (H1414)	44.94	—
Baobab (H1410)	46.47	—
Pomegranate (H1409)	48.77	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Carrot (H1416)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81087	81087	0.00	18.39

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group	Catechin extract (H1010)
Substance class	HCK - nutritional supplements (Hepart)
Report date	25/06/2020
Report number	80031-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Catechin extract (H1010)	7	0	14

Second-stage model

For differentiation of the substance/substance group *Catechin extract (H1010)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Catechin extract...	15000206/4	80849	40	from supplier
Hepart	Catechin extract...	17000409/0	80880	40	from supplier
Hepart	Catechin extract...	18001420	81144	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 7 reference samples from the substance/substance group *Catechin extract (H1010)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 22 551 spectra from a total of 433 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Catechin extract (H1010)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Catechin extract (H1010)	15000206	80872	40

- 20714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 23 spectra from 10 *Apo-Ident* customers from 15 batches from the substance/substance group *Catechin extract (H1010)*.
- Among them are spectra of independent samples from 14 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Catechin extract (H1010)	115000206/5	1
Hepart	Catechin extract (H1010)	17000409	1
Hepart / Unisan	Catechin extract (H1010)	170004092	1
Hepart AG	Catechin extract (H1010)	1574018601	1
Hepart AG	Catechin extract (H1010)	18601	2
Hepart AG	Catechin extract (H1010)	130208020	1
Hepart AG	Catechin extract (H1010)	15000206/2	1
Hepart AG	Catechin extract (H1010)	17000409/2	1
Hepart AG, CH-8280 Kreu...	Catechin extract (H1010)	1571025702	1
Hepart AG, CH-8280 Kreu...	Catechin extract (H1010)	18601	1
Hepart AG, CH-8280 Kreu...	Catechin extract (H1010)	62901	1
Unisan	Catechin extract (H1010)	1571025702	1
Unisan	Catechin extract (H1010)	1571681501	1
Unisan	Catechin extract (H1010)	25702	1
Unisan	Catechin extract (H1010)	130208020	1
Unisan	Catechin extract (H1010)	62801	1
Unisan	Catechin extract (H1010)	681501	1
Unisan	Catechin extract (H1010)	62901	1
Unisan	Catechin extract (H1010)	15000206/2	1
Unisan	Catechin extract (H1010)	17000409	1
Unisan/Hepart AG	Catechin extract (H1010)	18601	1
Hepart	Catechin extract (H1010)	17000409/0	1

- 1864 spectra from 19 *Apo-Ident* customers from a total of 844 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 *Catechin extract (H1010)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Catechin extract (H1010)*

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

	False positive	True positive	False negative	True negative
Type A	0	300	0	22 551
Type B	0	40	0	20 714
Type C	0	11	12	1864

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9309 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7281 %)	47.8261 % (> 34.7826 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Catechin extract (H1010)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium (H1008)	16.57	—
Ginkgo (H1024)	20.51	—
Green coffee extract (H1433)	20.64	—
Carnitine (L-) (H1038)	24.06	—
Vitamin complex (H1100)	26.18	—
Rhodiola (H1064)	28.44	—
Antioxidants NAT complex (H1004)	29.81	—
L-5-HTP (H1035)	32.73	—
Bioflavonoid complex (H1006)	34.36	—
Silymarin (H1071)	34.71	—
PET immune system (H1502)	38.23	—
Antibiosis forte complex (H1115)	41.12	—
Flavour orange (H1405)	41.87	—
Vitamin B1 (H1101)	44.47	—
Vitamin C (H1104)	45.85	—
PET basis (H1503)	45.93	—
Broccoli (H1415)	49.30	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Catechin extract (H1010)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80849	80849	0.00	31.34
81144	81144	0.00	42.54
80555	80555	0.00	32.86
80339	80339	0.00	43.80
80880	80880	0.00	25.82
80338	80338	0.00	32.73
80340	80340	0.00	20.64

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Chaga (H1011)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80032-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chaga (H1011)	4	1	4

Second-stage model

For differentiation of the substance/substance group *Chaga (H1011)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Chaga (H1011)	14000951	80466	40	from supplier
Hepart	Chaga (H1011)	14001688	80493	60	from supplier
Hepart	Chaga (H1011)	16000976	80825	40	from supplier
Hepart	Chaga (H1011)	17001560	80952	40	from supplier

Validation samples

A total of 45 492 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 *Chaga (H1011)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 671 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 60 spectra of 1 reference samples from the substance/substance group *Chaga (H1011)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Chaga (H1011)	16000235	80763	60

- 20 694 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 6 spectra from 2 *Apo-Ident* customers from 5 batches from the substance/substance group *Chaga (H1011)*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Purren Apotheke	Chaga (H1011)	1514675601	1
Unisan	Chaga (H1011)	64001	2
Unisan	Chaga (H1011)	16000235	1
Unisan	Chaga (H1011)	14001688	1
Unisan/Hepart AG	Chaga (H1011)	46701	1

- 1881 spectra from 19 *Apo-Ident* customers from a total of 854 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 *Chaga (H1011)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chaga (H1011)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	22 671
Type B	0	60	0	20 694
Type C	0	6	0	1881

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9311 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8823 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.7646 %)	n/a (n/a)

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

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chaga (H1011)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Walnut leaf (H1114)	24.17	—
Trace elements SE (H1082)	49.11	—
Iron (H1015)	52.59	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chaga (H1011)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80952	80952	0.00	31.55
80493	80493	0.00	41.23
80466	80466	0.00	82.18
80825	80825	0.00	32.83

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Chia protein (H1431)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81009-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chia protein (H1431)

Special notes

When selecting the *Chia protein (H1431)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chia protein (H1431)	3	0	0

Second-stage model

For differentiation of the substance/substance group *Chia protein (H1431)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Chia protein (H1431)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Chia protein (H1...	17001729	81009	40	from supplier
Hepart	Chia protein (H1...	19000342/0	81157	40	from supplier
Hepart	Chia protein (H1...	20000513	81227	40	from supplier

Validation samples

A total of 45 492 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 *Chia protein (H1431)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 731 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Chia protein (H1431)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Chia protein (H1431)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Chia protein (H1431)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chia protein (H1431)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	22 731
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Chia protein (H1431)* can be clearly distinguished from all other substances. In order 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 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chia protein (H1431)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
PET immune system (H1502)	28.96	—
PET basis (H1503)	41.27	—
Antibiosis forte complex (H1115)	43.02	—
Hemp protein (H1406)	44.89	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chia protein (H1431)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81157	81157	0.00	28.96
81227	81227	0.00	30.26
81009	81009	0.00	40.10

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Chondroitin sulfate (Sodium-) (H1065)**
Substance class HCK - nutritional supplements (Hepar)
Report date 25/06/2020
Report number 80093-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chondroitin sulfate (Sodium-) (H1065)	4	2	9

Second-stage model

For differentiation of the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Chondroitin sulf...	14001985	80532	60	from supplier
Hepart	Chondroitin sulf...	14001991	80533	60	from supplier
Hepart	Chondroitin sulf...	14001985/2	80779	60	from supplier
Hepart	Chondroitin sulf...	17000211	80871	40	from supplier

Validation samples

A total of 45 492 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 *Chondroitin sulfate (Sodium-) (H1065)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 631 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 100 spectra of 2 reference samples from the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Chondroitin sulfate (Sodium...	031801	80584	60
Hepart	Chondroitin sulfate (Sodium...	19000780	81180	40

- 20 654 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 20 spectra from 11 *Apo-Ident* customers from 9 batches from the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Chondroitin sulfate (Sodium...	1821031801	1
Hepart	Chondroitin sulfate (Sodium...	14001985/5	1
Hepart	Chondroitin sulfate (Sodium...	17000211/0	1
hepart ag	Chondroitin sulfate (Sodium...	31801	1
Hepart AG	Chondroitin sulfate (Sodium...	31801	1
Hepart AG	Chondroitin sulfate (Sodium...	31801/1	1
Hepart AG, CH-8280 Kreu...	Chondroitin sulfate (Sodium...	1820031801	1
Hepart AG, CH-8280 Kreu...	Chondroitin sulfate (Sodium...	31801	1
Purren Apotheke	Chondroitin sulfate (Sodium...	1821964101	1
Unisan	Chondroitin sulfate (Sodium...	1820001801	2
Unisan	Chondroitin sulfate (Sodium...	1801	2
Unisan	Chondroitin sulfate (Sodium...	31801	4
Unisan	Chondroitin sulfate (Sodium...	1821964101	1
Unisan/Hepart AG	Chondroitin sulfate (Sodium...	31801	2

- 1867 spectra from 19 *Apo-Ident* customers from a total of 850 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 *Chondroitin sulfate (Sodium-) (H1065)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chondroitin sulfate (Sodium-) (H1065)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	22 631
Type B	0	40	60	20 654
Type C	0	2	18	1867

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9310 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.8813 %)	40.0000 % (> 37.0000 %)
Type C	100.0000 % (> 98.7300 %)	10.0000 % (≥ 0.0000 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Coenzyme Q10 (H1013)	21.29	—
Vitamin E NAT (H1107)	39.38	—
Ginseng (H1018)	47.37	—
PET coenzyme Q10 (H0022)	56.16	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chondroitin sulfate (Sodium-) (H1065)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80871	80871	0.00	61.56
80532	80532	0.00	47.81
80779	80779	0.00	46.74
80533	80533	0.00	39.35

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Cocoa (H1424)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80922-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Cocoa (H1424)

Special notes

When selecting the *Cocoa (H1424)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cocoa (H1424)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Cocoa (H1424)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Cocoa (H1424)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Cocoa (H1424)	17000625	80922	40	from supplier
Hepart	Cocoa (H1424)	18001680	81147	40	from supplier

Validation samples

A total of 45 492 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 *Cocoa (H1424)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Cocoa (H1424)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Cocoa (H1424)	18001645/0	81112	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Cocoa (H1424)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cocoa (H1424)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cocoa (H1424)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	20	20	20 714
Type C	0	0	0	1887

The substance/substance group *Cocoa (H1424)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8834 %)	50.0000 % (> 42.5000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cocoa (H1424)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
PET immune system (H1502)	26.90	—
PET basis (H1503)	40.06	—
Ginkgo (H1024)	48.22	—
Vitamin C (H1104)	56.21	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Cocoa (H1424)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80922	80922	0.00	26.90
81147	81147	0.00	35.25

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Coconut (H1418)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81120-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Coconut (H1418)

Special notes

When selecting the *Coconut (H1418)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Coconut (H1418)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Coconut (H1418)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Coconut (H1418)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Coconut (H1418)	18000569	81120	40	from supplier
Hepart	Coconut (H1418)	18001678	81132	40	from supplier

Validation samples

A total of 45 492 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 *Coconut (H1418)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Coconut (H1418)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Coconut (H1418)	16001493	81121	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Coconut (H1418)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Coconut (H1418)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Coconut (H1418)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Coconut (H1418)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Coconut (H1418)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Vitamin E NAT (H1107)	16.27	—
Coenzyme Q10 (H1013)	22.54	—
Antioxidants NAT complex (H1004)	31.09	—
Isoflavones (H1025)	44.43	—
Antibiosis forte complex (H1115)	44.86	—
Flavour orange (H1405)	48.49	—
Calcium (H1008)	49.83	—
Glutamine (L-) (H1043)	51.04	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Coconut (H1418)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81120	81120	0.00	26.26
81132	81132	0.00	23.08

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Coenzyme Q10 (H1013)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80015-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Coenzyme Q10 (H1013)	8	3	14

Second-stage model

For differentiation of the substance/substance group *Coenzyme Q10 (H1013)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Coenzyme Q10 (H1...	14001546	80587	60	from supplier
Hepart	Coenzyme Q10 (H1...	16000402/0	80794	40	from supplier
Hepart	Coenzyme Q10 (H1...	16000402/0	80850	40	from supplier
Hepart	Coenzyme Q10 (H1...	16001598/4	80854	40	from supplier
Hepart	Coenzyme Q10 (H1...	16001598	80881	40	from supplier
Hepart	Coenzyme Q10 (H1...	18000792/0	81048	40	from supplier
Hepart	Coenzyme Q10 (H1...	18000806	81049	40	from supplier
Hepart	Coenzyme Q10 (H1...	19002493/4	81213	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 440 spectra of 10 reference samples from the substance/substance group *Coenzyme Q10 (H1013)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 22 411 spectra from a total of 433 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Coenzyme Q10 (H1013)*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Coenzyme Q10 (H1013)	16000402/4	80795	40
Hepart	Coenzyme Q10 (H1013)	16000402	80882	40
Hepart	Coenzyme Q10 (H1013)	20000802	81257	40

- 20634 spectra from a total of 444 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 59 spectra from 15 *Apo-Ident* customers from 18 batches from the substance/substance group *Coenzyme Q10 (H1013)*.
- Among them are spectra of independent samples from 14 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Coenzyme Q10 (H1013)	16001598/1	1
Hepart	Coenzyme Q10 (H1013)	16000402/1	1
Hepart	Coenzyme Q10 (H1013)	16001599	1
Hepart / Unisan	Coenzyme Q10 (H1013)	160015991	1
Hepart AG	Coenzyme Q10 (H1013)	1194015601	2
Hepart AG	Coenzyme Q10 (H1013)	15601	4
Hepart AG	Coenzyme Q10 (H1013)	130521-300	5
Hepart AG	Coenzyme Q10 (H1013)	16000402/0	1
Hepart AG	Coenzyme Q10 (H1013)	16001599/1	2
Hepart AG	Coenzyme Q10 (H1013)	16001599/2	12
Hepart AG, CH-8280 Kreu...	Coenzyme Q10 (H1013)	1194015601	1
Hepart AG, CH-8280 Kreu...	Coenzyme Q10 (H1013)	15601	1
Unisan	Coenzyme Q10 (H1013)	992501	1
Unisan	Coenzyme Q10 (H1013)	15601	4
Unisan	Coenzyme Q10 (H1013)	1194015601	2
Unisan	Coenzyme Q10 (H1013)	H101311	1
Unisan	Coenzyme Q10 (H1013)	130521-300	4
Unisan	Coenzyme Q10 (H1013)	14001546	2
Unisan	Coenzyme Q10 (H1013)	14001546/1	2
Unisan	Coenzyme Q10 (H1013)	16000402/0	2
Unisan	Coenzyme Q10 (H1013)	16000402	1
Unisan	Coenzyme Q10 (H1013)	16001598	1
Unisan	Coenzyme Q10 (H1013)	16001599	1
UNISAN	Coenzyme Q10 (H1013)	130521-300	2
UNISAN	Coenzyme Q10 (H1013)	14001546	2
Unisan 02.04.2016	Coenzyme Q10 (H1013)	14001546/3	1
Unisan 2.10.2015	Coenzyme Q10 (H1013)	14001546/2	1

- 1828 spectra from 19 *Apo-Ident* customers from a total of 841 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 *Coenzyme Q10 (H1013)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Coenzyme Q10 (H1013)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	440	0	22 411
Type B	0	120	0	20 634
Type C	0	43	16	1828

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9308 %)	100.0000 % (> 98.6364 %)
Type B	100.0000 % (> 99.8811 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7202 %)	72.8814 % (> 67.7966 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Coenzyme Q10 (H1013)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Vitamin E NAT (H1107)	16.61	—
Ginseng (H1018)	21.94	—
PET coenzyme Q10 (H0022)	40.35	—
Vitamin K2 (75µg Mono) (H1108)	45.87	—
Antibiosis forte complex (H1115)	46.81	—
Vitamin B1 (H1101)	47.98	—
Glutamine (L-) (H1043)	48.36	—
Antioxidants NAT complex (H1004)	48.81	—
Psyllium husks (H1432)	51.26	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Coenzyme Q10 (H1013)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80354	80354	0.00	29.70
80850	80850	0.00	22.69
80587	80587	0.00	46.81
80881	80881	0.00	36.12
80794	80794	0.00	26.73
80484	80484	0.00	25.61
80854	80854	0.00	23.59
81048	81048	0.00	31.21
81213	81213	0.00	32.94
81049	81049	0.00	38.98

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Creatine (H1031)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80149-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Creatine (H1031)	4	2	5

Second-stage model

For differentiation of the substance/substance group *Creatine (H1031)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Creatine (H1031)	15000750	80628	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 4 reference samples from the substance/substance group *Creatine (H1031)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 651 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Creatine (H1031)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Creatine (H1031)	17001177	80918	40
Hepart	Creatine (H1031)	18001411	81115	40

- 20 674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 9 spectra from 4 *Apo-Ident* customers from 7 batches from the substance/substance group *Creatine (H1031)*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart AG	Creatine (H1031)	15000749	1
Purren Apotheke	Creatine (H1031)	965201	1
Unisan	Creatine (H1031)	25003	2
Unisan	Creatine (H1031)	15000750/0	1
Unisan	Creatine (H1031)	15000750	1
Unisan	Creatine (H1031)	17001177	2
Unisan GmbH, 78465 Kons. ...	Creatine (H1031)	1830025003	1

- 1878 spectra from 19 *Apo-Ident* customers from a total of 852 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 *Creatine (H1031)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Creatine (H1031)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	22 651
Type B	0	80	0	20 674
Type C	0	9	0	1878

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9310 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8817 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7481 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Creatine (H1031)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Vitamin complex (H1100)	46.24	—
Flavour orange (H1405)	49.00	—
Antibiosis forte complex (H1115)	55.10	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Creatine (H1031)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80440	80440	0.00	46.86
80441	80441	0.00	53.76
80627	80627	0.00	44.06
80628	80628	0.00	49.50

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Curcumin and piperine (H1014)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80034-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Curcumin and piperine (H1014)	3	3	8

Second-stage model

For differentiation of the substance/substance group *Curcumin and piperine (H1014)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Curcumin and pip...	17000258	80883	40	from supplier

Validation samples

A total of 45 492 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 *Curcumin and piperine (H1014)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 711 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Curcumin and piperine (H1014)*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Curcumin and piperine (H1014)	16000369	80796	40
Hepart	Curcumin and piperine (H1014)	18001688	81128	40
Hepart	Curcumin and piperine (H1014)	18001687	81129	40

- 20 634 spectra from a total of 444 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 21 spectra from 8 *Apo-Ident* customers from 11 batches from the substance/substance group *Curcumin and piperine (H1014)*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Curcumin and piperine (H1014)	1017	1
Hepart	Curcumin and piperine (H1014)	17000259/0	1
Hepart	Curcumin and piperine (H1014)	180016870	1
Hepart AG	Curcumin and piperine (H1014)	1534002201	1
Hepart AG	Curcumin and piperine (H1014)	13901	3
Hepart AG	Curcumin and piperine (H1014)	72001	2
Hepart AG	Curcumin and piperine (H1014)	15001589	1
Hepart AG, CH-8280 Kreu...	Curcumin and piperine (H1014)	13901	1
Unisan	Curcumin and piperine (H1014)	13901	1
Unisan	Curcumin and piperine (H1014)	72001	4
Unisan	Curcumin and piperine (H1014)	14001017	1
Unisan	Curcumin and piperine (H1014)	14001017/6	1
Unisan	Curcumin and piperine (H1014)	17000259	1
Hepart	Curcumin and piperine (H1014)	17000258	2

- 1866 spectra from 19 *Apo-Ident* customers from a total of 848 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 *Curcumin and piperine (H1014)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Curcumin and piperine (H1014)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	22 711
Type B	0	120	0	20 634
Type C	0	8	13	1866

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9312 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.8811 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7293 %)	38.0952 % (> 23.8095 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Curcumin and piperine (H1014)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	35.63	—
Betaine hydrochloride (H1119)	80.88	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Curcumin and piperine (H1014)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80883	80883	0.00	35.63
80475	80475	0.00	37.75
80705	80705	0.00	37.58

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Detox complex (H1111) / Juniper (H1112)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80702-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Detox complex (H1118)	2	2	0
Juniper (H1112)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Detox complex (H1111) / Juniper (H1112)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Detox complex (H1111) / Juniper (H1112)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Detox complex (H...	16001075 (MM)	80894	40	from supplier
Hepart	Detox complex (H...	16001076	80895	40	from supplier
Hepart	Juniper (H1112)	15001004	80702	60	from supplier
Hepart	Juniper (H1112)	16000683	80891	40	from supplier

Validation samples

A total of 45 492 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 *Detox complex (H1111) / Juniper (H1112)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 671 spectra from a total of 436 batches from further 116 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Detox complex (H1111) / Juniper (H1112)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

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

- 20 674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Detox complex (H1111) / Juniper (H1112)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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
Type A	0	180	0	22 671
Type B	0	80	0	20 674
Type C	0	0	0	1887

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
Type A	100.0000 % (> 99.9311 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8817 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Detox complex (H1111) / Juniper (H1112)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Baobab (H1410)	19.39	—
Garcinia cambogia (H1017)	19.44	—
Ginseng (H1018)	19.90	—
Saffron style (H1434)	22.71	—
Saffron flowers (H1435)	24.52	—
Antioxidants NAT complex (H1004)	24.89	—
Artichoke extract (H1440)	26.75	—
Lycopene (H1058)	27.65	—
Calcium (H1008)	29.05	—
Vitamin K2 (75µg Mono) (H1108)	32.14	—
Silicium (H1070)	33.39	—
Gentian extract (H1438)	34.02	—
Boron (H1005)	34.21	—
Marshmallow extract (H1439)	35.05	—
PET coenzyme Q10 (H0022)	36.27	—
Orthovimin Neutral Complex (H1403)	36.59	—
Vitamin E NAT (H1107)	39.14	—
Glutathione (H1020)	39.55	—
Flavour orange (H1405)	40.78	—
Enzyme complex (H1118)	41.80	—
Vitamin B1 (H1101)	44.06	—
Coenzyme Q10 (H1013)	45.28	—
Ginger extract (H1437)	45.31	—
Zinc (H1110)	46.46	—
Iron (H1015)	46.67	—
Camu camu (H1411)	49.17	—
Orthocolon complex (H1800)	49.64	—
Cabbage extract (H1121)	50.39	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Detox complex (H1111) / Juniper (H1112)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80894	80894	0.00	20.15
80895	80895	0.00	21.56
80891	80891	0.00	32.66
80702	80702	0.00	24.52

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Enzyme complex (H1118)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80665-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Enzyme complex (H1118)

Special notes

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

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Enzyme complex (H1118)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Enzyme complex (H1118)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Enzyme complex (...)	15001134	80665	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 60 spectra of 1 reference samples from the substance/substance group *Enzyme complex (H1118)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 791 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Enzyme complex (H1118)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Enzyme complex (H1118)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Enzyme complex (H1118)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Enzyme complex (H1118)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	60	0	22 791
Type B	0	0	0	20 753
Type C	0	0	0	1887

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9321 %)	100.0000 % (> 90.0000 %)
Type B	100.0000 % (> 99.8825 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Enzyme complex (H1118)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ginseng (H1018)	14.11	—
Saffron flowers (H1435)	20.45	—

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Substanz	Distance in main model	Distance in second-stage model
Orthovimin Neutral Complex (H1403)	22.66	—
Psyllium husks (H1432)	24.40	—
Marshmallow extract (H1439)	24.50	—
Antioxidants NAT complex (H1004)	32.17	—
Folic acid (H1016)	35.36	—
Lycopene (H1058)	36.81	—
Artichoke extract (H1440)	37.07	—
Garcinia cambogia (H1017)	37.52	—
Zinc (H1110)	38.01	—
Vitamin B12 (H1102)	38.08	—
Vitamin E NAT (H1107)	38.21	—
Coenzyme Q10 (H1013)	38.81	—
Vitamin K2 (75µg Mono) (H1108)	40.21	—
Gentian extract (H1438)	40.98	—
Vitamin B1 (H1101)	41.33	—
Juniper (H1112)	41.76	—
Ginger extract (H1437)	44.19	—
Biotin (H1007)	45.04	—
Calcium (H1008)	47.21	—
Detox complex (H1118)	47.42	—
Iron (H1015)	48.78	—
Konjac (H1426)	49.81	—
Saffron style (H1434)	49.96	—
Baobab (H1410)	50.02	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Enzyme complex (H1118)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80665	80665	0.00	20.45

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group	Garcinia cambogia (H1017)
Substance class	HCK - nutritional supplements (Hepart)
Report date	25/06/2020
Report number	80037-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Garcinia cambogia (H1017)	5	2	5

Second-stage model

For differentiation of the substance/substance group *Garcinia cambogia* (H1017) the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Garcinia cambogi...	15001048 (F2)	80660	60	from supplier
Hepart	Garcinia cambogi...	17000873	80956	40	from supplier
Hepart	Garcinia cambogi...	18001849	81150	40	from supplier

Validation samples

A total of 45 492 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 *Garcinia cambogia* (H1017). These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 22 571 spectra from a total of 435 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 2 reference samples from the substance/substance group *Garcinia cambogia* (H1017).
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Garcinia cambogia (H1017)	15001048	80661	60
Hepart	Garcinia cambogia (H1017)	15001048(B1)	80662	60

- 20 634 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 8 spectra from 4 *Apo-Ident* customers from 6 batches from the substance/substance group *Garcinia cambogia (H1017)*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Garcinia cambogia (H1017)	16001252/1	1
Hepart AG	Garcinia cambogia (H1017)	1221007401	1
Hepart AG	Garcinia cambogia (H1017)	7401	2
Unisan	Garcinia cambogia (H1017)	1221007401	1
Unisan	Garcinia cambogia (H1017)	56601	1
Unisan	Garcinia cambogia (H1017)	16001252/0	1
Unisan	Garcinia cambogia (H1017)	17000873	1

- 1879 spectra from 19 *Apo-Ident* customers from a total of 853 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 *Garcinia cambogia (H1017)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Garcinia cambogia (H1017)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	22 571
Type B	0	120	0	20 634
Type C	0	4	4	1879

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9309 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.8811 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7522 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Garcinia cambogia* (H1017) in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pathogene complex (H1803)	18.53	—
Antioxidants NAT complex (H1004)	20.15	—
Camu camu (H1411)	23.47	—
Copper (H1032)	24.18	—
Baobab (H1410)	25.07	—
Calcium (H1008)	25.95	—
Seabuckthorn organic (H1412)	26.70	—
Juniper (H1112)	26.83	—
Iron (H1015)	28.86	—
Orthovimin Neutral Complex (H1403)	29.89	—
Silicium (H1070)	32.57	—
Detox complex (H1118)	35.01	—
Coenzyme Q10 (H1013)	35.44	—
Saffron style (H1434)	35.56	—
Psyllium husks (H1432)	37.67	—
Histamine block complex (H1117)	38.14	—
Isoflavones (H1025)	39.48	—
Orthocolon complex (H1800)	40.09	—
Ginkgo (H1024)	40.54	—
Magnesium (H1060)	40.89	—
Glutathione (H1020)	41.24	—
Betaine hydrochloride (H1119)	42.59	—
Vitamin E NAT (H1107)	43.31	—
Vitamin B1 (H1101)	43.43	—
Ginseng (H1018)	43.86	—
PET joints (H1501)	44.95	—
Silymarin (H1071)	45.50	—
Trace elements JK (H1080)	46.48	—
PET basis (H1503)	47.16	—
Boron (H1005)	48.34	—
Marshmallow extract (H1439)	49.81	—
Artichoke extract (H1440)	49.88	—
Broccoli (H1415)	50.77	—

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

stance/substance group *Garcinia cambogia* (H1017) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80346	80346	0.00	43.36
80477	80477	0.00	37.67
80490	80490	0.00	18.53
80660	80660	0.00	21.86
81150	81150	0.00	31.65
80956	80956	0.00	24.82

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Ginger extract (H1437)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81089-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ginger extract (H1437)

Special notes

When selecting the *Ginger extract (H1437)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ginger extract (H1437)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Ginger extract (H1437)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ginger extract (H1437)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Ginger extract (...)	18001115	81089	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Ginger extract (H1437)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Ginger extract (H1437)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Ginger extract (H1437)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ginger extract (H1437)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ginger extract (H1437)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Ginger extract (H1437)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ginger extract (H1437)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ginseng (H1018)	12.51	—
Saffron style (H1434)	14.25	—

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Substanz	Distance in main model	Distance in second-stage model
Vitamin K2 (75µg Mono) (H1108)	21.57	—
Coenzyme Q10 (H1013)	24.81	—
Lycopene (H1058)	25.21	—
Gentian extract (H1438)	26.14	—
Biotin (H1007)	29.48	—
Marshmallow extract (H1439)	29.95	—
Vitamin E NAT (H1107)	30.09	—
PET coenzyme Q10 (H0022)	30.48	—
Boron (H1005)	32.66	—
Zinc (H1110)	32.89	—
Folic acid (H1016)	35.42	—
Enzyme complex (H1118)	35.47	—
Chromium (H1012)	39.03	—
Acacia gum (H1001)	40.93	—
Psyllium husks (H1432)	41.08	—
Orthovimin Neutral Complex (H1403)	42.68	—
Silicium (H1070)	43.10	—
Vitamin B1 (H1101)	43.47	—
Baobab (H1410)	43.65	—
Antioxidants NAT complex (H1004)	43.73	—
Vitamin B12 (H1102)	45.29	—
Flavour orange (H1405)	46.30	—
Juniper (H1112)	46.46	—
Selenium yeast (H1068)	46.63	—
Saffron flowers (H1435)	46.76	—
Detox complex (H1118)	46.96	—
Calcium (H1008)	50.80	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ginger extract (H1437)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81089	81089	0.00	14.25

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Ginkgo (H1024)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80391-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ginkgo (H1024)	7	2	3

Second-stage model

For differentiation of the substance/substance group *Ginkgo (H1024)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Ginkgo (H1024)	15001038 (F3)	80657	60	from supplier
Hepart	Ginkgo (H1024)	15001038	80658	60	from supplier
Hepart	Ginkgo (H1024)	17001832	81005	40	from supplier
Hepart	Ginkgo (H1024)	18001386	81133	40	from supplier
Hepart	Ginkgo (H1024)	19002623	81215	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 420 spectra of 8 reference samples from the substance/substance group *Ginkgo (H1024)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 22 431 spectra from a total of 433 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 100 spectra of 2 reference samples from the substance/substance group *Ginkgo (H1024)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Ginkgo (H1024)	15001038 (F1)	80659	60
Hepart	Ginkgo (H1024)	18001110	81072	40

- 20 654 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 6 spectra from 4 *Apo-Ident* customers from 5 batches from the substance/substance group *Ginkgo (H1024)*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Ginkgo (H1024)	150010391	1
Hepart	Ginkgo (H1024)	18001110	1
Hepart AG	Ginkgo (H1024)	15001038	1
Hepart AG	Ginkgo (H1024)	15001039/1	1
Unisan	Ginkgo (H1024)	15001039/1	1
Hepart	Ginkgo (H1024)	17001832	1

- 1881 spectra from 19 *Apo-Ident* customers from a total of 854 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 *Ginkgo (H1024)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ginkgo (H1024)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	420	0	22 431
Type B	0	100	0	20 654
Type C	0	6	0	1881

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9308 %)	100.0000 % (> 98.5714 %)
Type B	100.0000 % (> 99.8813 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.7646 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ginkgo* (*H1024*) in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	10.39	—
Silymarin (H1071)	15.81	—
Calcium (H1008)	17.58	—
Rhodiola (H1064)	17.74	—
Carnitine (L-) (H1038)	21.28	—
Coenzyme Q10 (H1013)	23.96	—
PET basis (H1503)	23.98	—
Seabuckthorn organic (H1412)	24.13	—
Broccoli (H1415)	26.85	—
Green coffee extract (H1433)	28.59	—
Flavour orange (H1405)	29.88	—
Garcinia cambogia (H1017)	30.68	—
Pathogene complex (H1803)	30.69	—
PET immune system (H1502)	30.87	—
Vitamin C (H1104)	32.98	—
Betaine hydrochloride (H1119)	33.60	—
Vitamins BAG (H1090)	39.94	—
Yeast organic (H1007)	40.29	—
PET well-aging (H1500)	40.75	—
Vitamin B1 (H1101)	40.97	—
Antibiosis forte complex (H1115)	41.84	—
PET joints (H1501)	43.42	—
Orthocolon complex (H1800)	43.84	—
Copper (H1032)	43.95	—
Camu camu (H1411)	46.01	—
Iron (H1015)	47.47	—
Catechin extract (H1010)	48.61	—
Histamine block complex (H1117)	48.83	—
OPC Grape seed (H1066)	50.98	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ginkgo* (*H1024*) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81133	81133	0.00	25.21
81215	81215	0.00	23.69
80656	80656	0.00	14.57
81005	81005	0.00	11.92
80391	80391	0.00	29.31
80476	80476	0.00	24.04
80657	80657	0.00	23.98
80658	80658	0.00	29.79

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Glucosamine sulfate (H1019)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80094-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Glucosamine sulfate (H1019)	3	6	8

Second-stage model

For differentiation of the substance/substance group *Glucosamine sulfate (H1019)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Glucosamine sulfate (H1019)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 671 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Glucosamine sulfate (H1019)*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
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
Hepart	Glucosamine sulfate (H1019)	19000775	81181	40
Hepart	Glucosamine sulfate (H1019)	20000494	81261	40

- 20 514 spectra from a total of 441 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 17 spectra from 9 *Apo-Ident* customers from 9 batches from the substance/substance group *Glucosamine sulfate (H1019)*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Glucosamine sulfate (H1019)	17000073	1
Hepart	Glucosamine sulfate (H1019)	34001	1
Hepart	Glucosamine sulfate (H1019)	17001245	2
Hepart AG	Glucosamine sulfate (H1019)	38001	2
Hepart AG	Glucosamine sulfate (H1019)	1822038001	1
Unisan	Glucosamine sulfate (H1019)	1823954901	2
Unisan	Glucosamine sulfate (H1019)	38001	2
Unisan	Glucosamine sulfate (H1019)	75401	1
Unisan	Glucosamine sulfate (H1019)	17000073/0	1
Unisan	Glucosamine sulfate (H1019)	16000948	1
UNISAN	Glucosamine sulfate (H1019)	34001	1
Unisan GmbH, 78465 Kons...	Glucosamine sulfate (H1019)	38001	1
Unisan/Hepart AG	Glucosamine sulfate (H1019)	38001	1

- 1870 spectra from 19 *Apo-Ident* customers from a total of 850 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 *Glucosamine sulfate (H1019)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glucosamine sulfate (H1019)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	22 671
Type B	0	200	40	20 514
Type C	0	9	8	1870

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9311 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8805 %)	83.3333 % (> 82.0833 %)
Type C	100.0000 % (> 98.7326 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glucosamine sulfate (H1019)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Flavour orange (H1405)	33.45	—
Creatine (H1031)	54.10	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glucosamine sulfate (H1019)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80402	80402	0.00	50.69
80812	80812	0.00	70.30
80319	80319	0.00	86.85
80362	80362	0.00	83.74

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

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Glutamine (L-) (H1043)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80089-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Glutamine (L-) (H1043)	6	6	16

Second-stage model

For differentiation of the substance/substance group *Glutamine (L-) (H1043)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Glutamine (L-) (...)	061501	80336	40	from supplier
Hepart	Glutamine (L-) (...)	15000017	80551	60	from supplier
Hepart	Glutamine (L-) (...)	15000018	80552	60	from supplier
Hepart	Glutamine (L-) (...)	16000940	80802	40	from supplier
Hepart	Glutamine (L-) (...)	20001001	81263	40	from supplier
Hepart	Glutamine (L-) (...)	20001021	81264	40	from supplier

Validation samples

A total of 45 492 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 *Glutamine (L-) (H1043)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 22 571 spectra from a total of 434 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Glutamine (L-) (H1043)*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
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
Hepart	Glutamine (L-) (H1043)	19000531	81190	40
Hepart	Glutamine (L-) (H1043)	19000650/0	81191	40

- 20514 spectra from a total of 441 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 42 spectra from 10 *Apo-Ident* customers from 20 batches from the substance/substance group *Glutamine (L-) (H1043)*.
- Among them are spectra of independent samples from 16 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Glutamine (L-) (H1043)	16000941	2
Hepart	Glutamine (L-) (H1043)	16000942	2
Hepart	Glutamine (L-) (H1043)	17000901/1	1
Hepart	Glutamine (L-) (H1043)	17000901	1
Hepart / Unisan	Glutamine (L-) (H1043)	16000942	1
Hepart AG	Glutamine (L-) (H1043)	15000017/1	1
Hepart AG	Glutamine (L-) (H1043)	160009420	1
Hepart AG	Glutamine (L-) (H1043)	17000901/0	1
Unisan	Glutamine (L-) (H1043)	1814026901	5
Unisan	Glutamine (L-) (H1043)	26903	2
Unisan	Glutamine (L-) (H1043)	61501	8
Unisan	Glutamine (L-) (H1043)	26904	1
Unisan	Glutamine (L-) (H1043)	61501/4	1
Unisan	Glutamine (L-) (H1043)	15000017/0	1
Unisan	Glutamine (L-) (H1043)	15000017	1
Unisan	Glutamine (L-) (H1043)	15000018/0	1
Unisan	Glutamine (L-) (H1043)	15000018	1
Unisan	Glutamine (L-) (H1043)	16000940/0	2
Unisan	Glutamine (L-) (H1043)	16000940	1
Unisan	Glutamine (L-) (H1043)	16000941	1
Unisan	Glutamine (L-) (H1043)	16000942	1
UNISAN	Glutamine (L-) (H1043)	61501	2
UNISAN	Glutamine (L-) (H1043)	15000017/0	1
Unisan GmbH, 78465 Kons...	Glutamine (L-) (H1043)	26904	1
Unisan/Hepart AG	Glutamine (L-) (H1043)	26901	1
Unisan	Glutamine (L-) (H1043)		1

- 1845 spectra from 19 *Apo-Ident* customers from a total of 840 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 *Glutamine (L-) (H1043)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glutamine (L-) (H1043)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	22 571
Type B	0	240	0	20 514
Type C	0	39	3	1845

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 % (> 99.9309 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.8805 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 98.7222 %)	92.8571 % (> 85.7143 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glutamine (L-) (H1043)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Leaky gut complex (H1802)	35.04	—
Pumpkin protein (H1429)	36.14	—
PET skin and hair (H1504)	38.98	—
Antioxidants NAT complex (H1004)	39.66	—
PET joints (H1501)	40.00	—
Antibiosis forte complex (H1115)	40.46	—
Vitamin E NAT (H1107)	43.65	—
PET basis (H1503)	46.86	—
Aminomix NAC (H1002)	49.60	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glutamine (L-) (H1043)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80551	80551	0.00	40.46
80552	80552	0.00	38.98
80802	80802	0.00	44.03
81263	81263	0.00	44.90
81264	81264	0.00	42.85
80336	80336	0.00	35.04

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Glycine (H1021)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80168-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Glycine (H1021)	7	7	9

Second-stage model

For differentiation of the substance/substance group *Glycine (H1021)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Glycine (H1021)	16000239	80764	60	from supplier
Hepart	Glycine (H1021)	16000238	80765	60	from supplier
Hepart	Glycine (H1021)	16000933	80805	40	from supplier
Hepart	Glycine (H1021)	18000449	81027	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 7 reference samples from the substance/substance group *Glycine (H1021)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 22 511 spectra from a total of 433 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 300 spectra of 7 reference samples from the substance/substance group *Glycine (H1021)*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Glycine (H1021)	14001731	80495	60
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
Hepart	Glycine (H1021)	19001877	81216	40
Hepart	Glycine (H1021)	19001237	81217	40

- 20 454 spectra from a total of 440 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 19 spectra from 8 *Apo-Ident* customers from 11 batches from the substance/substance group *Glycine (H1021)*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Glycine (H1021)	16000239/0	1
Hepart	Glycine (H1021)	17001660/0	1
Hepart AG	Glycine (H1021)	1803028101	1
Hepart AG	Glycine (H1021)	28101	3
Hepart AG	Glycine (H1021)	75501	1
Hepart AG	Glycine (H1021)	14001730/2	1
Hepart AG	Glycine (H1021)	16000239/0	1
Hepart AG	Glycine (H1021)	17001660/1	1
Hepart AG	Glycine (H1021)	18000449/0	1
Hepart AG, CH-8280 Kreu...	Glycine (H1021)	28101	1
Unisan	Glycine (H1021)	28101	2
Unisan	Glycine (H1021)	14001730	1
Unisan	Glycine (H1021)	16000933	2
Unisan/Hepart AG	Glycine (H1021)	28101	1
HCK	Glycine (H1021)		1

- 1868 spectra from 19 *Apo-Ident* customers from a total of 848 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 *Glycine (H1021)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glycine (H1021)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following

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

	False positive	True positive	False negative	True negative
Type A	0	340	0	22 511
Type B	0	300	0	20 454
Type C	0	17	2	1868

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9308 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.8804 %)	100.0000 % (> 98.0000 %)
Type C	100.0000 % (> 98.7308 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glycine (H1021)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Threonine (L-) (H1052)	72.70	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glycine (H1021)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80494	80494	0.00	81.73
80348	80348	0.00	88.34
80805	80805	0.00	85.70
80436	80436	0.00	91.67
81027	81027	0.00	88.06

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80764	80764	0.00	92.06
80765	80765	0.00	86.42

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Green coffee extract (H1433)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81037-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Green coffee extract (H1433)

Special notes

When selecting the *Green coffee extract (H1433)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Green coffee extract (H1433)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Green coffee extract (H1433)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Green coffee extract (H1433)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Green coffee ext...	18000368	81037	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Green coffee extract (H1433)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Green coffee extract (H1433)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Green coffee extract (H1433)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Green coffee extract (H1433)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Green coffee extract (H1433)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Green coffee extract (H1433)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Green coffee extract (H1433)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ginkgo (H1024)	17.46	—
Antioxidants NAT complex (H1004)	27.85	—

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Substanz	Distance in main model	Distance in second-stage model
Carnitine (L-) (H1038)	29.63	—
PET basis (H1503)	32.07	—
Calcium (H1008)	35.65	—
Rhodiola (H1064)	36.02	—
Vitamin C (H1104)	36.62	—
Flavour orange (H1405)	41.04	—
Catechin extract (H1010)	42.43	—
PET immune system (H1502)	43.62	—
Antibiosis forte complex (H1115)	44.12	—
Yeast organic (H1007)	46.70	—
PET well-aging (H1500)	48.33	—
Broccoli (H1415)	51.16	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Green coffee extract (H1433)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81037	81037	0.00	23.57

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group	HCK classification I
Substance class	HCK - nutritional supplements (Hepart)
Report date	25/06/2020
Report number	80331-2020-06-25
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

HCK classification I; Acacia gum (H1001); Biotin (H1007); Chromium (H1012); Folic acid (H1016); Gentian extract (H1438); Ginseng (H1018); Konjac (H1426); Lycopene (H1058); Marshmallow extract (H1439); Saffron flowers (H1435); Selenium (H1067); Selenium yeast (H1068); Vitamin B12 (H1102); Vitamin D3 (H1105); Vitamin K2 (75µg Mono) (H1108)

Special notes

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

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Acacia gum (H1001)	1	0	0
Biotin (H1007)	3	0	0
Chromium (H1012)	2	3	11

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Substance	Type A	Type B	Type C
Folic acid (H1016)	5	3	13
Gentian extract (H1438)	1	0	0
Ginseng (H1018)	5	1	8
Konjac (H1426)	2	1	0
Lycopene (H1058)	3	0	0
Marshmallow extract (H1439)	1	0	0
Saffron flowers (H1435)	2	0	0
Selenium (H1067)	8	5	17
Selenium yeast (H1068)	1	0	0
Vitamin B12 (H1102)	5	2	12
Vitamin D3 (H1105)	5	3	17
Vitamin K2 (75µg Mono) (H1108)	2	0	0

Second-stage model

For differentiation of the substance/substance group *HCK classification I* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Acacia gum (H1001)	16000363/2	81013	40	from supplier
Hepart	Biotin (H1007)	029601	80365	40	from supplier
Hepart	Biotin (H1007)	029601	80385	40	from supplier
Hepart	Biotin (H1007)	15000735	80586	60	from supplier
Hepart	Biotin (H1007)	16001396	80855	40	from supplier
Hepart	Chromium (H1012)	16000520/0	80791	40	from supplier
Hepart	Chromium (H1012)	16000520/4	80792	40	from supplier
Hepart	Folic acid (H1016)	052301	80331	60	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	Folic acid (H1016)	15000125	80553	60	from supplier
Hepart	Folic acid (H1016)	19001346	81207	40	from supplier
Hepart	Gentian extract ...	18001096	81092	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	Ginseng (H1018)	14002047	80534	60	from supplier
Hepart	Ginseng (H1018)	15001047	80663	60	from supplier
Hepart	Ginseng (H1018)	15001047	80780	60	from supplier
Hepart	Konjac (H1426)	17000837	80927	40	from supplier
Hepart	Konjac (H1426)	19000132	81153	40	from supplier
Hepart	Lycopene (H1058)	053501	80335	40	from supplier
Hepart	Lycopene (H1058)	17000619	80913	40	from supplier
Hepart	Lycopene (H1058)	17000619/0	81024	40	from supplier
Hepart	Marshmallow extr...	18001095	81091	40	from supplier
Hepart	Saffron flowers ...	18000806	81056	40	from supplier
Hepart	Saffron flowers ...	19000801	81204	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	Selenium (H1067)	065701	80366	40	from supplier
Hepart	Selenium (H1067)	15000157	80530	60	from supplier
Hepart	Selenium (H1067)	15000158	80531	60	from supplier
Hepart	Selenium (H1067)	15000159	80535	60	from supplier
Hepart	Selenium (H1067)	065501	80706	60	from supplier
Hepart	Selenium (H1067)	16001349	80822	40	from supplier
Hepart	Selenium (H1067)	18000578	81025	40	from supplier
Hepart	Selenium yeast (...)	16001450/1	81014	40	from supplier
Hepart	Vitamin B12 (H11...)	025017	80353	40	from supplier
Hepart	Vitamin B12 (H11...)	15000993	80603	60	from supplier
Hepart	Vitamin B12 (H11...)	15000993 (B1)	80604	60	from supplier
Hepart	Vitamin B12 (H11...)	17000277	80910	40	from supplier
Hepart	Vitamin B12 (H11...)	19001114	81201	40	from supplier
Hepart	Vitamin D3 (H1105)	15000490	80580	60	from supplier
Hepart	Vitamin D3 (H1105)	16000952	80816	40	from supplier
Hepart	Vitamin D3 (H1105)	16001212	80863	40	from supplier
Hepart	Vitamin D3 (H1105)	18001951	81130	40	from supplier
Hepart	Vitamin D3 (H1105)	19001097	81206	40	from supplier
Hepart	Vitamin K2 (75µg...)	16001559	80874	40	from supplier
Hepart	Vitamin K2 (75µg...)	18001656	81126	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 2320 spectra of 51 reference samples from the substance/substance group *HCK classification I*. These samples are listed above in the *calibration samples* section. The reference samples come from 46 different batches.
- 20 531 spectra from a total of 395 batches from further 103 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this *chemometric model*, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 795 spectra of 20 reference samples from the substance/substance group *HCK classification I*.
- Among them are spectra of independent samples from 18 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Chromium (H1012)	977201	80033	15
Hepart	Chromium (H1012)	16000520/2	80793	40
Hepart	Chromium (H1012)	18002076	81148	40
Hepart	Folic acid (H1016)	16001098	80833	40
Hepart	Folic acid (H1016)	19002382	81223	40
Hepart	Folic acid (H1016)	20000403	81259	40
Hepart	Ginseng (H1018)	17000285	80873	40
Hepart	Konjac (H1426)	17000846	80985	40
Hepart	Selenium (H1067)	16001350	80823	40
Hepart	Selenium (H1067)	16001351	80824	40
Hepart	Selenium (H1067)	18000422	81026	40
Hepart	Selenium (H1067)	18001021	81078	40
Hepart	Selenium (H1067)	18001022	81079	40
Hepart	Vitamin B12 (H1102)	15000993(F2)	80605	60
Hepart	Vitamin B12 (H1102)	17000276	80911	40
Hepart	Vitamin D3 (H1105)	17000874	80959	40
Hepart	Vitamin D3 (H1105)	19001583	81224	40
Hepart	Vitamin D3 (H1105)	20000338	81266	40
Hepart	Ginseng (H1018)	067801	80403	40
Hepart	Ginseng (H1018)	17000285	81103	40

- 19959 spectra from a total of 428 batches from further 85 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 350 spectra from 15 *Apo-Ident* customers from 121 batches from the substance/substance group *HCK classification I*.
- Among them are spectra of independent samples from 103 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Acacia gum (H1001)	1211728201	2
Hepart	Acacia gum (H1001)	728201	2
Hepart AG	Acacia gum (H1001)	728201	1
Hepart AG, CH-8280 Kreu...	Acacia gum (H1001)	1211622002	2
Hepart AG, CH-8280 Kreu...	Acacia gum (H1001)	1211728201	1
Unisan	Acacia gum (H1001)	16000363/0	1
Unisan GmbH, 78465 Kons...	Acacia gum (H1001)	728201	1
Hepart	Biotin (H1007)	14000862/4	2
Hepart AG	Biotin (H1007)	1592029603	3
Hepart AG	Biotin (H1007)	29603	3
Hepart AG	Biotin (H1007)	29601	2
Hepart AG, CH-8280 Kreu...	Biotin (H1007)	1592029603	1
Ichthyol Gesellschaft C...	Biotin (H1007)	1591983601	1
Unisan	Biotin (H1007)	983601	1
Unisan	Biotin (H1007)	29603	3
Unisan	Biotin (H1007)	1591983601	1
Unisan	Biotin (H1007)	29601	2
Unisan	Biotin (H1007)	14000862	2

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Supplier	Substance	Batch	Spectra
Unisan	Biotin (H1007)	14000862/2	2
Unisan	Biotin (H1007)	15000735/0	1
Unisan	Biotin (H1007)	15000735	2
Unisan	Biotin (H1007)	15000735/5	1
Unisan	Biotin (H1007)	16001396	3
Unisan	Biotin (H1007)	16001396/0	1
Falcento	Chromium (H1012)	16000520	4
Hepart	Chromium (H1012)	16000520/3	3
Hepart	Chromium (H1012)	160005203	1
Hepart	Chromium (H1012)	16000520	1
Hepart	Chromium (H1012)	16000520/8	5
Hepart AG	Chromium (H1012)	1582977201	3
Hepart AG	Chromium (H1012)	977201	5
Hepart AG	Chromium (H1012)	H101221	1
Hepart AG	Chromium (H1012)	14000429/4	1
Hepart AG	Chromium (H1012)	16000520/7	4
Hepart AG, CH-8280 Kreu...	Chromium (H1012)	977201	2
Unisan	Chromium (H1012)	1581977201	1
Unisan	Chromium (H1012)	977201	3
Unisan	Chromium (H1012)	1582977201	1
Unisan	Chromium (H1012)	14000429	2
Unisan	Chromium (H1012)	16000520/0	1
UNISAN	Chromium (H1012)	14000429	4
Bombastus	Folic acid (H1016)	1613052301	1
Hepart AG	Folic acid (H1016)	1613030201	4
Hepart AG	Folic acid (H1016)	52301	3
Hepart AG	Folic acid (H1016)	15000125	1
Hepart AG	Folic acid (H1016)	16000931	1
Hepart AG	Folic acid (H1016)	16001098	1
Hepart AG, CH-8280 Kreu...	Folic acid (H1016)	52301	2
Hepart/Unisan	Folic acid (H1016)	15000125/0	1
Unisan	Folic acid (H1016)	30201	7
Unisan	Folic acid (H1016)	1613977701	2
Unisan	Folic acid (H1016)	977701	2
Unisan	Folic acid (H1016)	1613030201	2
Unisan	Folic acid (H1016)	52301	5
Unisan	Folic acid (H1016)	H101621	1
Unisan	Folic acid (H1016)	14000638	3
Unisan	Folic acid (H1016)	14000639/1	2
Unisan	Folic acid (H1016)	16000931	2
Unisan	Folic acid (H1016)	16001098	3
Unisan	Folic acid (H1016)	18000337	2
Unisan Gmbh, 78465 Kons...	Folic acid (H1016)	1611030201	1
Unisan Gmbh, 78465 Kons...	Folic acid (H1016)	30201	1
Unisan/Hepart AG	Folic acid (H1016)	30201	1
Euro OTC	Ginseng (H1018)	15001047/0	1
HCK	Ginseng (H1018)	14002047	1
HCK	Ginseng (H1018)	17000285	2
Hepart	Ginseng (H1018)	18000794/0	1
Hepart AG	Ginseng (H1018)	38802	1
Hepart AG	Ginseng (H1018)	15001047	1
Hepart AG	Ginseng (H1018)	17000285/0	1
Unisan	Ginseng (H1018)	38802	2
Unisan	Ginseng (H1018)	14002047/1	1
Unisan	Ginseng (H1018)	67801	2
Unisan	Ginseng (H1018)	14002047/2	1
UNISAN	Ginseng (H1018)	67801	1
Unisan/Hepart AG	Ginseng (H1018)	38802	1
HCK	Lycopene (H1058)	17000619/0	1
HCK	Lycopene (H1058)	17000619	1

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Supplier	Substance	Batch	Spectra
Hepart AG	Lycopene (H1058)	47301	1
Hepart AG	Lycopene (H1058)	53501	1
Unisan	Lycopene (H1058)	4501	4
Unisan	Lycopene (H1058)	47301	2
Unisan	Lycopene (H1058)	53501	7
Unisan	Lycopene (H1058)	H105811	1
Unisan	Lycopene (H1058)	14000803	1
Unisan	Lycopene (H1058)	53501/7	1
Unisan	Lycopene (H1058)	17000619/0	1
Unisan/Hepart AG	Lycopene (H1058)	47301	1
Bombastus	Selenium (H1067)	1144010201	1
Hedinger	Selenium (H1067)	10201	9
Hepart	Selenium (H1067)	15000158/1	1
Hepart	Selenium (H1067)	160013497/0	1
Hepart	Selenium (H1067)	16001350	1
Hepart AG	Selenium (H1067)	1144010201	3
Hepart AG	Selenium (H1067)	65701	1
Hepart AG	Selenium (H1067)	933301	1
Hepart AG	Selenium (H1067)	15000157/1	1
Hepart AG	Selenium (H1067)	15000158/0	1
Hepart AG	Selenium (H1067)	16001349/0	2
Hepart AG	Selenium (H1067)	16001350/0	15
Hepart AG, CH-8280 Kreu...	Selenium (H1067)	1144010201	1
Hepart AG, CH-8280 Kreu...	Selenium (H1067)	10201	1
Unisan	Selenium (H1067)	1144010201	1
Unisan	Selenium (H1067)	10201	10
Unisan	Selenium (H1067)	1144933301	1
Unisan	Selenium (H1067)	65701	4
Unisan	Selenium (H1067)	65601	3
Unisan	Selenium (H1067)	65501	1
Unisan	Selenium (H1067)	65601/1	1
Unisan	Selenium (H1067)	65601/2	1
Unisan	Selenium (H1067)	65501/2	1
Unisan	Selenium (H1067)	15000157	3
Unisan	Selenium (H1067)	15000158	1
Unisan	Selenium (H1067)	15000158/0	3
Unisan	Selenium (H1067)	15000159	1
Unisan	Selenium (H1067)	16001349	1
UNISAN	Selenium (H1067)	65601	3
UNISAN	Selenium (H1067)	65501	1
Hepart	Selenium yeast (H1068)	71901	2
Unisan	Selenium yeast (H1068)	9001	1
Unisan	Selenium yeast (H1068)	25709	1
Unisan	Selenium yeast (H1068)	16001450/0	1
HCK	Vitamin B12 (H1102)	15000993/0	1
Hepart	Vitamin B12 (H1102)	17000276	1
Hepart AG	Vitamin B12 (H1102)	1064026401	1
Hepart AG	Vitamin B12 (H1102)	1064025017	1
Hepart AG	Vitamin B12 (H1102)	25017	4
Hepart AG	Vitamin B12 (H1102)	15000993/0	1
Hepart AG	Vitamin B12 (H1102)	17000276/0	1
Hepart AG, CH-8280 Kreu...	Vitamin B12 (H1102)	1064026401	1
Unisan	Vitamin B12 (H1102)	1061025017	1
Unisan	Vitamin B12 (H1102)	1064025017	3
Unisan	Vitamin B12 (H1102)	26401	1
Unisan	Vitamin B12 (H1102)	25017	5
Unisan	Vitamin B12 (H1102)	3441377	1
Unisan	Vitamin B12 (H1102)	75301	5
Unisan	Vitamin B12 (H1102)	75301/2	1
Unisan	Vitamin B12 (H1102)	15000993	4

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Supplier	Substance	Batch	Spectra
Unisan	Vitamin B12 (H1102)	15000993/3	1
Unisan	Vitamin B12 (H1102)	17000276	2
Fagron	Vitamin D3 (H1105)	63701	1
HCK	Vitamin D3 (H1105)	8101	1
Hepart	Vitamin D3 (H1105)	16001212/0	1
Hepart	Vitamin D3 (H1105)	17000874	2
Hepart AG	Vitamin D3 (H1105)	1335008101	1
Hepart AG	Vitamin D3 (H1105)	8101	1
Hepart AG	Vitamin D3 (H1105)	64801	4
Hepart AG	Vitamin D3 (H1105)	63701	3
Hepart AG	Vitamin D3 (H1105)	14000481	3
Hepart AG	Vitamin D3 (H1105)	15000490/2	1
Hepart AG	Vitamin D3 (H1105)	16000952/1	1
Hepart AG, CH-8280 Kreu...	Vitamin D3 (H1105)	1336008101	2
Hepart AG, CH-8280 Kreu...	Vitamin D3 (H1105)	64801	1
Unisan	Vitamin D3 (H1105)	8101	7
Unisan	Vitamin D3 (H1105)	1335959601	1
Unisan	Vitamin D3 (H1105)	1335008108	1
Unisan	Vitamin D3 (H1105)	1335008101	2
Unisan	Vitamin D3 (H1105)	64801	5
Unisan	Vitamin D3 (H1105)	63701	4
Unisan	Vitamin D3 (H1105)	14000481	1
Unisan	Vitamin D3 (H1105)	14000481/2	3
Unisan	Vitamin D3 (H1105)	15000490/0	2
Unisan	Vitamin D3 (H1105)	15000490	4
Unisan	Vitamin D3 (H1105)	15000490/5	1
Unisan	Vitamin D3 (H1105)	16000952	2
Unisan	Vitamin D3 (H1105)	16001212/1	1
Unisan	Vitamin D3 (H1105)	16001212	3
UNISAN	Vitamin D3 (H1105)	63601	1
Unisan Gmbh, 78465 Kons...	Vitamin D3 (H1105)	63701	1
Unisan/Hepart	Vitamin D3 (H1105)	15000490/5	1
unisan	Chromium (H1012)		2
Hepart	Lycopene (H1058)	17000619	1
Hepart	Selenium (H1067)	15000158	1

- 1537 spectra from 19 *Apo-Ident* customers from a total of 739 batches from a further 53 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	2320	0	20 531
Type B	0	788	7	19 862
Type C	0	327	23	1536

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9306 %)	100.0000 % (> 99.7414 %)
Type B	100.0000 % (> 99.8802 %)	99.1195 % (> 98.7421 %)
Type C	100.0000 % (> 98.8384 %)	93.4286 % (> 92.5714 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *HCK classification I* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
PET coenzyme Q10 (H0022)	11.25	—
Enzyme complex (H1118)	14.03	—
Flavour orange (H1405)	14.46	—
Saffron style (H1434)	15.86	—
Vitamin E NAT (H1107)	19.17	—
Orthovimin Neutral Complex (H1403)	19.29	—
Juniper (H1112)	19.36	—
Detox complex (H1118)	19.67	—
Psyllium husks (H1432)	20.80	—
Zinc (H1110)	20.94	—
Vitamin B1 (H1101)	22.35	—
Ginger extract (H1437)	22.83	—
Coenzyme Q10 (H1013)	25.11	—
Antioxidants NAT complex (H1004)	26.27	—
Garcinia cambogia (H1017)	27.54	—
Baobab (H1410)	28.99	—
Silicium (H1070)	30.50	—
Boron (H1005)	31.04	—
Calcium (H1008)	32.06	—
Artichoke extract (H1440)	35.27	—
Iron (H1015)	38.62	—
Camu camu (H1411)	39.32	—
Trace elements BAG (H1078)	40.96	—
Glutathione (H1020)	41.94	—
Seabuckthorn organic (H1412)	47.52	—
Cabbage extract (H1121)	49.80	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81014	81014	0.00	26.39
81024	81024	0.00	25.11
81153	81153	0.00	20.80
80365	80365	0.00	31.71
80586	80586	0.00	27.89
80335	80335	0.00	22.68
81092	81092	0.00	20.28
81056	81056	0.00	14.03
80791	80791	0.00	36.11
80792	80792	0.00	32.93
81206	81206	0.00	40.80
80913	80913	0.00	29.60
80855	80855	0.00	31.53
81091	81091	0.00	15.86
81207	81207	0.00	35.57
80535	80535	0.00	29.69
80456	80456	0.00	22.39
80534	80534	0.00	11.25
80442	80442	0.00	26.23
80663	80663	0.00	23.85
80553	80553	0.00	29.94
80780	80780	0.00	21.83
81126	81126	0.00	20.44
80874	80874	0.00	23.18
81013	81013	0.00	37.38
80580	80580	0.00	37.16
80927	80927	0.00	28.60
80816	80816	0.00	38.19
81130	81130	0.00	36.89
80863	80863	0.00	38.45
80910	80910	0.00	37.45
80455	80455	0.00	16.46
80530	80530	0.00	35.80
81025	81025	0.00	37.97
80331	80331	0.00	29.49
81204	81204	0.00	19.36
80361	80361	0.00	50.99
80443	80443	0.00	31.80
80364	80364	0.00	53.59
80449	80449	0.00	26.85
80366	80366	0.00	53.12
80451	80451	0.00	27.20
80478	80478	0.00	25.83
80531	80531	0.00	37.31
80353	80353	0.00	26.54
80706	80706	0.00	45.19

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80603	80603	0.00	29.14
80822	80822	0.00	32.17
80604	80604	0.00	29.52
81201	81201	0.00	40.51
80385	80385	0.00	22.83

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group	HCK classification II
Substance class	HCK - nutritional supplements (Hepart)
Report date	25/06/2020
Report number	80311-2020-06-25
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

HCK classification II; Acerola (H1413); Antioxidants NAT complex (H1004); Bioflavonoid complex (H1006); Broccoli (H1415); Cabbage extract (H1121); Calcium (H1008); Camu camu (H1411); Cranberry (H1408); Flavour orange (H1405); Glutathione (H1020); Isoflavones (H1025); OPC Grape seed (H1066); Orthocolon complex (H1800); Rhodiola (H1064); Seabuckthorn organic (H1412); Vitamin B1 (H1101); Wild berry (H1417)

Special notes

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

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Acerola (H1413)	1	1	0
Antioxidants NAT complex (H1004)	28	60	50

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Substance	Type A	Type B	Type C
Bioflavonoid complex (H1006)	3	1	12
Broccoli (H1415)	2	0	0
Cabbage extract (H1121)	2	2	0
Calcium (H1008)	23	48	33
Camu camu (H1411)	2	1	0
Cranberry (H1408)	1	1	0
Flavour orange (H1405)	4	3	0
Glutathione (H1020)	2	1	11
Isoflavones (H1025)	3	1	10
OPC Grape seed (H1066)	5	2	8
Orthocolon complex (H1800)	3	2	0
Rhodiola (H1064)	3	2	3
Seabuckthorn organic (H1412)	3	1	0
Vitamin B1 (H1101)	5	2	14
Wild berry (H1417)	1	1	0

Second-stage model

For differentiation of the substance/substance group *HCK classification II* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Acerola (H1413)	18000568/5	81033	40	from supplier
Hepart	Antioxidants NAT...	051901	80311	60	from supplier
Hepart	Antioxidants NAT...	052001	80313	60	from supplier
Hepart	Antioxidants NAT...	052201	80315	50	from supplier
Hepart	Antioxidants NAT...	052101	80317	50	from supplier
Hepart	Antioxidants NAT...	051902	80318	60	from supplier
Hepart	Antioxidants NAT...	067301	80404	40	from supplier
Hepart	Antioxidants NAT...	067201	80405	40	from supplier
Hepart	Antioxidants NAT...	14000044	80419	40	from supplier
Hepart	Antioxidants NAT...	14000965	80469	40	from supplier
Hepart	Antioxidants NAT...	14000964	80473	40	from supplier
Hepart	Antioxidants NAT...	14001849	80504	60	from supplier
Hepart	Antioxidants NAT...	14001850	80505	60	from supplier
Hepart	Antioxidants NAT...	14001851	80506	60	from supplier
Hepart	Antioxidants NAT...	14001846	80507	60	from supplier
Hepart	Antioxidants NAT...	14001848	80508	60	from supplier
Hepart	Antioxidants NAT...	14001847	80509	60	from supplier
Hepart	Antioxidants NAT...	15000875(B1)	80607	60	from supplier
Hepart	Antioxidants NAT...	15000880	80609	60	from supplier
Hepart	Antioxidants NAT...	15000877(B1)	80613	60	from supplier
Hepart	Antioxidants NAT...	15000878(B1)	80616	60	from supplier
Hepart	Antioxidants NAT...	15000874	80618	60	from supplier
Hepart	Antioxidants NAT...	15000874(B1)	80619	60	from supplier
Hepart	Antioxidants NAT...	15000879	80621	60	from supplier
Hepart	Antioxidants NAT...	15000876	80624	60	from supplier
Hepart	Antioxidants NAT...	16000378	80783	40	from supplier
Hepart	Antioxidants NAT...	17000260	80946	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antioxidants NAT...	17000261	80986	40	from supplier
Hepart	Antioxidants NAT...	17001756	80987	40	from supplier
Hepart	Bioflavonoid com...	068101	80342	40	from supplier
Hepart	Bioflavonoid com...	14001675	80492	60	from supplier
Hepart	Bioflavonoid com...	17000256	80878	40	from supplier
Hepart	Broccoli (H1415)	18001334	81098	40	from supplier
Hepart	Broccoli (H1415)	19000456/0	81166	40	from supplier
Hepart	Cabbage extract ...	15001355	80676	60	from supplier
Hepart	Cabbage extract ...	16000657	80819	40	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	Calcium (H1008)	14000106	80422	40	from supplier
Hepart	Calcium (H1008)	14001933	80521	60	from supplier
Hepart	Calcium (H1008)	14001934	80522	60	from supplier
Hepart	Calcium (H1008)	14001937	80525	60	from supplier
Hepart	Calcium (H1008)	14001938	80526	60	from supplier
Hepart	Calcium (H1008)	14001939	80527	60	from supplier
Hepart	Calcium (H1008)	15001669	80707	60	from supplier
Hepart	Calcium (H1008)	15001672(B1)	80709	60	from supplier
Hepart	Calcium (H1008)	15001671	80711	60	from supplier
Hepart	Calcium (H1008)	15001673(MM)	80712	60	from supplier
Hepart	Calcium (H1008)	15001668(B1)	80715	60	from supplier
Hepart	Calcium (H1008)	15001667(MM)	80719	60	from supplier
Hepart	Calcium (H1008)	15001666(MM)	80722	60	from supplier
Hepart	Calcium (H1008)	15001665(B1)	80724	60	from supplier
Hepart	Calcium (H1008)	15001670(B2)	80729	60	from supplier
Hepart	Calcium (H1008)	15001675(B2)	80732	60	from supplier
Hepart	Calcium (H1008)	15001676(MM)	80734	60	from supplier
Hepart	Calcium (H1008)	15001677(B1)	80740	60	from supplier
Hepart	Calcium (H1008)	15001674(B2)	80741	60	from supplier
Hepart	Camu camu (H1411)	18000789/0	81044	40	from supplier
Hepart	Camu camu (H1411)	20000230	81253	40	from supplier
Hepart	Cranberry (H1408)	18000790/0	81034	40	from supplier
Hepart	Flavour orange (...)	16000262	80768	60	from supplier
Hepart	Flavour orange (...)	17000491/0	81016	40	from supplier
Hepart	Flavour orange (...)	19000149	81151	40	from supplier
Hepart	Flavour orange (...)	19000607/0	81170	40	from supplier
Hepart	Glutathione (H10...	074901	80430	40	from supplier
Hepart	Glutathione (H10...	15000478	80583	60	from supplier
Hepart	Isoflavones (H10...	056701	80345	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 (...)	130208-77	80337	40	from supplier
Hepart	OPC Grape seed (...)	068301	80352	40	from supplier
Hepart	OPC Grape seed (...)	070401	80380	40	from supplier
Hepart	OPC Grape seed (...)	070401	80398	40	from supplier
Hepart	OPC Grape seed (...)	16001439	80864	40	from supplier
Hepart	OPC Grape seed (...)	17001805	81001	40	from supplier
Hepart	Orthocolon compl...	18000636	81041	40	from supplier
Hepart	Orthocolon compl...	18000641	81042	40	from supplier
Hepart	Orthocolon compl...	19000177	81202	40	from supplier
Hepart	Rhodiola (H1064)	070501	80390	40	from supplier
Hepart	Rhodiola (H1064)	070501	80632	60	from supplier
Hepart	Rhodiola (H1064)	15001045	80672	60	from supplier
Hepart	Rhodiola (H1064)	18000413	81136	40	from supplier
Hepart	Seabuckthorn org...	16001154	80923	40	from supplier
Hepart	Seabuckthorn org...	18001314	81102	40	from supplier
Hepart	Seabuckthorn org...	19001040/0	81200	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin B1 (H1101)	053301	80316	60	from supplier
Hepart	Vitamin B1 (H1101)	075001	80392	40	from supplier
Hepart	Vitamin B1 (H1101)	075001	80479	40	from supplier
Hepart	Vitamin B1 (H1101)	075001	80529	60	from supplier
Hepart	Vitamin B1 (H1101)	17000914	80953	40	from supplier
Hepart	Vitamin B1 (H1101)	17001075	80980	40	from supplier
Hepart	Vitamin B1 (H1101)	19000685	81183	40	from supplier
Hepart	Wild berry (H1417)	18000975/0	81070	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 4750 spectra of 95 reference samples from the substance/substance group *HCK classification II*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 91 different batches.
- 18 101 spectra from a total of 349 batches from further 101 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 6069 spectra of 130 reference samples from the substance/substance group *HCK classification II*.
- Among them are spectra of independent samples from 129 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Acerola (H1413)	18001312	81097	40
Hepart	Antioxidants NAT complex (H1...	14000043	80424	40
Hepart	Antioxidants NAT complex (H1...	14000042	80428	40
Hepart	Antioxidants NAT complex (H1...	14000961	80470	40
Hepart	Antioxidants NAT complex (H1...	14000962	80471	39
Hepart	Antioxidants NAT complex (H1...	14000963	80472	40
Hepart	Antioxidants NAT complex (H1...	14000966	80474	40
Hepart	Antioxidants NAT complex (H1...	15000875	80606	60
Hepart	Antioxidants NAT complex (H1...	15000875 (F2)	80608	60

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Supplier	Substance	Batch	Sample ID	Spectra
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(F2)	80614	60
Hepart	Antioxidants NAT complex (H1...	15000878	80615	60
Hepart	Antioxidants NAT complex (H1...	15000878(F2)	80617	60
Hepart	Antioxidants NAT complex (H1...	15000874(F2)	80620	60
Hepart	Antioxidants NAT complex (H1...	15000879(B1)	80622	60
Hepart	Antioxidants NAT complex (H1...	15000879(F2)	80623	60
Hepart	Antioxidants NAT complex (H1...	15000876(B1)	80625	60
Hepart	Antioxidants NAT complex (H1...	15000876(F2)	80626	60
Hepart	Antioxidants NAT complex (H1...	16000380	80784	40
Hepart	Antioxidants NAT complex (H1...	16000376	80785	40
Hepart	Antioxidants NAT complex (H1...	16000377	80786	40
Hepart	Antioxidants NAT complex (H1...	16000965	80834	40
Hepart	Antioxidants NAT complex (H1...	16000966	80835	40
Hepart	Antioxidants NAT complex (H1...	16000967	80836	40
Hepart	Antioxidants NAT complex (H1...	16000968	80837	40
Hepart	Antioxidants NAT complex (H1...	16000969	80838	40
Hepart	Antioxidants NAT complex (H1...	16000970	80839	40
Hepart	Antioxidants NAT complex (H1...	16000971	80840	40
Hepart	Antioxidants NAT complex (H1...	16000972	80841	40
Hepart	Antioxidants NAT complex (H1...	16000973	80842	40
Hepart	Antioxidants NAT complex (H1...	16000974	80843	40
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...	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	Antioxidants NAT complex (H1...	18001181	81084	40
Hepart	Antioxidants NAT complex (H1...	18001182	81085	40
Hepart	Antioxidants NAT complex (H1...	18001812	81138	40
Hepart	Antioxidants NAT complex (H1...	18001814	81139	40
Hepart	Antioxidants NAT complex (H1...	18001815	81140	40
Hepart	Antioxidants NAT complex (H1...	18001816	81141	40
Hepart	Antioxidants NAT complex (H1...	18001817	81142	40
Hepart	Antioxidants NAT complex (H1...	18001818	81143	40
Hepart	Antioxidants NAT complex (H1...	19000449	81192	40
Hepart	Antioxidants NAT complex (H1...	19000603	81193	40
Hepart	Antioxidants NAT complex (H1...	19002532	81221	40
Hepart	Antioxidants NAT complex (H1...	20000224	81232	40
Hepart	Antioxidants NAT complex (H1...	20000225	81233	40
Hepart	Antioxidants NAT complex (H1...	20000805	81244	40
Hepart	Antioxidants NAT complex (H1...	20000806	81245	40
Hepart	Antioxidants NAT complex (H1...	20000720	81246	40
Hepart	Antioxidants NAT complex (H1...	20000722	81247	40
Hepart	Bioflavonoid complex (H1006)	17000257	80879	40
Hepart	Cabbage extract (H1121)	15001474	80677	60
Hepart	Cabbage extract (H1121)	18001647	81118	40
Hepart	Calcium (H1008)	055301	80324	60
Hepart	Calcium (H1008)	055401	80325	60
Hepart	Calcium (H1008)	055501	80326	60
Hepart	Calcium (H1008)	14000110	80406	40
Hepart	Calcium (H1008)	14000107	80412	40

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Calcium (H1008)	14000111	80414	40
Hepart	Calcium (H1008)	14000108	80415	40
Hepart	Calcium (H1008)	14000109	80417	30
Hepart	Calcium (H1008)	14001935	80523	60
Hepart	Calcium (H1008)	14001936	80524	60
Hepart	Calcium (H1008)	15001672 (B2)	80708	60
Hepart	Calcium (H1008)	15001672 (MM)	80710	60
Hepart	Calcium (H1008)	15001673 (B2)	80713	60
Hepart	Calcium (H1008)	15001673 (B1)	80714	60
Hepart	Calcium (H1008)	15001668 (MM)	80716	60
Hepart	Calcium (H1008)	15001667 (F2)	80717	60
Hepart	Calcium (H1008)	15001667 (B1)	80718	60
Hepart	Calcium (H1008)	15001666 (B1)	80720	60
Hepart	Calcium (H1008)	15001666 (F2)	80721	60
Hepart	Calcium (H1008)	15001670 (B1)	80723	60
Hepart	Calcium (H1008)	15001670 (MM)	80725	60
Hepart	Calcium (H1008)	15001665 (F2)	80726	60
Hepart	Calcium (H1008)	15001665 (MM)	80727	60
Hepart	Calcium (H1008)	15001668 (F2)	80728	60
Hepart	Calcium (H1008)	15001675 (MM)	80730	60
Hepart	Calcium (H1008)	15001675 (B1)	80731	60
Hepart	Calcium (H1008)	15001675/4	80733	60
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)	15001674 (B1)	80742	60
Hepart	Calcium (H1008)	15001674 (MM)	80743	60
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	Calcium (H1008)	18001413	81105	40
Hepart	Calcium (H1008)	18001414/0	81106	40
Hepart	Calcium (H1008)	18001415/0	81107	40
Hepart	Calcium (H1008)	18001416/0	81108	40
Hepart	Calcium (H1008)	18001417/0	81109	40
Hepart	Calcium (H1008)	18001418	81110	40
Hepart	Camu camu (H1411)	18001526/0	81104	40
Hepart	Cranberry (H1408)	18001311	81083	40
Hepart	Flavour orange (H1405)	18000770	81064	40
Hepart	Flavour orange (H1405)	18001327	81095	40
Hepart	Flavour orange (H1405)	18001422/0	81096	40
Hepart	Glutathione (H1020)	16000938	80813	40
Hepart	Isoflavones (H1025)	15000205	80556	60
Hepart	OPC Grape seed (H1066)	16001439 (B1)	80865	40
Hepart	OPC Grape seed (H1066)	16001439 (F1)	80866	40
Hepart	Orthocolon complex (H1800)	18000640	81043	40
Hepart	Orthocolon complex (H1800)	19000937	81185	40
Hepart	Rhodiola (H1064)	17000278	80915	40
Hepart	Rhodiola (H1064)	20000088	81235	40
Hepart	Seabuckthorn organic (H1412)	16001709	80924	40
Hepart	Vitamin B1 (H1101)	14001112	80480	40
Hepart	Vitamin B1 (H1101)	14001113	80481	40

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Wild berry (H1417)	18001313	81094	40
Hepart	Antioxidants NAT complex (H1...	17000261	80945	40

- 14685 spectra from a total of 317 batches from further 76 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 293 spectra from 19 *Apo-Ident* customers from 155 batches from the substance/substance group *HCK classification II*.
- Among them are spectra of independent samples from 140 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Antioxidants NAT complex (H1...	16000970	1
Hedinger	Antioxidants NAT complex (H1...	51901	1
Hepart	Antioxidants NAT complex (H1...	16000968	1
Hepart	Antioxidants NAT complex (H1...	16000970	1
Hepart	Antioxidants NAT complex (H1...	17000265	1
Hepart	Antioxidants NAT complex (H1...	17000264	2
Hepart	Antioxidants NAT complex (H1...	18001182	1
Hepart	Antioxidants NAT complex (H1...	17001754	1
hepart ag	Antioxidants NAT complex (H1...	19901	1
Hepart AG	Antioxidants NAT complex (H1...	1034019901	1
Hepart AG	Antioxidants NAT complex (H1...	1034030902	1
Hepart AG	Antioxidants NAT complex (H1...	1034030904	1
Hepart AG	Antioxidants NAT complex (H1...	1037030904	1
Hepart AG	Antioxidants NAT complex (H1...	1034030901	1
Hepart AG	Antioxidants NAT complex (H1...	52101	3
Hepart AG	Antioxidants NAT complex (H1...	51902	1
Hepart AG	Antioxidants NAT complex (H1...	52201	2
Hepart AG	Antioxidants NAT complex (H1...	67301	2
Hepart AG	Antioxidants NAT complex (H1...	67201	1
Hepart AG	Antioxidants NAT complex (H1...	67501	1
Hepart AG	Antioxidants NAT complex (H1...	14000963	3
Hepart AG	Antioxidants NAT complex (H1...	15000878/0	2
Hepart AG	Antioxidants NAT complex (H1...	16000376	1
Hepart AG	Antioxidants NAT complex (H1...	16000378	1
Hepart AG	Antioxidants NAT complex (H1...	16000970/0	1
Hepart AG	Antioxidants NAT complex (H1...	17000264/0	1
Hepart AG	Antioxidants NAT complex (H1...	17000266/0	1
Hepart AG	Antioxidants NAT complex (H1...	18001182/1	1
Hepart AG	Antioxidants NAT complex (H1...	17001754/0	1
Hepart AG, CH-8280 Kreu...	Antioxidants NAT complex (H1...	1034030901	1
Hepart AG, CH-8280 Kreu...	Antioxidants NAT complex (H1...	52101	1
Hepart AG, CH-8280 Kreu...	Antioxidants NAT complex (H1...	1034019901	1
Hepart/Unisan	Antioxidants NAT complex (H1...	15000877/1	1
Hepart/Unisan	Antioxidants NAT complex (H1...	16000376/0	1
Hepart/Unisan	Antioxidants NAT complex (H1...	16000967	1
Phönix	Antioxidants NAT complex (H1...	16000376	1

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Supplier	Substance	Batch	Spectra
unisan	Antioxidants NAT complex (H1...	15000877	2
Unisan	Antioxidants NAT complex (H1...	11001	1
Unisan	Antioxidants NAT complex (H1...	30903	3
Unisan	Antioxidants NAT complex (H1...	1034030904	1
Unisan	Antioxidants NAT complex (H1...	30904	1
Unisan	Antioxidants NAT complex (H1...	51901	2
Unisan	Antioxidants NAT complex (H1...	51902	1
Unisan	Antioxidants NAT complex (H1...	52001	2
Unisan	Antioxidants NAT complex (H1...	68201	4
Unisan	Antioxidants NAT complex (H1...	67601	2
Unisan	Antioxidants NAT complex (H1...	67201	4
Unisan	Antioxidants NAT complex (H1...	67501	1
Unisan	Antioxidants NAT complex (H1...	1400042	1
Unisan	Antioxidants NAT complex (H1...	14000044	1
Unisan	Antioxidants NAT complex (H1...	14000961	1
Unisan	Antioxidants NAT complex (H1...	14000963	2
Unisan	Antioxidants NAT complex (H1...	14001847/0	2
Unisan	Antioxidants NAT complex (H1...	14001848/0	1
Unisan	Antioxidants NAT complex (H1...	14001847/1	1
Unisan	Antioxidants NAT complex (H1...	14001851/0	1
Unisan	Antioxidants NAT complex (H1...	1851	1
Unisan	Antioxidants NAT complex (H1...	15000877/0	1
Unisan	Antioxidants NAT complex (H1...	15000880	1
Unisan	Antioxidants NAT complex (H1...	16000376	1
Unisan	Antioxidants NAT complex (H1...	16000378	1
Unisan	Antioxidants NAT complex (H1...	16000966/0	2
Unisan	Antioxidants NAT complex (H1...	16000966	1
Unisan	Antioxidants NAT complex (H1...	16000968/0	1
Unisan	Antioxidants NAT complex (H1...	16000970/0	3
Unisan	Antioxidants NAT complex (H1...	16000970	1
Unisan	Antioxidants NAT complex (H1...	17000260	2
Unisan	Antioxidants NAT complex (H1...	17000264	1
Unisan	Antioxidants NAT complex (H1...	19901	2
UNISAN	Antioxidants NAT complex (H1...	14000042	1
UNISAN	Antioxidants NAT complex (H1...	14000961	1
Unisan 02.04.2016	Antioxidants NAT complex (H1...	15000874/0	2
Unisan Gmbh, 78465 Kons...	Antioxidants NAT complex (H1...	52201	1
Unisan Gmbh, 78465 Kons...	Antioxidants NAT complex (H1...	67301	1
HCK	Bioflavonoid complex (H1006)	17000256	1
Hepart	Bioflavonoid complex (H1006)	14001675/5	1
Hepart AG	Bioflavonoid complex (H1006)	1284019001	1
Hepart AG	Bioflavonoid complex (H1006)	1284042501	1
Hepart AG	Bioflavonoid complex (H1006)	42501	1
Hepart AG	Bioflavonoid complex (H1006)	56001	2
Hepart AG	Bioflavonoid complex (H1006)	68101	1
Hepart AG	Bioflavonoid complex (H1006)	14001675/1	1
Hepart AG, CH-8280 Kreu...	Bioflavonoid complex (H1006)	56001	1
Unisan	Bioflavonoid complex (H1006)	1284648802	1
Unisan	Bioflavonoid complex (H1006)	1284019001	1
Unisan	Bioflavonoid complex (H1006)	1284042501	1
Unisan	Bioflavonoid complex (H1006)	68101	1
Unisan	Bioflavonoid complex (H1006)	14001675	2
Unisan	Bioflavonoid complex (H1006)	14001675/4	1
Unisan	Bioflavonoid complex (H1006)	17000256	1
Unisan	Bioflavonoid complex (H1006)	42501	1
Unisan	Bioflavonoid complex (H1006)	1281683901	1
Unisan 02.04.2016	Bioflavonoid complex (H1006)	14001675/2	1
Unisan 2.10.2015	Bioflavonoid complex (H1006)	14001675/1	1
HCK	Calcium (H1008)	15001672	2
Hepart	Calcium (H1008)	15001667/0	1

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Supplier	Substance	Batch	Spectra
Hepart	Calcium (H1008)	150016740	1
Hepart	Calcium (H1008)	17000204	1
Hepart	Calcium (H1008)	170002040	1
Hepart	Calcium (H1008)	17000206	1
Hepart	Calcium (H1008)	17000205	1
Hepart	Calcium (H1008)	17000251/0	1
Hepart / Unisan	Calcium (H1008)	17000250	1
Hepart AG	Calcium (H1008)	1104008901	6
Hepart AG	Calcium (H1008)	8901	2
Hepart AG	Calcium (H1008)	55001	1
Hepart AG	Calcium (H1008)	55501	5
Hepart AG	Calcium (H1008)	55201	1
Hepart AG	Calcium (H1008)	55401	4
Hepart AG	Calcium (H1008)	55301	2
Hepart AG	Calcium (H1008)	14001933	1
Hepart AG	Calcium (H1008)	15001668/0	2
Hepart AG	Calcium (H1008)	17000203/0	2
Hepart AG	Calcium (H1008)	17000205/0	2
Hepart AG, CH-8280 Kreu...	Calcium (H1008)	1104008901	4
Hepart AG, CH-8280 Kreu...	Calcium (H1008)	55501	2
Hepart/Unisan	Calcium (H1008)	14001938/1	1
unisan	Calcium (H1008)	55001	1
Unisan	Calcium (H1008)	1105008901	1
Unisan	Calcium (H1008)	956001	1
Unisan	Calcium (H1008)	8901	5
Unisan	Calcium (H1008)	55601	2
Unisan	Calcium (H1008)	55001	1
Unisan	Calcium (H1008)	55101	3
Unisan	Calcium (H1008)	55301	1
Unisan	Calcium (H1008)	55401	1
Unisan	Calcium (H1008)	14000110	1
Unisan	Calcium (H1008)	14000108	1
Unisan	Calcium (H1008)	14001934/0	1
Unisan	Calcium (H1008)	55501	1
Unisan	Calcium (H1008)	14001938/0	1
Unisan	Calcium (H1008)	15001666	1
Unisan	Calcium (H1008)	15001666/0	1
Unisan	Calcium (H1008)	15001667	2
Unisan	Calcium (H1008)	15001672/0	1
Unisan	Calcium (H1008)	15001672	1
Unisan	Calcium (H1008)	17000201	1
UNISAN	Calcium (H1008)	14000110	1
Unisan Gmbh, 78465 Kons...	Calcium (H1008)	55401	1
Unisan/Hepart AG	Calcium (H1008)	8901	1
HCK	Glutathione (H1020)	15000478	1
Hepart	Glutathione (H1020)	16000938/0	2
Hepart AG	Glutathione (H1020)	1254025703	1
Hepart AG	Glutathione (H1020)	1254040201	1
Hepart AG	Glutathione (H1020)	16000938/2	1
Hepart AG, CH-8280 Kreu...	Glutathione (H1020)	1251019703	1
Hepart AG, CH-8280 Kreu...	Glutathione (H1020)	40201	1
Hepart AG, CH-8280 Kreu...	Glutathione (H1020)	1251025703	1
Purren Apotheke	Glutathione (H1020)	1254955501	1
Unisan	Glutathione (H1020)	1251019703	1
Unisan	Glutathione (H1020)	25703	1
Unisan	Glutathione (H1020)	40201	3
Unisan	Glutathione (H1020)	1254025703	1
Unisan	Glutathione (H1020)	74901	3
Unisan	Glutathione (H1020)	16000938	1
UNISAN	Glutathione (H1020)	74901	1

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Supplier	Substance	Batch	Spectra
Hepart	Isoflavones (H1025)	16001644	1
Hepart AG	Isoflavones (H1025)	1314025704	1
Hepart AG	Isoflavones (H1025)	1314038801	1
Hepart AG	Isoflavones (H1025)	56701	1
Hepart AG	Isoflavones (H1025)	38801	1
Purren Apotheke	Isoflavones (H1025)	1314955701	1
Unisan	Isoflavones (H1025)	56701	2
Unisan	Isoflavones (H1025)	15000205/0	3
Unisan	Isoflavones (H1025)	15000205	1
Unisan	Isoflavones (H1025)	15000205/3	1
Unisan 02.04.2016	Isoflavones (H1025)	15000205/1	1
Unisan/Hepart AG	Isoflavones (H1025)	38801	1
Hepart	OPC Grape seed (H1066)	17001805/1	1
Hepart AG	OPC Grape seed (H1066)	1504018401	2
Hepart AG	OPC Grape seed (H1066)	18401	1
Hepart AG	OPC Grape seed (H1066)	70401	2
Hepart AG	OPC Grape seed (H1066)	16000637	1
Hepart AG, CH-8280 Kreu...	OPC Grape seed (H1066)	130208	1
Unisan	OPC Grape seed (H1066)	18401	1
Unisan	OPC Grape seed (H1066)	68301	4
Unisan	OPC Grape seed (H1066)	70401	2
Unisan	OPC Grape seed (H1066)	16000637	1
Unisan	OPC Grape seed (H1066)	16001439	2
Unisan	OPC Grape seed (H1066)	16001439/0	1
UNISAN	OPC Grape seed (H1066)	70401	1
Hepart AG	Rhodiola (H1064)	70501	1
Hepart AG	Rhodiola (H1064)	15001045/4	1
Unisan	Rhodiola (H1064)	15001045/8	1
Hepart AG	Vitamin B1 (H1101)	1622030202	2
Hepart AG	Vitamin B1 (H1101)	1621030202	1
Hepart AG	Vitamin B1 (H1101)	53301	2
Hepart AG	Vitamin B1 (H1101)	14001112	1
Hepart AG	Vitamin B1 (H1101)	15001622/0	1
Hepart AG	Vitamin B1 (H1101)	16000698/0	1
Hepart AG, CH-8280 Kreu...	Vitamin B1 (H1101)	53301	1
Hepart AG, Unisan GmbH	Vitamin B1 (H1101)	15001622/0	1
Unisan	Vitamin B1 (H1101)	1622977301	1
Unisan	Vitamin B1 (H1101)	977301	2
Unisan	Vitamin B1 (H1101)	30202	2
Unisan	Vitamin B1 (H1101)	14001112/0	1
Unisan	Vitamin B1 (H1101)	15001620/0	1
Unisan	Vitamin B1 (H1101)	15001622/0	1
Unisan	Vitamin B1 (H1101)	15001622	1
Unisan	Vitamin B1 (H1101)	16000698	1
Unisan	Vitamin B1 (H1101)	17001075	1
UNISAN	Vitamin B1 (H1101)	75001	1
Unisan/Hepart AG	Vitamin B1 (H1101)	53301	1
Hepart	Antioxidants NAT complex (H1...	17000260	1
Unisan	Antioxidants NAT complex (H1...		3
Hepart	Bioflavonoid complex (H1006)	17000256	1
Hepart	Glutathione (H1020)	15000478	1
Hepart	OPC Grape seed (H1066)	16001439	1
Hepart	OPC Grape seed (H1066)	17001805	2
Hepart	Rhodiola (H1064)	15001045	1
Hepart	Vitamin B1 (H1101)	17000914	1

- 1594 spectra from 17 *Apo-Ident* customers from a total of 705 batches from a further 55 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented

within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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	4732	18	18 101
Type B	0	5970	99	14 685
Type C	0	266	27	1594

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 % (> 99.9306 %)	99.6211 % (> 99.5579 %)
Type B	100.0000 % (> 99.8800 %)	98.3688 % (> 98.3193 %)
Type C	100.0000 % (> 98.7162 %)	90.7850 % (> 89.7611 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *HCK classification II* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Silymarin (H1071)	13.91	—
Beetroot (H1414)	17.10	—
Ginkgo (H1024)	18.32	—
Coenzyme Q10 (H1013)	18.99	—
Garcinia cambogia (H1017)	19.81	—
Carrot (H1416)	20.44	—
Pathogene complex (H1803)	20.78	—
Detox complex (H1118)	21.51	—
Orthovimin Neutral Complex (H1403)	21.78	—
Leaky gut complex (H1802)	22.16	—
Catechin extract (H1010)	23.22	—
PET basis (H1503)	23.93	—
Baobab (H1410)	25.09	—
Juniper (H1112)	27.49	—

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Substanz	Distance in main model	Distance in second-stage model
Aminomix NAC (H1002)	29.76	—
Ginseng (H1018)	31.75	—
Copper (H1032)	31.97	—
Betaine hydrochloride (H1119)	32.78	—
Carnitine (L-) (H1038)	33.10	—
Antibiosis forte complex (H1115)	34.35	—
Vitamins BAG (H1090)	35.34	—
PET joints (H1501)	35.44	—
Vitamin C (H1104)	35.58	—
Vitamin E NAT (H1107)	36.09	—
L-5-HTP (H1035)	37.92	—
Green coffee extract (H1433)	38.15	—
Vitamin complex (H1100)	40.18	—
Yeast organic (H1007)	40.77	—
PET well-aging (H1500)	41.65	—
Psyllium husks (H1432)	42.05	—
Silicium (H1070)	42.31	—
Saffron flowers (H1435)	42.39	—
Iron (H1015)	42.84	—
Boron (H1005)	45.16	—
Histamine block complex (H1117)	45.65	—
Sunflower protein (H1430)	45.94	—
Artichoke extract (H1440)	47.17	—
Creatine (H1031)	48.03	—
Zinc (H1110)	48.23	—
Walnut leaf (H1114)	48.38	—
Magnesium (H1060)	51.14	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80707	80707	0.00	49.54
80318	80318	0.00	43.85
80709	80709	0.00	48.46
80404	80404	0.00	32.79
80405	80405	0.00	34.10
80419	80419	0.00	38.95
80469	80469	0.00	44.94
80473	80473	0.00	44.45
80504	80504	0.00	41.28
80946	80946	0.00	23.54
80505	80505	0.00	37.11
80337	80337	0.00	38.07
80506	80506	0.00	39.26

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81202	81202	0.00	23.52
80507	80507	0.00	35.50
80422	80422	0.00	45.95
80508	80508	0.00	39.79
80525	80525	0.00	42.73
80509	80509	0.00	38.11
80526	80526	0.00	38.24
80607	80607	0.00	41.78
81034	81034	0.00	38.90
81102	81102	0.00	25.23
81044	81044	0.00	23.21
80609	80609	0.00	44.85
80345	80345	0.00	43.37
81070	81070	0.00	21.50
81253	81253	0.00	26.19
80613	80613	0.00	43.36
80616	80616	0.00	44.77
80853	80853	0.00	31.25
80352	80352	0.00	13.06
80618	80618	0.00	42.22
80768	80768	0.00	33.75
80380	80380	0.00	18.35
80632	80632	0.00	29.55
80619	80619	0.00	44.01
81151	81151	0.00	61.22
80398	80398	0.00	19.54
80621	80621	0.00	44.98
81170	81170	0.00	59.12
80980	80980	0.00	43.01
80624	80624	0.00	30.32
81041	81041	0.00	30.54
80783	80783	0.00	36.54
80316	80316	0.00	34.13
81042	81042	0.00	29.40
80712	80712	0.00	49.86
80715	80715	0.00	50.48
80719	80719	0.00	42.11
80986	80986	0.00	19.34
80864	80864	0.00	19.42
80722	80722	0.00	47.62
80987	80987	0.00	18.17
81001	81001	0.00	19.94
80724	80724	0.00	47.71
80732	80732	0.00	46.81
81016	81016	0.00	35.68
80734	80734	0.00	51.56
80740	80740	0.00	46.06
80342	80342	0.00	22.02
80492	80492	0.00	33.08
80741	80741	0.00	49.21
80878	80878	0.00	36.49

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81033	81033	0.00	32.56
80390	80390	0.00	27.59
80672	80672	0.00	23.93
81136	81136	0.00	28.69
80322	80322	0.00	40.79
80323	80323	0.00	45.08
80327	80327	0.00	49.43
81200	81200	0.00	20.44
80329	80329	0.00	34.97
80521	80521	0.00	43.71
80819	80819	0.00	26.62
80711	80711	0.00	46.39
81098	81098	0.00	34.65
80923	80923	0.00	20.78
80729	80729	0.00	49.35
81166	81166	0.00	36.52
80953	80953	0.00	39.16
80815	80815	0.00	44.42
80430	80430	0.00	27.61
80583	80583	0.00	22.16
80311	80311	0.00	42.88
80313	80313	0.00	44.56
80392	80392	0.00	34.35
80315	80315	0.00	42.65
80479	80479	0.00	38.50
80317	80317	0.00	42.49
80529	80529	0.00	36.08
80522	80522	0.00	48.87
81183	81183	0.00	42.08
80527	80527	0.00	40.97
80676	80676	0.00	41.16

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Hemp protein (H1406)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81099-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hemp protein (H1406)

Special notes

When selecting the *Hemp protein (H1406)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Hemp protein (H1406)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Hemp protein (H1406)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hemp protein (H1406)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Hemp protein (H1...	18001330	81099	40	from supplier
Hepart	Hemp protein (H1...	18001679	81134	40	from supplier

Validation samples

A total of 45 492 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 *Hemp protein (H1406)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Hemp protein (H1406)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Hemp protein (H1406)	20000392	81256	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Hemp protein (H1406)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hemp protein (H1406)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hemp protein (H1406)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Hemp protein (H1406)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hemp protein (H1406)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	32.60	—
PET skin and hair (H1504)	39.58	—
Amino V complex (H1400)	41.32	—
Pumpkin protein (H1429)	47.49	—
Pea protein complex (H1428)	47.50	—
Aminomix NAC (H1002)	54.75	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hemp protein (H1406)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81099	81099	0.00	32.60
81134	81134	0.00	34.71

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Histamine block complex (H1117)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80896-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Histamine block complex (H1117)

Special notes

When selecting the *Histamine block complex (H1117)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Histamine block complex (H1117)	1	1	0

Second-stage model

For differentiation of the substance/substance group *Histamine block complex (H1117)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Histamine block complex (H1117)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Histamine block ...	16001078	80896	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Histamine block complex (H1117)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Histamine block complex (H1117)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Histamine block complex (H11...	16001079	80897	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Histamine block complex (H1117)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Histamine block complex (H1117)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Histamine block complex (H1117)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Histamine block complex (H1117)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Histamine block complex (H1117)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pathogene complex (H1803)	16.81	—
Garcinia cambogia (H1017)	21.06	—
Antibiosis mite complex (H1113)	28.88	—
Antioxidants NAT complex (H1004)	33.83	—
Ginkgo (H1024)	34.50	—
Seabuckthorn organic (H1412)	35.59	—
Copper (H1032)	35.75	—
PET basis (H1503)	37.78	—
Iron (H1015)	42.94	—
PET joints (H1501)	44.03	—
Walnut leaf (H1114)	46.49	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Histamine block complex (H1117)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80896	80896	0.00	16.81

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Inositol hexanicotinate (H1022)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80087-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Inositol hexanicotinate (H1022)	4	2	5

Second-stage model

For differentiation of the substance/substance group *Inositol hexanicotinate (H1022)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Inositol hexanic...	18001390/0	81116	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 4 reference samples from the substance/substance group *Inositol hexanicotinate (H1022)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 651 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Inositol hexanicotinate (H1022)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Inositol hexanicotinate (H10...	16000750	80814	40
Hepart	Inositol hexanicotinate (H10...	20000182	81231	40

- 20 674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 10 spectra from 3 *Apo-Ident* customers from 7 batches from the substance/substance group *Inositol hexanicotinate (H1022)*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Inositol hexanicotinate (H10...	1811046001	1
HCK	Inositol hexanicotinate (H10...	19000750/4	1
Hepart AG	Inositol hexanicotinate (H10...	1811979201	1
Hepart AG	Inositol hexanicotinate (H10...	15000013	1
Hepart AG	Inositol hexanicotinate (H10...	16000750/4	1
Purren Apotheke	Inositol hexanicotinate (H10...	1811979201	1
unisan	Inositol hexanicotinate (H10...	15000013	1
Unisan	Inositol hexanicotinate (H10...	46001	1
Unisan	Inositol hexanicotinate (H10...	14000920	1
Unisan/Hepart AG	Inositol hexanicotinate (H10...	46001	1

- 1877 spectra from 19 *Apo-Ident* customers from a total of 852 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 *Inositol hexanicotinate (H1022)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Inositol hexanicotinate (H1022)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	22 651
Type B	0	63	17	20 674
Type C	0	5	5	1877

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9310 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8817 %)	78.7500 % (> 75.0000 %)
Type C	100.0000 % (> 98.7448 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Inositol hexanicotinate (H1022)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	54.78	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Inositol hexanicotinate (H1022)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80320	80320	0.00	81.15
80465	80465	0.00	85.83
80554	80554	0.00	79.58
81116	81116	0.00	54.78

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Iron (H1015) / Copper (H1032)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80341-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Copper (H1032)	3	1	11
Iron (H1015)	5	6	15

Second-stage model

For differentiation of the substance/substance group *Iron (H1015) / Copper (H1032)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Copper (H1032)	130415	80341	40	from supplier
Hepart	Copper (H1032)	15000211	80536	60	from supplier
Hepart	Copper (H1032)	19001347	81222	40	from supplier
Hepart	Iron (H1015)	14000285	80510	60	from supplier
Hepart	Iron (H1015)	040901	80511	60	from supplier
Hepart	Iron (H1015)	040901	80568	60	from supplier
Hepart	Iron (H1015)	14000285	80569	60	from supplier
Hepart	Iron (H1015)	15001258	80650	60	from supplier
Hepart	Iron (H1015)	15001259(B1)	80651	60	from supplier
Hepart	Iron (H1015)	15001259	80653	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 560 spectra of 10 reference samples from the substance/substance group *Iron (H1015) / Copper (H1032)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 22 291 spectra from a total of 432 batches from further 116 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 380 spectra of 8 reference samples from the substance/substance group *Iron (H1015) / Copper (H1032)*.

- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Copper (H1032)	15000211/5	80875	40
Hepart	Iron (H1015)	15001259(F2)	80649	60
Hepart	Iron (H1015)	15001258(F2)	80652	60
Hepart	Iron (H1015)	15001258(B1)	80654	60
Hepart	Iron (H1015)	17000279	80917	40
Hepart	Iron (H1015)	20000399	81254	40
Hepart	Iron (H1015)	20000089/0	81255	40
Hepart	Iron (H1015)	14000285	80413	40

- 20374 spectra from a total of 439 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 73 spectra from 13 *Apo-Ident* customers from 30 batches from the substance/substance group *Iron (H1015) / Copper (H1032)*.
- Among them are spectra of independent samples from 26 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Copper (H1032)	933901	1
Hepart	Copper (H1032)	15000211/5	1
Hepart	Copper (H1032)	150002117	1
Hepart AG	Copper (H1032)	1544007901	1
Hepart AG	Copper (H1032)	1544046401	1
Hepart AG	Copper (H1032)	46401	1
Hepart AG	Copper (H1032)	13041501	1
Hepart AG	Copper (H1032)	130415-K1	1
Unisan	Copper (H1032)	7901	1
Unisan	Copper (H1032)	46401	2
Unisan	Copper (H1032)	933901	1
Unisan	Copper (H1032)	13041501	5
Unisan	Copper (H1032)	15000211	1
Unisan	Copper (H1032)	15000211/0	1
Unisan	Copper (H1032)	1542933901	1
Unisan/Hepart AG	Copper (H1032)	13041501	1
HCK	Iron (H1015)	15001258/1	1
HCK	Iron (H1015)	1259	1
Hepart	Iron (H1015)	15001259/2	2
Hepart AG	Iron (H1015)	1114998701	1
Hepart AG	Iron (H1015)	1114040901	2
Hepart AG	Iron (H1015)	40901	3
Hepart AG	Iron (H1015)	15001258/0	1
Hepart AG, CH-8280 Kreu...	Iron (H1015)	1114998701	1
Hepart/Unisan	Iron (H1015)	15001258/1	1

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Supplier	Substance	Batch	Spectra
Unisan	Iron (H1015)	998701	6
Unisan	Iron (H1015)	1114603206	1
Unisan	Iron (H1015)	1114998701	3
Unisan	Iron (H1015)	1114040901	2
Unisan	Iron (H1015)	40901	9
Unisan	Iron (H1015)	14000285	1
Unisan	Iron (H1015)	14000285/1	2
Unisan	Iron (H1015)	14000285/5	1
Unisan	Iron (H1015)	15001258/0	1
Unisan	Iron (H1015)	15001259	2
Unisan	Iron (H1015)	15001258/2	2
UNISAN	Iron (H1015)	14000285	1
Unisan 02.04.2016	Iron (H1015)	15001258/0	1
Unisan 11.08.2105	Iron (H1015)	14000285/2	1
Unisan 2.10.2015	Iron (H1015)	14000285/3	2
Unisan/Hepart	Iron (H1015)	15001259/0	1
Unisan/Hepart AG	Iron (H1015)	40901	1
Hepart	Iron (H1015)	15001258	2

- 1814 spectra from 19 *Apo-Ident* customers from a total of 829 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 *Iron (H1015) / Copper (H1032)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Iron (H1015) / Copper (H1032)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	560	0	22 291
Type B	0	380	0	20 374
Type C	0	72	1	1814

The substance/substance group *Iron (H1015) / Copper (H1032)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9307 %)	100.0000 % (> 98.9286 %)
Type B	100.0000 % (> 99.8803 %)	100.0000 % (> 98.4211 %)
Type C	100.0000 % (> 98.7192 %)	98.6301 % (> 94.5205 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Iron (H1015) / Copper (H1032)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Argentum (H1116)	12.01	—
Trace elements SE (H1082)	36.10	—
Antioxidants NAT complex (H1004)	57.81	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Iron (H1015) / Copper (H1032)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80510	80510	0.00	20.04
80511	80511	0.00	20.87
80568	80568	0.00	17.87
80569	80569	0.00	20.21
80650	80650	0.00	12.55
80651	80651	0.00	12.01
80653	80653	0.00	12.21
80341	80341	0.00	26.35
80536	80536	0.00	38.19
81222	81222	0.00	24.25

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Isoleucine (L-) (H1045)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80134-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Isoleucine (L-) (H1045)	4	2	7

Second-stage model

For differentiation of the substance/substance group *Isoleucine (L-) (H1045)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Isoleucine (L-) ...	066301	80368	40	from supplier
Hepart	Isoleucine (L-) ...	14001772	80498	60	from supplier
Hepart	Isoleucine (L-) ...	15001641	80678	60	from supplier
Hepart	Isoleucine (L-) ...	15001640	80679	60	from supplier

Validation samples

A total of 45 492 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 *Isoleucine (L-) (H1045)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 631 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Isoleucine (L-) (H1045)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Isoleucine (L-) (H1045)	17000900	80909	40
Hepart	Isoleucine (L-) (H1045)	18001412	81111	40

- 20 674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 16 spectra from 7 *Apo-Ident* customers from 9 batches from the substance/substance group *Isoleucine (L-) (H1045)*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fritz Schiele	Isoleucine (L-) (H1045)	1805027701	1
HCK	Isoleucine (L-) (H1045)	15001641	2
Hepart	Isoleucine (L-) (H1045)	17000900	1
Hepart AG	Isoleucine (L-) (H1045)	1805027701	2
Hepart AG	Isoleucine (L-) (H1045)	66301	1
Hepart AG	Isoleucine (L-) (H1045)	15001640/2	1
Hepart AG	Isoleucine (L-) (H1045)	15001641	1
Hepart AG, CH-8280 Kreu...	Isoleucine (L-) (H1045)	1804968701	1
Hepart AG, CH-8280 Kreu...	Isoleucine (L-) (H1045)	66301	1
Unisan	Isoleucine (L-) (H1045)	27701	1
Unisan	Isoleucine (L-) (H1045)	1805968701	1
Unisan	Isoleucine (L-) (H1045)	66301	2
Unisan	Isoleucine (L-) (H1045)	15001640	1

- 1871 spectra from 19 *Apo-Ident* customers from a total of 850 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 *Isoleucine (L-) (H1045)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Isoleucine (L-) (H1045)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	22 631
Type B	0	80	0	20 674
Type C	0	10	6	1871

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9310 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.8817 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7337 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Isoleucine* (L-) (*H1045*) in the substance class *HCK - nutritional supplements* (*Hepart*). Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Valine (L-) (<i>H1056</i>)	29.71	–
Leucine (L-) (<i>H1046</i>)	34.24	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Isoleucine* (L-) (*H1045*) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80498	80498	0.00	32.95
80678	80678	0.00	33.29
80679	80679	0.00	29.71
80368	80368	0.00	32.24

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **L-5-HTP (H1035)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80111-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
L-5-HTP (H1035)	2	0	0

Second-stage model

For differentiation of the substance/substance group L-5-HTP (H1035) the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group 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 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 80 spectra of 2 reference samples from the substance/substance group L-5-HTP (H1035). These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group L-5-HTP (H1035).
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 15 spectra from 5 *Apo-Ident* customers from 10 batches from the substance/substance group L-5-HTP (*H1035*).
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	L-5-HTP (<i>H1035</i>)	16000441	1
Hepart	L-5-HTP (<i>H1035</i>)	18000913	1
Hepart AG	L-5-HTP (<i>H1035</i>)	1837999801	1
Hepart AG	L-5-HTP (<i>H1035</i>)	15001503/2	3
Hepart AG	L-5-HTP (<i>H1035</i>)	15001503	1
Hepart AG	L-5-HTP (<i>H1035</i>)	16000441/0	1
Unisan	L-5-HTP (<i>H1035</i>)	26102	1
Unisan	L-5-HTP (<i>H1035</i>)	25006	3
Unisan	L-5-HTP (<i>H1035</i>)	15001503/5	2
Unisan	L-5-HTP (<i>H1035</i>)	25006/12	1

- 1872 spectra from 19 *Apo-Ident* customers from a total of 849 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 L-5-HTP (*H1035*) can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with L-5-HTP (*H1035*) and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	0	0	20 754
Type C	0	3	12	1872

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7349 %)	n/a (n/a)

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

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group L-5-HTP (H1035) in the substance class HCK - nutritional supplements (Hepart). Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium (H1008)	12.73	—
Silymarin (H1071)	28.73	—
Vitamin complex (H1100)	32.12	—
Antioxidants NAT complex (H1004)	33.89	—
Carnitine (L-) (H1038)	40.62	—
OPC Grape seed (H1066)	43.24	—
Rhodiola (H1064)	48.97	—
Catechin extract (H1010)	55.93	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group L-5-HTP (H1035) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80851	80851	0.00	32.24
80797	80797	0.00	30.45

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Leaky gut complex (H1802)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81039-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Leaky gut complex (H1802)

Special notes

When selecting the *Leaky gut complex (H1802)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Leaky gut complex (H1802)	1	1	0

Second-stage model

For differentiation of the substance/substance group *Leaky gut complex (H1802)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Leaky gut complex (H1802)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Leaky gut comple...	18000638	81039	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Leaky gut complex (H1802)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Leaky gut complex (H1802)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Leaky gut complex (H1802)	18000639	81040	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Leaky gut complex (H1802)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Leaky gut complex (H1802)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Leaky gut complex (H1802)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Leaky gut complex (H1802)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Leaky gut complex (H1802)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	19.39	—
Coenzyme Q10 (H1013)	20.35	—
Vitamin E NAT (H1107)	26.70	—
Ginseng (H1018)	29.68	—
PET joints (H1501)	31.24	—
Flavour orange (H1405)	32.95	—
Calcium (H1008)	36.64	—
Glutamine (L-) (H1043)	36.97	—
Camu camu (H1411)	37.22	—
Glutathione (H1020)	44.50	—
Isoflavones (H1025)	48.05	—
Antibiosis forte complex (H1115)	49.56	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Leaky gut complex (H1802)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81039	81039	0.00	31.24

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Leucine (L-) (H1046)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80150-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Leucine (L-) (H1046)	2	2	8

Second-stage model

For differentiation of the substance/substance group *Leucine (L-) (H1046)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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 45 492 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 [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 751 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 100 spectra of 2 reference samples from the substance/substance group *Leucine (L-) (H1046)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Leucine (L-) (H1046)	15000283	80570	60
Hepart	Leucine (L-) (H1046)	18001305	81074	40

- 20 654 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 15 spectra from 8 *Apo-Ident* customers from 9 batches from the substance/substance group *Leucine (L-) (H1046)*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Leucine (L-) (H1046)	965101	1
Hepart	Leucine (L-) (H1046)	18001305	1
Hepart	Leucine (L-) (H1046)	15000283	1
Hepart AG	Leucine (L-) (H1046)	1809994101	1
Hepart AG	Leucine (L-) (H1046)	15000283/1	1
Hepart AG	Leucine (L-) (H1046)	18001305/0	1
Hepart AG, CH-8280 Kreu...	Leucine (L-) (H1046)	52601	2
Purren Apotheke	Leucine (L-) (H1046)	1809965101	1
Unisan	Leucine (L-) (H1046)	1809965101	1
Unisan	Leucine (L-) (H1046)	52601	1
Unisan	Leucine (L-) (H1046)	15000283/0	1
Unisan	Leucine (L-) (H1046)	15000283	1
Unisan	Leucine (L-) (H1046)	15000283/1	1
Unisan/Hepart AG	Leucine (L-) (H1046)	52601	1

- 1872 spectra from 19 *Apo-Ident* customers from a total of 850 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 *Leucine (L-) (H1046)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Leucine (L-) (H1046)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	100	0	22 751
Type B	0	100	0	20 654
Type C	0	12	3	1872

The substance/substance group *Leucine (L-) (H1046)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9315 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8813 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.7349 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Leucine* (L-) (*H1046*) in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Isoleucine (L-) (<i>H1045</i>)	36.75	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Leucine* (L-) (*H1046*) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80333	80333	0.00	42.48
80410	80410	0.00	49.19

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Liver kidney complex (H1801)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81036-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Liver kidney complex (H1801)

Special notes

When selecting the *Liver kidney complex (H1801)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Liver kidney complex (H1801)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Liver kidney complex (H1801)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Liver kidney complex (H1801)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Liver kidney com...	18000635	81036	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Liver kidney complex (H1801)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Liver kidney complex (H1801)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Liver kidney complex (H1801)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Liver kidney complex (H1801)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Liver kidney complex (H1801)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Liver kidney complex (H1801)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Liver kidney complex (H1801)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	31.47	—
Antioxidants NAT complex (H1004)	63.30	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Liver kidney complex (H1801)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81036	81036	0.00	31.47

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Lupin protein complex (H1427)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81008-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lupin protein complex (H1427)

Special notes

When selecting the *Lupin protein complex (H1427)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Lupin protein complex (H1427)	2	2	0

Second-stage model

For differentiation of the substance/substance group *Lupin protein complex (H1427)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lupin protein complex (H1427)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Lupin protein co...	17001732	81008	40	from supplier
Hepart	Lupin protein co...	19000532	81165	40	from supplier

Validation samples

A total of 45 492 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 *Lupin protein complex (H1427)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Lupin protein complex (H1427)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Lupin protein complex (H1427)	18000948	81065	40
Hepart	Lupin protein complex (H1427)	20000644	81258	40

- 20 674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Lupin protein complex (H1427)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lupin protein complex (H1427)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lupin protein complex (H1427)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	80	0	20 674
Type C	0	0	0	1887

The substance/substance group *Lupin protein complex (H1427)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9817 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lupin protein complex (H1427)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Amino V complex (H1400)	22.31	—
Coenzyme Q10 (H1013)	22.47	—
Antibiosis forte complex (H1115)	28.09	—
Pumpkin protein (H1429)	31.35	—
Aminomix NAC (H1002)	38.96	—
Pea protein complex (H1428)	41.53	—
Glutamine (L-) (H1043)	44.45	—
Antioxidants NAT complex (H1004)	47.14	—
Vitamin B1 (H1101)	53.62	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lupin protein complex (H1427)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81008	81008	0.00	23.16
81165	81165	0.00	27.73

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Lysine (L-) (H1047)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80151-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Lysine (L-) (H1047)	6	3	12

Second-stage model

For differentiation of the substance/substance group *Lysine (L-) (H1047)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Lysine (L-) (H10...	16001395/0	80847	40	from supplier
Hepart	Lysine (L-) (H10...	18001389	81131	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 8 reference samples from the substance/substance group *Lysine (L-) (H1047)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 22 511 spectra from a total of 434 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Lysine (L-) (H1047)*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Lysine (L-) (H1047)	16001503/0	80848	40
Hepart	Lysine (L-) (H1047)	19001154	81208	40
Hepart	Lysine (L-) (H1047)	20000950	81268	40

- 20634 spectra from a total of 444 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 19 spectra from 9 *Apo-Ident* customers from 13 batches from the substance/substance group *Lysine (L-) (H1047)*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Lysine (L-) (H1047)	16001395	3
Hepart	Lysine (L-) (H1047)	16001503	1
Hepart AG	Lysine (L-) (H1047)	65401	1
Hepart AG	Lysine (L-) (H1047)	15000372/2	1
Hepart AG	Lysine (L-) (H1047)	16001395/1	3
Hepart AG	Lysine (L-) (H1047)	16001503/0	2
Hepart AG	Lysine (L-) (H1047)	16001503/1	1
Hepart AG, CH-8280 Kreu...	Lysine (L-) (H1047)	1800955002	1
Unisan	Lysine (L-) (H1047)	1800017302	1
Unisan	Lysine (L-) (H1047)	14000944	1
Unisan	Lysine (L-) (H1047)	15000372/0	1
Unisan	Lysine (L-) (H1047)	65401/4	1
Unisan	Lysine (L-) (H1047)	1801028801	1
Unisan/Hepart AG	Lysine (L-) (H1047)	65401	1

- 1868 spectra from 19 *Apo-Ident* customers from a total of 846 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 *Lysine (L-) (H1047)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lysine (L-) (H1047)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	22 511
Type B	0	120	0	20 634
Type C	0	17	2	1868

The substance/substance group *Lysine* (L-) (*H1047*) can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9308 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.8811 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7308 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lysine* (L-) (*H1047*) in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	52.67	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lysine* (L-) (*H1047*) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80562	80562	0.00	61.49
80360	80360	0.00	63.16
80343	80343	0.00	52.67
80468	80468	0.00	64.52
80453	80453	0.00	54.71
81131	81131	0.00	68.13
80458	80458	0.00	55.69
80847	80847	0.00	72.39

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Magnesium (H1060)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80061-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Magnesium (H1060)	6	30	28

Second-stage model

For differentiation of the substance/substance group *Magnesium (H1060)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Magnesium (H1060)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Magnesium (H1060)	069601	80378	40	from supplier
Hepart	Magnesium (H1060)	14001893	80515	60	from supplier
Hepart	Magnesium (H1060)	16000264	80767	60	from supplier
Hepart	Magnesium (H1060)	16000269	80770	60	from supplier
Hepart	Magnesium (H1060)	16001702	80856	40	from supplier
Hepart	Magnesium (H1060)	18000949	81058	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 6 reference samples from the substance/substance group *Magnesium (H1060)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 22 551 spectra from a total of 434 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1420 spectra of 30 reference samples from the substance/substance group *Magnesium (H1060)*.
- Among them are spectra of independent samples from 30 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Magnesium (H1060)	043601	80351	40
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)	14001895	80516	60
Hepart	Magnesium (H1060)	14001889	80517	60
Hepart	Magnesium (H1060)	14001891	80518	60
Hepart	Magnesium (H1060)	14001894	80519	60
Hepart	Magnesium (H1060)	16000270	80769	60
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
Hepart	Magnesium (H1060)	19001559/0	81175	40
Hepart	Magnesium (H1060)	19001153	81176	40
Hepart	Magnesium (H1060)	19001558	81177	40
Hepart	Magnesium (H1060)	19001560	81178	40
Hepart	Magnesium (H1060)	19001561	81179	40

- 19334 spectra from a total of 417 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 75 spectra from 14 *Apo-Ident* customers from 30 batches from the substance/substance group *Magnesium (H1060)*.
- Among them are spectra of independent samples from 28 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Magnesium (H1060)	16000272	1
Hepart	Magnesium (H1060)	16000269/0	1
Hepart	Magnesium (H1060)	16000272	1
Hepart	Magnesium (H1060)	16001704/0	1
Hepart	Magnesium (H1060)	16001704	1
Hepart AG	Magnesium (H1060)	1134973501	5
Hepart AG	Magnesium (H1060)	43601	2
Hepart AG	Magnesium (H1060)	43501	1

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Supplier	Substance	Batch	Spectra
Hepart AG	Magnesium (H1060)	43602	4
Hepart AG	Magnesium (H1060)	43701	1
Hepart AG	Magnesium (H1060)	69901	3
Hepart AG	Magnesium (H1060)	14001894/0	1
Hepart AG	Magnesium (H1060)	14001895/2	1
Hepart AG	Magnesium (H1060)	16000269	1
Hepart AG	Magnesium (H1060)	16000272/0	2
Hepart AG	Magnesium (H1060)	16001705/0	2
Hepart AG	Magnesium (H1060)	16001703/0	1
Hepart AG	Magnesium (H1060)	16001704/0	2
Hepart AG, CH-8280 Kreu...	Magnesium (H1060)	1134973501	2
Hepart AG, CH-8280 Kreu...	Magnesium (H1060)	1134043601	1
Hepart AG, CH-8280 Kreu...	Magnesium (H1060)	43602	1
Hepart/Unisan	Magnesium (H1060)	16000267/0	1
unisan	Magnesium (H1060)	43702	1
unisan	Magnesium (H1060)	14001895	2
Unisan	Magnesium (H1060)	973501	2
Unisan	Magnesium (H1060)	1134973501	2
Unisan	Magnesium (H1060)	43501	2
Unisan	Magnesium (H1060)	43601	1
Unisan	Magnesium (H1060)	H106021	1
Unisan	Magnesium (H1060)	43701	3
Unisan	Magnesium (H1060)	69701	3
Unisan	Magnesium (H1060)	69801	4
Unisan	Magnesium (H1060)	69601	1
Unisan	Magnesium (H1060)	14001895	4
Unisan	Magnesium (H1060)	69801/2	1
Unisan	Magnesium (H1060)	14001893	1
Unisan	Magnesium (H1060)	16000265/0	1
Unisan	Magnesium (H1060)	16000265/1	1
Unisan	Magnesium (H1060)	16000265	1
Unisan	Magnesium (H1060)	16000272	1
UNISAN	Magnesium (H1060)	69701	3
Unisan GmbH, 78465 Kons...	Magnesium (H1060)	43702	1
Unisan/Hepart AG	Magnesium (H1060)	973501	1
Unisan/Hepart AG	Magnesium (H1060)	43601	1
Hepart	Magnesium (H1060)	16000269	1

- 1812 spectra from 19 *Apo-Ident* customers from a total of 829 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 *Magnesium (H1060)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Magnesium (H1060)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	22 551
Type B	0	1398	22	19 334
Type C	0	57	18	1812

The substance/substance group *Magnesium (H1060)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9309 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.8801 %)	98.4507 % (> 98.2394 %)
Type C	100.0000 % (> 98.7191 %)	76.0000 % (> 72.0000 %)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Magnesium (H1060)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Trace elements JK (H1080)	22.31	—
Antioxidants NAT complex (H1004)	53.42	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Magnesium (H1060)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80770	80770	0.00	30.01
80378	80378	0.00	29.47
80515	80515	0.00	33.81
80767	80767	0.00	29.98
80856	80856	0.00	22.72
81058	81058	0.00	25.40

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Methylsulfonylmethane (MSM) (H1062)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80102-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Methylsulfonylmethane (MSM) (H1062)	6	1	7

Second-stage model

For differentiation of the substance/substance group *Methylsulfonylmethane (MSM) (H1062)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	120	from supplier
Hepart	Methylsulfonylme...	17001247	80957	40	from supplier
Hepart	Methylsulfonylme...	18001387	81117	40	from supplier
Hepart	Methylsulfonylme...	20000221	81262	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 6 reference samples from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 22 511 spectra from a total of 434 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Methylsulfonylmethane (MSM) ...	16000449/0	80782	40

- 20714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 12 spectra from 5 *Apo-Ident* customers from 9 batches from the substance/substance group *Methylsulfonylmethane (MSM) (H1062)*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Methylsulfonylmethane (MSM) ...	1400921/1	1
Hepart AG	Methylsulfonylmethane (MSM) ...	15001371	1
Unisan	Methylsulfonylmethane (MSM) ...	26101	1
Unisan	Methylsulfonylmethane (MSM) ...	25013	2
Unisan	Methylsulfonylmethane (MSM) ...	56201	2
Unisan	Methylsulfonylmethane (MSM) ...	979401	1
Unisan	Methylsulfonylmethane (MSM) ...	15001371	1
Unisan	Methylsulfonylmethane (MSM) ...	16000449/1	1
Unisan/Hepart AG	Methylsulfonylmethane (MSM) ...	1819025013	1
Hepart	Methylsulfonylmethane (MSM) ...	17001247	1

- 1875 spectra from 19 *Apo-Ident* customers from a total of 850 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 *Methylsulfonylmethane (MSM) (H1062)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methylsulfonylmethane (MSM) (H1062)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	22 511
Type B	0	40	0	20 714
Type C	0	10	2	1875

The substance/substance group *Methylsulfonylmethane (MSM) (H1062)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9308 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7399 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Methylsulfonylmethane (MSM) (H1062)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	54.48	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methylsulfonylmethane (MSM) (H1062)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80332	80332	0.00	64.17
80467	80467	0.00	72.40
81262	81262	0.00	54.96
80957	80957	0.00	54.74
81117	81117	0.00	54.48
80703	80703	0.00	68.00

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Ornithine (L-) (H1048)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80175-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ornithine (L-) (H1048)	4	1	5

Second-stage model

For differentiation of the substance/substance group *Ornithine (L-) (H1048)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Ornithine (L-) (...)	15000004	80629	60	from supplier
Hepart	Ornithine (L-) (...)	15001364	80667	60	from supplier
Hepart	Ornithine (L-) (...)	15001364(F1)	80669	60	from supplier
Hepart	Ornithine (L-) (...)	16000935	80811	40	from supplier

Validation samples

A total of 45 492 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 *Ornithine (L-) (H1048)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 631 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 60 spectra of 1 reference samples from the substance/substance group *Ornithine (L-) (H1048)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Ornithine (L-) (H1048)	15001364(F2)	80668	60

- 20 694 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 11 spectra from 7 *Apo-Ident* customers from 6 batches from the substance/substance group *Ornithine (L-) (H1048)*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart / Unisan	Ornithine (L-) (H1048)	15000004	2
Purren Apotheke	Ornithine (L-) (H1048)	1817979301	1
Unisan	Ornithine (L-) (H1048)	979301	2
Unisan	Ornithine (L-) (H1048)	1816979301	1
Unisan	Ornithine (L-) (H1048)	16000935/0	3
Unisan/Hepart AG	Ornithine (L-) (H1048)	27001	2

- 1876 spectra from 19 *Apo-Ident* customers from a total of 853 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 *Ornithine (L-) (H1048)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ornithine (L-) (H1048)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	22 631
Type B	0	60	0	20 694
Type C	0	6	5	1876

The substance/substance group *Ornithine (L-) (H1048)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9310 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.8823 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.7421 %)	n/a (n/a)

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

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ornithine (L-) (H1048)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Lysine (L-) (H1047)	43.58	—
Tyrosine (L-) (H1054)	47.00	—
Antibiosis forte complex (H1115)	66.66	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ornithine (L-) (H1048)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80629	80629	0.00	76.09
80667	80667	0.00	72.21
80669	80669	0.00	76.82
80811	80811	0.00	66.66

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Orthovimin Neutral Complex (H1403)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80744-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Orthovimin Neutral Complex (H1403)

Special notes

When selecting the *Orthovimin Neutral Complex (H1403)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Orthovimin Neutral Complex (H1403)	4	2	0

Second-stage model

For differentiation of the substance/substance group *Orthovimin Neutral Complex (H1403)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Orthovimin Neutr...	15001850	80744	60	from supplier
Hepart	Orthovimin Neutr...	17001152	81020	40	from supplier
Hepart	Orthovimin Neutr...	18001065	81073	40	from supplier
Hepart	Orthovimin Neutr...	19000033	81149	40	from supplier

Validation samples

A total of 45 492 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 *Orthovimin Neutral Complex (H1403)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 671 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Orthovimin Neutral Complex (H1403)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Orthovimin Neutral Complex (...)	17001625	80983	40
Hepart	Orthovimin Neutral Complex (...)	19001312	81182	40

- 20674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Orthovimin Neutral Complex (H1403)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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
Type A	0	180	0	22 671
Type B	0	80	0	20 674
Type C	0	0	0	1887

The substance/substance group *Orthovimin Neutral Complex (H1403)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9311 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8817 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Orthovimin Neutral Complex (H1403)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zinc (H1110)	14.98	—
Antioxidants NAT complex (H1004)	15.71	—
Folic acid (H1016)	15.85	—
Calcium (H1008)	19.68	—
Garcinia cambogia (H1017)	21.32	—
Konjac (H1426)	23.93	—
Boron (H1005)	23.94	—
Ginseng (H1018)	24.99	—
Psyllium husks (H1432)	26.74	—
Artichoke extract (H1440)	27.86	—
Lycopene (H1058)	28.00	—
Baobab (H1410)	28.71	—
Juniper (H1112)	29.56	—
Vitamin B1 (H1101)	29.90	—
Silicium (H1070)	29.97	—
Marshmallow extract (H1439)	31.10	—
Orthocolon complex (H1800)	32.15	—
Detox complex (H1118)	33.87	—
Saffron style (H1434)	35.64	—
Selenium (H1067)	38.49	—
Trace elements JK (H1080)	39.58	—
Vitamin B12 (H1102)	40.01	—
Vitamin K2 (75µg Mono) (H1108)	40.79	—
Broccoli (H1415)	40.92	—
Gentian extract (H1438)	41.89	—
Selenium yeast (H1068)	42.07	—
Ginger extract (H1437)	43.08	—
Saffron flowers (H1435)	43.80	—
Iron (H1015)	44.34	—
Trace elements BAG (H1078)	45.02	—
Vitamin D3 (H1105)	45.24	—
Silymarin (H1071)	45.41	—
Glutathione (H1020)	46.31	—
Magnesium (H1060)	46.32	—
Coenzyme Q10 (H1013)	47.29	—
Enzyme complex (H1118)	48.30	—
Betaine hydrochloride (H1119)	49.18	—
Vitamin E NAT (H1107)	49.48	—
Cabbage extract (H1121)	49.83	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Orthovimin Neutral Complex (H1403)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80744	80744	0.00	26.74
81149	81149	0.00	24.47
81073	81073	0.00	23.94
81020	81020	0.00	23.93

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Pea protein complex (H1428) / Amino V complex (H1400)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80749-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pea protein complex (H1428) / Amino V complex (H1400); Amino V complex (H1400); Pea protein complex (H1428)

Special notes

When selecting the *Pea protein complex (H1428) / Amino V complex (H1400)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Amino V complex (H1400)	8	20	0
Pea protein complex (H1428)	4	3	0

Second-stage model

For differentiation of the substance/substance group *Pea protein complex (H1428) / Amino V complex (H1400)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pea protein complex (H1428) / Amino V complex (H1400)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Amino V complex ...	15001365 (MM)	80749	60	from supplier
Hepart	Amino V complex ...	15001366 (B1)	80750	60	from supplier
Hepart	Amino V complex ...	16001268	80820	40	from supplier
Hepart	Amino V complex ...	16001229	80821	40	from supplier
Hepart	Amino V complex ...	15001365	80862	40	from supplier
Hepart	Amino V complex ...	17000382	80885	40	from supplier
Hepart	Amino V complex ...	18000194	80995	40	from supplier
Hepart	Amino V complex ...	18000803	81051	40	from supplier
Hepart	Pea protein comp...	17001708	81006	40	from supplier
Hepart	Pea protein comp...	17001707	81007	40	from supplier
Hepart	Pea protein comp...	18001019	81075	40	from supplier
Hepart	Pea protein comp...	19001643	81220	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 520 spectra of 12 reference samples from the substance/substance group *Pea protein complex (H1428) / Amino V complex (H1400)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 12 different batches.
- 22 331 spectra from a total of 428 batches from further 116 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1080 spectra of 23 reference samples from the substance/substance group *Pea protein complex (H1428) / Amino V complex (H1400)*.

- Among them are spectra of independent samples from 23 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Amino V complex (H1400)	15001365(F2)	80745	60
Hepart	Amino V complex (H1400)	15001365(B1)	80746	60
Hepart	Amino V complex (H1400)	15001366(MM)	80747	60
Hepart	Amino V complex (H1400)	15001366(F2)	80748	60
Hepart	Amino V complex (H1400)	15001366	80884	40
Hepart	Amino V complex (H1400)	18000192	80996	40
Hepart	Amino V complex (H1400)	17001819	80997	40
Hepart	Amino V complex (H1400)	18000195	80998	40
Hepart	Amino V complex (H1400)	18000193	80999	40
Hepart	Amino V complex (H1400)	18000822	81052	40
Hepart	Amino V complex (H1400)	18000823	81053	40
Hepart	Amino V complex (H1400)	18000824	81054	40
Hepart	Amino V complex (H1400)	18000825	81066	40
Hepart	Amino V complex (H1400)	18000826	81067	40
Hepart	Amino V complex (H1400)	18001324	81100	40
Hepart	Amino V complex (H1400)	18001328	81101	40
Hepart	Amino V complex (H1400)	18001675	81122	60
Hepart	Amino V complex (H1400)	18001674	81123	60
Hepart	Amino V complex (H1400)	18001575	81124	60
Hepart	Amino V complex (H1400)	18001676	81125	60
Hepart	Pea protein complex (H1428)	18001020	81076	40
Hepart	Pea protein complex (H1428)	20000371	81236	40
Hepart	Pea protein complex (H1428)	20000372	81237	40

- 19674 spectra from a total of 424 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Pea protein complex (H1428) / Amino V complex (H1400)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pea protein complex (H1428) / 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 *Pea protein complex (H1428) / Amino V complex (H1400)* and it was evaluated how many

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

	False positive	True positive	False negative	True negative
Type A	0	520	0	22 331
Type B	0	1080	0	19 674
Type C	0	0	0	1887

The substance/substance group *Pea protein complex (H1428) / Amino V complex (H1400)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9307 %)	100.0000 % (> 98.8462 %)
Type B	100.0000 % (> 99.8801 %)	100.0000 % (> 99.4444 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pea protein complex (H1428) / Amino V complex (H1400)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	19.88	—
Lupin protein complex (H1427)	31.48	—
Pumpkin protein (H1429)	37.90	—
Coenzyme Q10 (H1013)	41.68	—
Glutamine (L-) (H1043)	53.64	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pea protein complex (H1428) / Amino V complex (H1400)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80749	80749	0.00	23.27
80750	80750	0.00	23.34
81220	81220	0.00	22.14
80820	80820	0.00	23.99
80821	80821	0.00	24.48
81007	81007	0.00	21.01
80995	80995	0.00	22.32
81051	81051	0.00	22.41
81006	81006	0.00	19.88
81075	81075	0.00	20.86
80885	80885	0.00	22.72
80862	80862	0.00	21.77

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **PET basis (H1503)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80566-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
PET basis (H1503)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET basis (H1503)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *PET basis (H1503)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET basis (H1503)	15000402	80566	60	from supplier
Hepart	PET basis (H1503)	15000402	80636	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *PET basis (H1503)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 731 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *PET basis (H1503)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET basis (H1503)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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
Type A	0	120	0	22 731
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *PET basis (H1503)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *PET basis (H1503)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
PET joints (H1501)	19.59	—
Antioxidants NAT complex (H1004)	22.60	—

continued on the next page

continued from previous page

Substanz	Distance in main model	Distance in second-stage model
PET well-aging (H1500)	25.86	—
Ginkgo (H1024)	30.03	—
Vitamin B1 (H1101)	30.99	—
PET immune system (H1502)	31.09	—
Rhodiola (H1064)	36.10	—
Yeast organic (H1007)	40.39	—
Antibiosis forte complex (H1115)	45.39	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET basis (H1503)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80566	80566	0.00	28.13
80636	80636	0.00	19.59

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **PET coenzyme Q10 (H0022)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80561-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
PET coenzyme Q10 (H0022)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET coenzyme Q10 (H0022)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *PET coenzyme Q10 (H0022)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET coenzyme Q10...	15000401	80561	60	from supplier
Hepart	PET coenzyme Q10...	15000401	80635	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *PET coenzyme Q10 (H0022)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 731 spectra from a total of 440 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *PET coenzyme Q10 (H0022)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET coenzyme Q10 (H0022)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *PET coenzyme Q10 (H0022)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET coenzyme Q10 (H0022)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	22 731
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *PET coenzyme Q10 (H0022)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *PET coenzyme Q10 (H0022)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Vitamin E NAT (H1107)	12.74	—
Ginseng (H1018)	13.53	—

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Substanz	Distance in main model	Distance in second-stage model
Flavour orange (H1405)	30.76	—
Coenzyme Q10 (H1013)	32.31	—
Vitamin K2 (75µg Mono) (H1108)	44.85	—
Antioxidants NAT complex (H1004)	46.61	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET coenzyme Q10 (H0022)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80635	80635	0.00	19.31
80561	80561	0.00	21.63

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **PET immune system (H1502)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80564-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
PET immune system (H1502)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET immune system (H1502)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *PET immune system (H1502)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET immune syste...	15000405	80564	60	from supplier
Hepart	PET immune syste...	15000405	80634	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *PET immune system (H1502)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 731 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *PET immune system (H1502)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET immune system (H1502)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *PET immune system (H1502)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET immune system (H1502)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	22 731
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *PET immune system (H1502)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *PET immune system (H1502)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
PET basis (H1503)	24.35	—
Ginkgo (H1024)	28.71	—

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Substanz	Distance in main model	Distance in second-stage model
PET well-aging (H1500)	36.23	—
Stomach complex (H1120)	39.00	—
Chia protein (H1431)	39.19	—
Yeast organic (H1007)	43.84	—
Antibiosis forte complex (H1115)	45.60	—
Antioxidants NAT complex (H1004)	48.17	—
PET joints (H1501)	55.43	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET immune system (H1502)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80564	80564	0.00	25.91
80634	80634	0.00	24.35

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **PET joints (H1501)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80567-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
PET joints (H1501)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET joints (H1501)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *PET joints (H1501)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET joints (H1501)	15000404	80567	60	from supplier
Hepart	PET joints (H1501)	15000404	80630	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *PET joints (H1501)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 731 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *PET joints (H1501)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET joints (H1501)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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
Type A	0	120	0	22 731
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *PET joints (H1501)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *PET joints (H1501)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
PET basis (H1503)	15.50	—
Antioxidants NAT complex (H1004)	15.99	—

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Substanz	Distance in main model	Distance in second-stage model
Coenzyme Q10 (H1013)	31.95	—
Rhodiola (H1064)	34.81	—
Calcium (H1008)	39.05	—
Flavour orange (H1405)	42.70	—
PET well-aging (H1500)	44.33	—
Antibiosis forte complex (H1115)	48.54	—
Glutamine (L-) (H1043)	49.72	—
Vitamin B1 (H1101)	50.11	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET joints (H1501)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80567	80567	0.00	15.50
80630	80630	0.00	17.67

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **PET skin and hair (H1504)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80565-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
PET skin and hair (H1504)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET skin and hair (H1504)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *PET skin and hair (H1504)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET skin and hai...	15000403	80565	60	from supplier
Hepart	PET skin and hai...	15000403	80633	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *PET skin and hair (H1504)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 731 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *PET skin and hair (H1504)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET skin and hair (H1504)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *PET skin and hair (H1504)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *PET skin and hair (H1504)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	22 731
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *PET skin and hair (H1504)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *PET skin and hair (H1504)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	49.94	—
a-Lipoic acid (H1000)	73.14	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET skin and hair (H1504)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80565	80565	0.00	50.75
80633	80633	0.00	49.94

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **PET well-aging (H1500)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80563-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
PET well-aging (H1500)	2	0	0

Second-stage model

For differentiation of the substance/substance group *PET well-aging (H1500)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *PET well-aging (H1500)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET well-aging (...)	15000401	80563	60	from supplier
Hepart	PET well-aging (...)	15000406	80631	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *PET well-aging (H1500)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 731 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *PET well-aging (H1500)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *PET well-aging (H1500)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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
Type A	0	120	0	22 731
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *PET well-aging (H1500)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *PET well-aging (H1500)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
PET basis (H1503)	14.50	—
PET joints (H1501)	28.34	—

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Substanz	Distance in main model	Distance in second-stage model
Vitamin B1 (H1101)	28.41	—
Antioxidants NAT complex (H1004)	29.40	—
Rhodiola (H1064)	30.80	—
Ginkgo (H1024)	32.90	—
PET immune system (H1502)	34.30	—
Antibiosis forte complex (H1115)	46.01	—
Green coffee extract (H1433)	46.72	—
Calcium (H1008)	47.51	—
Flavour orange (H1405)	48.27	—
Vitamins BAG (H1090)	49.30	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET well-aging (H1500)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80563	80563	0.00	15.96
80631	80631	0.00	14.50

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Phenylalanine (L-) (H1049)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80090-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Phenylalanine (L-) (H1049)	3	1	8

Second-stage model

For differentiation of the substance/substance group *Phenylalanine (L-) (H1049)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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
Hepart	Phenylalanine (L...	19000779	81167	40	from supplier

Validation samples

A total of 45 492 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 *Phenylalanine (L-) (H1049)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 731 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Phenylalanine (L-) (H1049)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Phenylalanine (L-) (H1049)	17000876	80916	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 20 spectra from 6 *Apo-Ident* customers from 9 batches from the substance/substance group *Phenylalanine (L-) (H1049)*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Phenylalanine (L-) (H1049)	17000876	1
Hepart	Phenylalanine (L-) (H1049)	170008760	3
Hepart	Phenylalanine (L-) (H1049)	17000876/1	3
Hepart AG	Phenylalanine (L-) (H1049)	74401/1	1
Hepart AG	Phenylalanine (L-) (H1049)	17000876/0	1
Unisan	Phenylalanine (L-) (H1049)	25009	7
Unisan	Phenylalanine (L-) (H1049)	74401/0	1
Unisan	Phenylalanine (L-) (H1049)	16001096	2
Unisan/Hepart AG	Phenylalanine (L-) (H1049)	1828025009	1

- 1867 spectra from 19 *Apo-Ident* customers from a total of 850 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 *Phenylalanine (L-) (H1049)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Phenylalanine (L-) (H1049)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	22 731
Type B	0	40	0	20 714
Type C	0	11	9	1867

The substance/substance group *Phenylalanine (L-) (H1049)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7300 %)	55.0000 % (> 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.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Phenylalanine (L-) (H1049)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tryptophan (L-) (H1053)	24.50	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Phenylalanine (L-) (H1049)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80400	80400	0.00	39.86
80852	80852	0.00	38.84
81167	81167	0.00	39.41

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Pomegranate (H1409)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81035-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pomegranate (H1409)

Special notes

When selecting the *Pomegranate (H1409)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Pomegranate (H1409)	1	1	0

Second-stage model

For differentiation of the substance/substance group *Pomegranate (H1409)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pomegranate (H1409)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Pomegranate (H14...	18000566/0	81035	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Pomegranate (H1409)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Pomegranate (H1409)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Pomegranate (H1409)	18001310	81086	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were

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

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Pomegranate (H1409)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pomegranate (H1409)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pomegranate (H1409)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	29	11	20 714
Type C	0	0	0	1887

The substance/substance group *Pomegranate (H1409)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8834 %)	72.5000 % (> 65.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pomegranate (H1409)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cabbage extract (H1121)	24.20	—
Vitamin B1 (H1101)	27.94	—
Calcium (H1008)	28.92	—
Flavour orange (H1405)	32.91	—
Antioxidants NAT complex (H1004)	35.66	—
Marshmallow extract (H1439)	37.47	—
Ginseng (H1018)	38.02	—
Glutathione (H1020)	41.27	—
Gentian extract (H1438)	45.24	—
Creatine (H1031)	45.96	—
Baobab (H1410)	47.49	—
Silymarin (H1071)	49.93	—
OPC Grape seed (H1066)	50.23	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pomegranate (H1409)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81035	81035	0.00	24.20

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Potassium (H1030)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80043-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Potassium (H1030)	7	11	21

Second-stage model

For differentiation of the substance/substance group *Potassium (H1030)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Potassium (H1030)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Potassium (H1030)	039302	80372	40	from supplier
Hepart	Potassium (H1030)	15000597	80571	60	from supplier
Hepart	Potassium (H1030)	15000598(B1)	80574	60	from supplier
Hepart	Potassium (H1030)	15000599	80576	60	from supplier
Hepart	Potassium (H1030)	15000600	80578	60	from supplier
Hepart	Potassium (H1030)	16001645	80868	40	from supplier
Hepart	Potassium (H1030)	19000026	81154	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 7 reference samples from the substance/substance group *Potassium (H1030)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 22 491 spectra from a total of 433 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 530 spectra of 11 reference samples from the substance/substance group *Potassium (H1030)*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Potassium (H1030)	130328001	80347	40
Hepart	Potassium (H1030)	069201	80376	30
Hepart	Potassium (H1030)	15000597(B1)	80572	60
Hepart	Potassium (H1030)	15000598	80573	60
Hepart	Potassium (H1030)	15000598(F2)	80575	60
Hepart	Potassium (H1030)	15000599(F2)	80577	60
Hepart	Potassium (H1030)	15000600(B1)	80579	60
Hepart	Potassium (H1030)	16001646	80869	40
Hepart	Potassium (H1030)	16001647	80870	40
Hepart	Potassium (H1030)	19000027	81155	40
Hepart	Potassium (H1030)	19000028	81156	40

- 20 224 spectra from a total of 436 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 56 spectra from 12 *Apo-Ident* customers from 24 batches from the substance/substance group *Potassium (H1030)*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Potassium (H1030)	39301	1
HCK	Potassium (H1030)	15000599	1
Hepart	Potassium (H1030)	15000599/1	1
Hepart	Potassium (H1030)	15000598	1
Hepart	Potassium (H1030)	16001646	1
Hepart / Unisan	Potassium (H1030)	160016460	1
Hepart AG	Potassium (H1030)	1124944201	1
Hepart AG	Potassium (H1030)	1124028903	1
Hepart AG	Potassium (H1030)	39302	1
Hepart AG	Potassium (H1030)	39301	1
Hepart AG	Potassium (H1030)	15000597/0	1
Hepart AG	Potassium (H1030)	16001645/0	4
Hepart AG	Potassium (H1030)	16001646/0	5
Unisan	Potassium (H1030)	944201	3
Unisan	Potassium (H1030)	288903	1
Unisan	Potassium (H1030)	39301	8
Unisan	Potassium (H1030)	28903	1
Unisan	Potassium (H1030)	1124944201	1
Unisan	Potassium (H1030)	130328001	3
Unisan	Potassium (H1030)	69201	3
Unisan	Potassium (H1030)	39302	1
Unisan	Potassium (H1030)	69301	3
Unisan	Potassium (H1030)	69401	1
Unisan	Potassium (H1030)	15000597/0	1
Unisan	Potassium (H1030)	69401/0	1
Unisan	Potassium (H1030)	15000597/1	1
Unisan	Potassium (H1030)	15000599/0	1

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Supplier	Substance	Batch	Spectra
Unisan	Potassium (H1030)	15000599	1
Unisan	Potassium (H1030)	15000598	1
Unisan	Potassium (H1030)	15000600	2
UNISAN	Potassium (H1030)	69201	1
Unisan/Hepart AG	Potassium (H1030)	39302	1
Hepart	Potassium (H1030)	16001645	1

- 1831 spectra from 19 *Apo-Ident* customers from a total of 835 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 *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	360	0	22 491
Type B	0	529	1	20 224
Type C	0	49	7	1831

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 % (> 99.9308 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.8802 %)	99.8113 % (> 99.2453 %)
Type C	100.0000 % (> 98.7205 %)	87.5000 % (> 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.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Potassium (H1030)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	31.14	—
Iron (H1015)	38.33	—
Calcium (H1008)	48.12	—
Vitamin C (H1104)	54.25	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Potassium (H1030)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80868	80868	0.00	51.20
80372	80372	0.00	38.73
81154	81154	0.00	46.34
80571	80571	0.00	49.90
80574	80574	0.00	51.10
80576	80576	0.00	51.64
80578	80578	0.00	51.12

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Proline (-L) NF (H1050)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80905-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Proline (-L) NF (H1050)	3	0	0

Second-stage model

For differentiation of the substance/substance group *Proline (-L) NF (H1050)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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
Hepart	Proline (-L) NF ...	16000951	81146	40	from supplier

Validation samples

A total of 45 492 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 *Proline (-L) NF (H1050)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 731 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Proline (-L) NF (H1050)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

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

- 20 674 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 2 spectra from 2 *Apo-Ident* customers from 1 batches from the substance/substance group *Proline (-L) NF (H1050)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Proline (-L) NF (H1050)	17000952	2

- 1885 spectra from 19 *Apo-Ident* customers from a total of 858 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
Type A	0	120	0	22 731
Type B	0	34	46	20 674
Type C	0	2	0	1885

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
Type A	100.0000 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8817 %)	42.5000 % (> 38.7500 %)
Type C	100.0000 % (> 98.8633 %)	n/a (n/a)

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

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Proline (-L) NF (H1050)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	26.59	—
Yeast organic (H1007)	69.60	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Proline (-L) NF (H1050)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80935	80935	0.00	29.38
81146	81146	0.00	26.59
81023	81023	0.00	32.98

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Psyllium husks (H1432)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81012-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Psyllium husks (H1432)

Special notes

When selecting the *Psyllium husks (H1432)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Psyllium husks (H1432)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Psyllium husks (H1432)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Psyllium husks (H1432)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Psyllium husks (...)	17001728	81012	40	from supplier
Hepart	Psyllium husks (...)	19000338/0	81161	40	from supplier

Validation samples

A total of 45 492 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 *Psyllium husks (H1432)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Psyllium husks (H1432)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Psyllium husks (H1432)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Psyllium husks (H1432)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Psyllium husks (H1432)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Psyllium husks (H1432)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Psyllium husks (H1432)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Vitamin B1 (H1101)	28.94	—
Ginseng (H1018)	30.66	—

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Substanz	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	32.74	—
Saffron flowers (H1435)	33.08	—
Garcinia cambogia (H1017)	37.13	—
Iron (H1015)	39.80	—
Orthovimin Neutral Complex (H1403)	40.35	—
Marshmallow extract (H1439)	46.56	—
Juniper (H1112)	53.47	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Psyllium husks (H1432)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81161	81161	0.00	39.42
81012	81012	0.00	33.08

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Pumpkin protein (H1429)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81010-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pumpkin protein (H1429)

Special notes

When selecting the *Pumpkin protein (H1429)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Pumpkin protein (H1429)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Pumpkin protein (H1429)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pumpkin protein (H1429)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Pumpkin protein ...	17001731	81010	40	from supplier
Hepart	Pumpkin protein ...	19000340/0	81164	40	from supplier

Validation samples

A total of 45 492 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 *Pumpkin protein (H1429)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Pumpkin protein (H1429)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Pumpkin protein (H1429)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pumpkin protein (H1429)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pumpkin protein (H1429)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Pumpkin protein (H1429)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pumpkin protein (H1429)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glutamine (L-) (H1043)	25.41	—
Antibiosis forte complex (H1115)	27.57	—

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Substanz	Distance in main model	Distance in second-stage model
Amino V complex (H1400)	31.23	—
Aminomix NAC (H1002)	33.32	—
Lupin protein complex (H1427)	34.21	—
Pea protein complex (H1428)	38.39	—
Antioxidants NAT complex (H1004)	42.95	—
Coenzyme Q10 (H1013)	45.77	—
Hemp protein (H1406)	45.84	—
PET skin and hair (H1504)	47.94	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pumpkin protein (H1429)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81010	81010	0.00	27.57
81164	81164	0.00	27.70

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Saffron style (H1434)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81090-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Saffron style (H1434)

Special notes

When selecting the *Saffron style (H1434)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Saffron style (H1434)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Saffron style (H1434)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Saffron style (H1434)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Saffron style (H...	18001093	81090	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Saffron style (H1434)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 0 spectra of 0 reference samples from the substance/substance group *Saffron style (H1434)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.
- 20 754 spectra from a total of 447 batches from further 92 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Saffron style (H1434)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Saffron style (H1434)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Saffron style (H1434)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	0	0	20 754
Type C	0	0	0	1887

The substance/substance group *Saffron style (H1434)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8835 %)	n/a (n/a)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Saffron style (H1434)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Vitamin K2 (75µg Mono) (H1108)	14.40	—
Ginseng (H1018)	15.66	—

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Substanz	Distance in main model	Distance in second-stage model
Marshmallow extract (H1439)	16.78	—
Ginger extract (H1437)	17.24	—
Gentian extract (H1438)	19.16	—
Lycopene (H1058)	26.90	—
Detox complex (H1118)	27.60	—
Baobab (H1410)	28.19	—
Boron (H1005)	28.37	—
Orthovimin Neutral Complex (H1403)	29.08	—
Zinc (H1110)	29.51	—
Silicium (H1070)	29.89	—
Vitamin E NAT (H1107)	32.47	—
Coenzyme Q10 (H1013)	32.53	—
Folic acid (H1016)	33.04	—
Enzyme complex (H1118)	33.13	—
Antioxidants NAT complex (H1004)	33.30	—
PET coenzyme Q10 (H0022)	33.95	—
Vitamin B1 (H1101)	35.54	—
Juniper (H1112)	35.76	—
Psyllium husks (H1432)	36.21	—
Calcium (H1008)	39.10	—
Biotin (H1007)	41.09	—
Selenium yeast (H1068)	43.73	—
Garcinia cambogia (H1017)	45.22	—
Saffron flowers (H1435)	46.28	—
Acacia gum (H1001)	47.32	—
Artichoke extract (H1440)	50.82	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Saffron style (H1434)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81090	81090	0.00	14.40

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

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Silicium (H1070)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80906-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Silicium (H1070)	4	3	0

Second-stage model

For differentiation of the substance/substance group *Silicium (H1070)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Silicium (H1070)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Silicium (H1070)	17000817	80914	40	from supplier
Hepart	Silicium (H1070)	18000448	81022	30	from supplier
Hepart	Silicium (H1070)	18001681	81127	40	from supplier
Hepart	Silicium (H1070)	19001317	81205	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 150 spectra of 4 reference samples from the substance/substance group *Silicium (H1070)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 701 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 130 spectra of 4 reference samples from the substance/substance group *Silicium (H1070)*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Silicium (H1070)	17000326	80906	40
Hepart	Silicium (H1070)	19000534	81184	40
Hepart	Silicium (H1070)	20001082	81265	40

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Silicium (H1070)	18000448	81022 [†]	10

- 20 624 spectra from a total of 443 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Silicium (H1070)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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
Type A	0	150	0	22 701
Type B	0	90	40	20 624
Type C	0	0	0	1887

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
Type A	100.0000 % (> 99.9312 %)	100.0000 % (> 96.0000 %)
Type B	100.0000 % (> 99.8810 %)	69.2308 % (> 66.9231 %)
Type C	100.0000 % (> 98.7704 %)	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

[†]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*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Silicium (H1070)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Boron (H1005)	10.25	—
Marshmallow extract (H1439)	21.24	—
Baobab (H1410)	22.17	—
Orthovimin Neutral Complex (H1403)	25.41	—
Detox complex (H1118)	25.45	—
Saffron style (H1434)	25.90	—
Calcium (H1008)	30.77	—
Ginseng (H1018)	31.70	—
Zinc (H1110)	31.73	—
Antioxidants NAT complex (H1004)	32.85	—
Ginger extract (H1437)	34.22	—
Gentian extract (H1438)	34.63	—
Folic acid (H1016)	37.19	—
Lycopene (H1058)	38.28	—
Selenium yeast (H1068)	39.07	—
PET coenzyme Q10 (H0022)	39.45	—
Vitamin B1 (H1101)	39.88	—
Juniper (H1112)	40.70	—
Vitamin K2 (75µg Mono) (H1108)	41.01	—
Coenzyme Q10 (H1013)	42.75	—
Konjac (H1426)	42.87	—
Vitamin E NAT (H1107)	43.11	—
Trace elements JK (H1080)	43.59	—
Garcinia cambogia (H1017)	45.69	—
Magnesium (H1060)	46.60	—
Psyllium husks (H1432)	48.40	—
Acacia gum (H1001)	49.06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Silicium (H1070)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81205	81205	0.00	10.25
80914	80914	0.00	11.72

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81127	81127	0.00	10.59
81022	81022	0.00	14.77

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Silymarin (H1071)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80068-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Silymarin (H1071)	2	2	11

Second-stage model

For differentiation of the substance/substance group *Silymarin (H1071)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Silymarin (H1071)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Silymarin (H1071)	15001046	80671	60	from supplier
Hepart	Silymarin (H1071)	16001084	80861	40	from supplier

Validation samples

A total of 45 492 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 *Silymarin (H1071)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 751 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Silymarin (H1071)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Silymarin (H1071)	067701	80375	40
Hepart	Silymarin (H1071)	16001084/0	81159	40

- 20 674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 22 spectra from 9 *Apo-Ident* customers from 12 batches from the substance/substance group *Silymarin (H1071)*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Silymarin (H1071)	15001046/0	1
hepart ag	Silymarin (H1071)	1244950401	1
Hepart AG	Silymarin (H1071)	1244029901	1
Hepart AG	Silymarin (H1071)	67701	1
Hepart AG, CH-8280 Kreu...	Silymarin (H1071)	1241950401	1
Hepart AG, CH-8280 Kreu...	Silymarin (H1071)	1241046101	1
Hepart AG, CH-8280 Kreu...	Silymarin (H1071)	29901	2
Unisan	Silymarin (H1071)	46101	1
Unisan	Silymarin (H1071)	950401	1
Unisan	Silymarin (H1071)	29901	3
Unisan	Silymarin (H1071)	67701	2
Unisan	Silymarin (H1071)	67701/7	1
Unisan	Silymarin (H1071)	15001046	2
Unisan	Silymarin (H1071)	15001046/1	1
UNISAN	Silymarin (H1071)	67701	1
Unisan/Hepart AG	Silymarin (H1071)	29901	1
Hepart	Silymarin (H1071)	15001046	1

- 1865 spectra from 19 *Apo-Ident* customers from a total of 847 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 *Silymarin (H1071)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Silymarin (H1071)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	100	0	22 751
Type B	0	80	0	20 674
Type C	0	15	7	1865

The substance/substance group *Silymarin (H1071)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9315 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8817 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7286 %)	68.1818 % (> 54.5455 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Silymarin (H1071)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	17.60	—
Calcium (H1008)	19.74	—
OPC Grape seed (H1066)	21.53	—
Coenzyme Q10 (H1013)	22.85	—
Betaine hydrochloride (H1119)	23.36	—
Rhodiola (H1064)	26.45	—
Orthocolon complex (H1800)	29.57	—
Carnitine (L-) (H1038)	30.67	—
Garcinia cambogia (H1017)	35.83	—
Sunflower protein (H1430)	37.57	—
Ginkgo (H1024)	42.55	—
Vitamin B1 (H1101)	44.47	—
Broccoli (H1415)	46.75	—
L-5-HTP (H1035)	47.65	—
Isoflavones (H1025)	47.99	—
PET basis (H1503)	48.23	—
Antibiosis forte complex (H1115)	49.12	—
Bioflavonoid complex (H1006)	49.62	—
Orthovimin Neutral Complex (H1403)	50.65	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Silymarin (H1071)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80671	80671	0.00	32.19
80861	80861	0.00	25.95

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Stomach complex (H1120)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80666-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Stomach complex (H1120)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Stomach complex (H1120)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Stomach complex (H1120)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Stomach complex ...	15001350	80666	60	from supplier
Hepart	Stomach complex ...	16001138	80888	40	from supplier

Validation samples

A total of 45 492 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 *Stomach complex (H1120)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 751 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Stomach complex (H1120)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Stomach complex (H1120)	16001139	80889	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Stomach complex (H1120)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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
Type A	0	100	0	22 751
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Stomach complex (H1120)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9315 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Stomach complex (H1120)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
PET immune system (H1502)	24.86	—
Yeast organic (H1007)	25.01	—
PET basis (H1503)	30.62	—
Antioxidants NAT complex (H1004)	31.46	—
Antibiosis forte complex (H1115)	38.68	—
Carnitine (L-) (H1038)	46.87	—
Coenzyme Q10 (H1013)	49.35	—
Hemp protein (H1406)	49.78	—
Vitamin B1 (H1101)	54.16	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Stomach complex (H1120)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80888	80888	0.00	26.56
80666	80666	0.00	24.86

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Sunflower protein (H1430)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 81011-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sunflower protein (H1430)

Special notes

When selecting the *Sunflower protein (H1430)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sunflower protein (H1430)	1	1	0

Second-stage model

For differentiation of the substance/substance group *Sunflower protein (H1430)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sunflower protein (H1430)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Sunflower protei...	17001730	81011	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 40 spectra of 1 reference samples from the substance/substance group *Sunflower protein (H1430)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 811 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Sunflower protein (H1430)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Sunflower protein (H1430)	19000339/0	81163	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Sunflower protein (H1430)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sunflower protein (H1430)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sunflower protein (H1430)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	22 811
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Sunflower protein (H1430)* can be clearly distinguished from all other substances. In order 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 % (> 99.9328 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sunflower protein (H1430)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	23.30	—
Coenzyme Q10 (H1013)	27.78	—
Carnitine (L-) (H1038)	28.46	—
Vitamin B1 (H1101)	37.07	—
Isoflavones (H1025)	37.11	—
Calcium (H1008)	38.26	—
Flavour orange (H1405)	40.56	—
Antibiosis forte complex (H1115)	40.81	—
Silymarin (H1071)	41.18	—
Leaky gut complex (H1802)	42.51	—
PET joints (H1501)	49.49	—
Aminomix NAC (H1002)	50.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sunflower protein (H1430)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81011	81011	0.00	37.11

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Taurine (H1084)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80071-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Taurine (H1084)	3	2	11

Second-stage model

For differentiation of the substance/substance group *Taurine (H1084)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Taurine (H1084)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Taurine (H1084)	14001767	80497	60	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 45 492 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 *Taurine (H1084)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 671 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Taurine (H1084)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Taurine (H1084)	16000947	80810	40
Hepart	Taurine (H1084)	19000847	81160	40

- 20 674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 37 spectra from 12 *Apo-Ident* customers from 13 batches from the substance/substance group *Taurine (H1084)*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Taurine (H1084)	16000947	4
Hepart	Taurine (H1084)	160009470	1
Hepart AG	Taurine (H1084)	28001	2
Hepart AG	Taurine (H1084)	14001767/3	4
Hepart AG	Taurine (H1084)	16000947/0	1
Hepart AG	Taurine (H1084)	2656905/0	2
Hepart AG	Taurine (H1084)	16000947/2	2
Hepart AG, CH-8280 Kreu...	Taurine (H1084)	25710	3
Hepart/Unisan	Taurine (H1084)	14001767/3	1
unisan	Taurine (H1084)	14001767	2
Unisan	Taurine (H1084)	1294960201	2
Unisan	Taurine (H1084)	28001	8
Unisan	Taurine (H1084)	14001767/0	1
Unisan	Taurine (H1084)	16000946/1	1
Unisan	Taurine (H1084)	16000946	1
Unisan/Hepart AG	Taurine (H1084)	28001	1
Hepart	Taurine (H1084)	16000946	1

- 1850 spectra from 19 *Apo-Ident* customers from a total of 846 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 *Taurine (H1084)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Taurine (H1084)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	22 671
Type B	0	80	0	20 674
Type C	0	22	15	1850

The substance/substance group *Taurine (H1084)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9311 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8817 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7232 %)	59.4595 % (> 51.3514 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Taurine (H1084)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antibiosis forte complex (H1115)	59.21	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Taurine (H1084)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80809	80809	0.00	61.51
81063	81063	0.00	60.01
80887	80887	0.00	61.02
80497	80497	0.00	59.21

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Threonine (L-) (H1052)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80107-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Threonine (L-) (H1052)	1	2	7

Second-stage model

For differentiation of the substance/substance group *Threonine (L-) (H1052)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Threonine (L-) (H1052)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Threonine (L-) (...)	14001718	80496	60	from supplier
Hepart	Threonine (L-) (...)	14001718	81018	40	from supplier

Validation samples

A total of 45 492 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 *Threonine (L-) (H1052)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 751 spectra from a total of 439 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Threonine (L-) (H1052)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Threonine (L-) (H1052)	17000875	80920	40
Hepart	Threonine (L-) (H1052)	18001023	81077	40

- 20 674 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 14 spectra from 7 *Apo-Ident* customers from 8 batches from the substance/substance group *Threonine (L-) (H1052)*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Threonine (L-) (H1052)	14001718/9	1
Hepart	Threonine (L-) (H1052)	17000875	1
Hepart AG	Threonine (L-) (H1052)	25708	3
Hepart/Unisan	Threonine (L-) (H1052)	14001718/3	1
Purren Apotheke	Threonine (L-) (H1052)	1833014901	1
unisan	Threonine (L-) (H1052)	25708	1
Unisan	Threonine (L-) (H1052)	25708	1
Unisan	Threonine (L-) (H1052)	14001718/1	1
Unisan	Threonine (L-) (H1052)	14001718	2
Unisan	Threonine (L-) (H1052)	14001718/7	1
UNISAN	Threonine (L-) (H1052)	25708	1

- 1873 spectra from 19 *Apo-Ident* customers from a total of 851 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 *Threonine (L-) (H1052)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Threonine (L-) (H1052)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	100	0	22 751
Type B	0	80	0	20 674
Type C	0	8	6	1873

The substance/substance group *Threonine (L-) (H1052)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9315 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8817 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7363 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Threonine (L-) (H1052)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine (H1021)	47.38	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Threonine (L-) (H1052)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80496	80496	0.00	54.17
81018	81018	0.00	57.46

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Trace elements BAG (H1078) / Zinc (H1110)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80503-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Trace elements BAG (H1078) / Zinc (H1110); Trace elements BAG (H1078); Zinc (H1110)

Special notes

When selecting the *Trace elements BAG (H1078) / Zinc (H1110)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Trace elements BAG (H1078)	2	1	0
Zinc (H1110)	5	2	12

Second-stage model

For differentiation of the substance/substance group *Trace elements BAG (H1078) / Zinc (H1110)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Trace elements BAG (H1078) / Zinc (H1110)*:

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
Hepart	Zinc (H1110)	14001803	80503	60	from supplier
Hepart	Zinc (H1110)	16000196	80761	60	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 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Trace elements BAG (H1078) / Zinc (H1110)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 22 531 spectra from a total of 433 batches from further 116 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 140 spectra of 3 reference samples from the substance/substance group *Trace elements BAG (H1078) / Zinc (H1110)*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Trace elements BAG (H1078)	16000797	80801	40
Hepart	Zinc (H1110)	14001753	80489	60
Hepart	Zinc (H1110)	16000519	80790	40

- 20614 spectra from a total of 444 batches from further 90 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 60 spectra from 12 *Apo-Ident* customers from 15 batches from the substance/substance group *Trace elements BAG (H1078) / Zinc (H1110)*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Zinc (H1110)	16000519	1
Hepart	Zinc (H1110)	16000519/0	1
Hepart AG	Zinc (H1110)	1164991001	3
Hepart AG	Zinc (H1110)	991001	3
Hepart AG	Zinc (H1110)	41501	7
Hepart AG	Zinc (H1110)	14001803/2	1
Hepart AG	Zinc (H1110)	16000518/1	1
Hepart AG	Zinc (H1110)	16000519/0	9
Hepart AG, CH-8280 Kreu...	Zinc (H1110)	1164991001	1
Hepart/Unisan	Zinc (H1110)	14001803/2	1
Unisan	Zinc (H1110)	1164991001	2
Unisan	Zinc (H1110)	991001	7
Unisan	Zinc (H1110)	41501	5
Unisan	Zinc (H1110)	14001803	3
Unisan	Zinc (H1110)	14001753/0	1
Unisan	Zinc (H1110)	14001753	1
Unisan	Zinc (H1110)	14001803/1	1
Unisan	Zinc (H1110)	16000196	3
Unisan	Zinc (H1110)	16000518	1
Unisan	Zinc (H1110)	1164949701	1
Unisan GmbH, 78465 Kons...	Zinc (H1110)	991001	1
Unisan/Hepart	Zinc (H1110)	16000196/0	2
Hepart	Zinc (H1110)	16000518	2
Hepart	Zinc (H1110)	16000196	2

- 1827 spectra from 19 *Apo-Ident* customers from a total of 844 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) / 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 *Trace elements BAG (H1078) / 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	320	0	22 531
Type B	0	140	0	20 614
Type C	0	60	0	1827

The substance/substance group *Trace elements BAG (H1078) / 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 % (> 99.9308 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.8809 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 98.7201 %)	100.0000 % (> 90.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Trace elements BAG (H1078) / Zinc (H1110)* in the substance class *HCK - nutritional supplements (Hep-art)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Folic acid (H1016)	15.38	—
Vitamin B12 (H1102)	16.20	—
Ginseng (H1018)	19.35	—
Selenium (H1067)	20.29	—
Orthovimin Neutral Complex (H1403)	20.56	—
Vitamin D3 (H1105)	26.55	—
Konjac (H1426)	29.03	—
Trace elements JK (H1080)	29.07	—
Biotin (H1007)	29.62	—
Chromium (H1012)	29.92	—
Psyllium husks (H1432)	34.27	—
Magnesium (H1060)	34.77	—
Selenium yeast (H1068)	35.60	—
Lycopene (H1058)	39.75	—
Boron (H1005)	45.62	—
Antioxidants NAT complex (H1004)	46.30	—
Vitamin E NAT (H1107)	46.70	—
Coenzyme Q10 (H1013)	49.52	—
Enzyme complex (H1118)	50.34	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Trace elements BAG (H1078) / Zinc (H1110)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80799	80799	0.00	20.56
80503	80503	0.00	15.31
80800	80800	0.00	21.00
80761	80761	0.00	18.20
81068	81068	0.00	16.36
81069	81069	0.00	21.41
80789	80789	0.00	16.01

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group	Trace elements JK (H1080)
Substance class	HCK - nutritional supplements (Hepart)
Report date	25/06/2020
Report number	80069-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Trace elements JK (H1080)	5	7	15

Second-stage model

For differentiation of the substance/substance group *Trace elements JK (H1080)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Trace elements J...	15000526	80766	60	from supplier
Hepart	Trace elements J...	18000455	81029	40	from supplier

Validation samples

A total of 45 492 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 *Trace elements JK (H1080)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 22 571 spectra from a total of 435 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 300 spectra of 7 reference samples from the substance/substance group *Trace elements JK (H1080)*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Trace elements JK (H1080)	15000525	80673	60
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

- 20 454 spectra from a total of 440 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 39 spectra from 12 *Apo-Ident* customers from 16 batches from the substance/substance group *Trace elements JK (H1080)*.
- Among them are spectra of independent samples from 15 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Trace elements JK (H1080)	15000526/0	1
Hepart	Trace elements JK (H1080)	15000529/0	1
Hepart	Trace elements JK (H1080)	17000869	1
Hepart	Trace elements JK (H1080)	17000869/0	1
Hepart AG	Trace elements JK (H1080)	1026011701	2
Hepart AG	Trace elements JK (H1080)	11701	8
Hepart AG	Trace elements JK (H1080)	72701	1
Hepart AG	Trace elements JK (H1080)	15000525	1
Hepart AG	Trace elements JK (H1080)	17000870/0	3
Hepart AG	Trace elements JK (H1080)	15000528/0	1
Hepart AG	Trace elements JK (H1080)	17000869	1
Hepart AG	Trace elements JK (H1080)	17000869/0	1
Unisan	Trace elements JK (H1080)	1026956901	1
Unisan	Trace elements JK (H1080)	11701	3
Unisan	Trace elements JK (H1080)	1026011701	1
Unisan	Trace elements JK (H1080)	1028956901	1
Unisan	Trace elements JK (H1080)	72701	1
Unisan	Trace elements JK (H1080)	15000525/0	1
Unisan	Trace elements JK (H1080)	15000526	1
Unisan	Trace elements JK (H1080)	72901	1
Unisan	Trace elements JK (H1080)	17000870	2
UNISAN	Trace elements JK (H1080)	72701	1
Unisan GmbH, 78465 Kons...	Trace elements JK (H1080)	1026011701	1
Unisan/Hepart AG	Trace elements JK (H1080)	11701	3

- 1848 spectra from 19 *Apo-Ident* customers from a total of 843 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 JK (H1080)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Trace elements JK (H1080)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	22 571
Type B	0	300	0	20 454
Type C	0	19	20	1848

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 % (> 99.9309 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.8804 %)	100.0000 % (> 98.0000 %)
Type C	100.0000 % (> 98.7228 %)	48.7179 % (> 41.0256 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Trace elements JK (H1080)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium (H1060)	12.62	—
Trace elements BAG (H1078)	29.37	—
Psyllium husks (H1432)	47.32	—
Antioxidants NAT complex (H1004)	59.87	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Trace elements JK (H1080)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80387	80387	0.00	27.09
80388	80388	0.00	25.42
80389	80389	0.00	27.51
80701	80701	0.00	25.45
81029	81029	0.00	26.74
80766	80766	0.00	27.24

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group	Trace elements SE (H1082)
Substance class	HCK - nutritional supplements (Hepart)
Report date	25/06/2020
Report number	80070-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Trace elements SE (H1082)	8	17	12

Second-stage model

For differentiation of the substance/substance group *Trace elements SE (H1082)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Trace elements S...	15000556(B1)	80592	60	from supplier
Hepart	Trace elements S...	15000557	80594	60	from supplier
Hepart	Trace elements S...	15000558	80597	60	from supplier
Hepart	Trace elements S...	15000553(B1)	80601	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 460 spectra of 9 reference samples from the substance/substance group *Trace elements SE (H1082)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 22 391 spectra from a total of 432 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 990 spectra of 21 reference samples from the substance/substance group *Trace elements SE (H1082)*.
- Among them are spectra of independent samples from 17 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Trace elements SE (H1082)	042301	80278	15
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(F2)	80593	60
Hepart	Trace elements SE (H1082)	15000557(B1)	80595	60
Hepart	Trace elements SE (H1082)	15000557(F2)	80596	60
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(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)	19001256	81186	40
Hepart	Trace elements SE (H1082)	19001260	81187	40
Hepart	Trace elements SE (H1082)	20000407	81260	40
Hepart	Trace elements SE (H1082)	042301	80290	15
Hepart	Trace elements SE (H1082)	14000722	80462	40
Hepart	Trace elements SE (H1082)	14000720	80463	40
Hepart	Trace elements SE (H1082)	15000558	80979	40

- 19764 spectra from a total of 427 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 37 spectra from 11 *Apo-Ident* customers from 16 batches from the substance/substance group *Trace elements SE (H1082)*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart AG	Trace elements SE (H1082)	42301	3
Hepart AG	Trace elements SE (H1082)	937201	4
Hepart AG	Trace elements SE (H1082)	31301	5
Hepart AG	Trace elements SE (H1082)	120435-14	1
Hepart AG	Trace elements SE (H1082)	14000720	2
Hepart AG	Trace elements SE (H1082)	41401	1
Hepart AG	Trace elements SE (H1082)	15000556	1
Hepart AG, CH-8280 Kreu...	Trace elements SE (H1082)	937201	1
Hepart AG, CH-8280 Kreu...	Trace elements SE (H1082)	31301	1
Unisan	Trace elements SE (H1082)	1024012401	1
Unisan	Trace elements SE (H1082)	937201	2
Unisan	Trace elements SE (H1082)	1024929202	1
Unisan	Trace elements SE (H1082)	31301	4
Unisan	Trace elements SE (H1082)	42301	1
Unisan	Trace elements SE (H1082)	14000720	1
Unisan	Trace elements SE (H1082)	14000721/0	1
Unisan	Trace elements SE (H1082)	14000721	1

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Supplier	Substance	Batch	Spectra
Unisan	Trace elements SE (H1082)	14000722	2
Unisan	Trace elements SE (H1082)	15000553	1
Unisan	Trace elements SE (H1082)	15000556/0	1
Unisan	Trace elements SE (H1082)	15000555	1
Unisan	Trace elements SE (H1082)	1024042301	1

- 1850 spectra from 19 *Apo-Ident* customers from a total of 844 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 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	460	0	22 391
Type B	0	960	30	19 764
Type C	0	12	25	1850

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 % (> 99.9308 %)	100.0000 % (> 98.6957 %)
Type B	100.0000 % (> 99.8801 %)	96.9697 % (> 96.6667 %)
Type C	100.0000 % (> 98.7232 %)	32.4324 % (> 24.3243 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Trace elements SE (H1082)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Copper (H1032)	22.00	—
Magnesium (H1060)	30.42	—
Iron (H1015)	31.45	—
Argentum (H1116)	39.00	—
Garcinia cambogia (H1017)	40.53	—
Walnut leaf (H1114)	49.96	—
Trace elements JK (H1080)	53.86	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Trace elements SE (H1082)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80588	80588	0.00	46.04
80592	80592	0.00	37.90
80594	80594	0.00	44.00
80597	80597	0.00	55.64
80601	80601	0.00	47.75
80459	80459	0.00	30.42
80460	80460	0.00	31.74
80461	80461	0.00	30.98
80464	80464	0.00	31.80

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Tryptophan (L-) (H1053)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80127-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tryptophan (L-) (H1053)	4	2	16

Second-stage model

For differentiation of the substance/substance group *Tryptophan (L-) (H1053)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tryptophan (L-) (H1053)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Tryptophan (L-) ...	074501	80401	40	from supplier
Hepart	Tryptophan (L-) ...	15000441	80581	60	from supplier
Hepart	Tryptophan (L-) ...	16001394	80845	40	from supplier
Hepart	Tryptophan (L-) ...	16001404	80846	40	from supplier

Validation samples

A total of 45 492 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 *Tryptophan (L-) (H1053)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 671 spectra from a total of 436 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 100 spectra of 2 reference samples from the substance/substance group *Tryptophan (L-) (H1053)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Tryptophan (L-) (H1053)	15000443	80582	60
Hepart	Tryptophan (L-) (H1053)	19001101	81219	40

- 20 654 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 35 spectra from 9 *Apo-Ident* customers from 19 batches from the substance/substance group *Tryptophan (L-) (H1053)*.
- Among them are spectra of independent samples from 16 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Tryptophan (L-) (H1053)	15000441/4	1
Caelo	Tryptophan (L-) (H1053)	15000443/0	1
HCK	Tryptophan (L-) (H1053)	15000441	1
HCK	Tryptophan (L-) (H1053)	16001404	1
Hepart	Tryptophan (L-) (H1053)	16001394/0	1
Hepart AG	Tryptophan (L-) (H1053)	1824027901	2
Hepart AG	Tryptophan (L-) (H1053)	27901	4
Hepart AG	Tryptophan (L-) (H1053)	27902	1
Hepart AG	Tryptophan (L-) (H1053)	16001404/3	3
Hepart AG	Tryptophan (L-) (H1053)	160001404/3	1
Hepart AG, CH-8280 Kreu...	Tryptophan (L-) (H1053)	27901	1
Purren Apotheke	Tryptophan (L-) (H1053)	1825950001	1
Purren Apotheke	Tryptophan (L-) (H1053)	978501	1
Unisan	Tryptophan (L-) (H1053)	1824950001	2
Unisan	Tryptophan (L-) (H1053)	950001	1
Unisan	Tryptophan (L-) (H1053)	27901	1
Unisan	Tryptophan (L-) (H1053)	27902	2
Unisan	Tryptophan (L-) (H1053)	74501	2
Unisan	Tryptophan (L-) (H1053)	150000441	1
Unisan	Tryptophan (L-) (H1053)	74501/4	1
Unisan	Tryptophan (L-) (H1053)	15000443/0	1
Unisan	Tryptophan (L-) (H1053)	15000443	2
Unisan	Tryptophan (L-) (H1053)	15000441/4	1
Unisan/Hepart AG	Tryptophan (L-) (H1053)	27901	1
unisan	Tryptophan (L-) (H1053)		1

- 1852 spectra from 19 *Apo-Ident* customers from a total of 841 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 *Tryptophan (L-) (H1053)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tryptophan (L-) (H1053)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect.

The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	22 671
Type B	0	100	0	20 654
Type C	0	16	19	1852

The substance/substance group *Tryptophan (L-) (H1053)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9311 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8813 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.7236 %)	45.7143 % (> 37.1429 %)

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.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tryptophan (L-) (H1053)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Phenylalanine (L-) (H1049)	33.07	–
Antibiosis forte complex (H1115)	74.55	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tryptophan (L-) (H1053)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80846	80846	0.00	60.53
80401	80401	0.00	35.11
80845	80845	0.00	60.88
80581	80581	0.00	47.44

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Tyrosine (L-) (H1054)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80121-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tyrosine (L-) (H1054)	3	1	8

Second-stage model

For differentiation of the substance/substance group *Tyrosine (L-) (H1054)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tyrosine (L-) (H1054)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Tyrosine (L-) (H...	074601	80386	100	from supplier
Hepart	Tyrosine (L-) (H...	15001380	80704	60	from supplier
Hepart	Tyrosine (L-) (H...	18000412	81050	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 3 reference samples from the substance/substance group *Tyrosine (L-) (H1054)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 651 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Tyrosine (L-) (H1054)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Tyrosine (L-) (H1054)	20000220	81267	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 17 spectra from 7 *Apo-Ident* customers from 8 batches from the substance/substance group *Tyrosine (L-) (H1054)*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Tyrosine (L-) (H1054)	1380	1
Hepart	Tyrosine (L-) (H1054)	18000412/0	2
Hepart AG	Tyrosine (L-) (H1054)	29502	1
Hepart AG	Tyrosine (L-) (H1054)	74601	1
Hepart AG	Tyrosine (L-) (H1054)	15001380/0	2
Unisan	Tyrosine (L-) (H1054)	29501	3
Unisan	Tyrosine (L-) (H1054)	29502	4
Unisan	Tyrosine (L-) (H1054)	979102	1
Unisan	Tyrosine (L-) (H1054)	74601/3	1
UNISAN	Tyrosine (L-) (H1054)	74601	1

- 1870 spectra from 19 *Apo-Ident* customers from a total of 851 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 *Tyrosine (L-) (H1054)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tyrosine (L-) (H1054)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	22 651
Type B	0	40	0	20 714
Type C	0	8	9	1870

The substance/substance group *Tyrosine (L-) (H1054)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9310 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7326 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tyrosine (L-) (H1054)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine (H1021)	66.25	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tyrosine (L-) (H1054)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80704	80704	0.00	87.66
81050	81050	0.00	83.13
80386	80386	0.00	84.88

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Valine (L-) (H1056)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80145-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Valine (L-) (H1056)	2	1	6

Second-stage model

For differentiation of the substance/substance group *Valine (L-) (H1056)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Valine (L-) (H1056)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Valine (L-) (H10...	14001947	80520	60	from supplier
Hepart	Valine (L-) (H10...	16001380/0	80844	40	from supplier

Validation samples

A total of 45 492 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 *Valine (L-) (H1056)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 751 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 60 spectra of 1 reference samples from the substance/substance group *Valine (L-) (H1056)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Valine (L-) (H1056)	15001436	80670	60

- 20 694 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 6 *Apo-Ident* customers from 8 batches from the substance/substance group *Valine (L-) (H1056)*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart AG	Valine (L-) (H1056)	1807025012	1
Hepart AG	Valine (L-) (H1056)	15001436	1
Hepart AG	Valine (L-) (H1056)	16001380/0	1
Purren Apotheke	Valine (L-) (H1056)	1807936701	1
Unisan	Valine (L-) (H1056)	25012	2
Unisan	Valine (L-) (H1056)	1807961101	2
Unisan	Valine (L-) (H1056)	15001436	2
Unisan	Valine (L-) (H1056)	15001436/1	1
Hepart AG	Valine (L-) (H1056)		1

- 1875 spectra from 19 *Apo-Ident* customers from a total of 851 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 *Valine (L-) (H1056)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Valine (L-) (H1056)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	100	0	22 751
Type B	0	48	12	20 694
Type C	0	11	1	1875

The substance/substance group *Valine (L-) (H1056)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9315 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8823 %)	80.0000 % (> 75.0000 %)
Type C	100.0000 % (> 98.7399 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Valine (L-) (H1056)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Isoleucine (L-) (H1045)	63.02	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Valine (L-) (H1056)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80520	80520	0.00	73.87
80844	80844	0.00	63.86

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Vitamin B6 (H1103)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80074-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Vitamin B6 (H1103)	3	1	11

Second-stage model

For differentiation of the substance/substance group *Vitamin B6 (H1103)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Vitamin B6 (H1103)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin B6 (H1103)	15000279	80550	60	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 45 492 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 *Vitamin B6 (H1103)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 671 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 100 spectra of 2 reference samples from the substance/substance group *Vitamin B6 (H1103)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin B6 (H1103)	19000782	81168	40
Hepart	Vitamin B6 (H1103)	15000279	80781	60

- 20 654 spectra from a total of 445 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 21 spectra from 9 *Apo-Ident* customers from 12 batches from the substance/substance group *Vitamin B6 (H1103)*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Vitamin B6 (H1103)	15000279/1	1
Hepart	Vitamin B6 (H1103)	15000879	1
Hepart	Vitamin B6 (H1103)	14001576/2	1
Hepart	Vitamin B6 (H1103)	554938001	1
Hepart AG	Vitamin B6 (H1103)	1554020101	1
Hepart AG	Vitamin B6 (H1103)	1552025711	1
Hepart AG	Vitamin B6 (H1103)	25711	1
Hepart AG, CH-8280 Kreu...	Vitamin B6 (H1103)	25711	1
Hepart AG, CH-8280 Kreu...	Vitamin B6 (H1103)	1552025711	1
Hepart AG, Unisan GmbH	Vitamin B6 (H1103)	15000279/0	1
Purren Apotheke	Vitamin B6 (H1103)	1554938001	1
Unisan	Vitamin B6 (H1103)	25711	3
Unisan	Vitamin B6 (H1103)	20101	1
Unisan	Vitamin B6 (H1103)	14001576	3
Unisan	Vitamin B6 (H1103)	14001576/2	1
Unisan	Vitamin B6 (H1103)	15000279/2	1
Unisan	Vitamin B6 (H1103)	15000279/0	1

- 1866 spectra from 19 *Apo-Ident* customers from a total of 847 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 *Vitamin B6 (H1103)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin B6 (H1103)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	22 671
Type B	0	100	0	20 654
Type C	0	20	1	1866

The substance/substance group *Vitamin B6 (H1103)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9311 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8813 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.7293 %)	95.2381 % (> 80.9524 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Vitamin B6 (H1103)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Flavour orange (H1405)	36.78	–
Creatine (H1031)	40.34	–
Antioxidants NAT complex (H1004)	63.16	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vitamin B6 (H1103)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80798	80798	0.00	41.32
80550	80550	0.00	53.61
80886	80886	0.00	58.78
80919	80919	0.00	55.48

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Vitamin C (H1104)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80009-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Vitamin C (H1104)	14	17	21

Second-stage model

For differentiation of the substance/substance group *Vitamin C (H1104)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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
Hepart	Vitamin C (H1104)	074201	80418	38	from supplier
Hepart	Vitamin C (H1104)	044602	80438	40	from supplier
Hepart	Vitamin C (H1104)	14001780	80499	60	from supplier
Hepart	Vitamin C (H1104)	14001788	80500	60	from supplier
Hepart	Vitamin C (H1104)	14001794	80501	60	from supplier
Hepart	Vitamin C (H1104)	14001797	80502	60	from supplier
Hepart	Vitamin C (H1104)	16000200	80751	60	from supplier
Hepart	Vitamin C (H1104)	16000198	80753	60	from supplier
Hepart	Vitamin C (H1104)	16000229	80756	60	from supplier
Hepart	Vitamin C (H1104)	16000230	80760	60	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 758 spectra of 15 reference samples from the substance/substance group *Vitamin C (H1104)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 14 different batches.
- 22 093 spectra from a total of 426 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 800 spectra of 17 reference samples from the substance/substance group *Vitamin C (H1104)*.
- Among them are spectra of independent samples from 17 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin C (H1104)	16000197	80752	60
Hepart	Vitamin C (H1104)	16000199	80754	60
Hepart	Vitamin C (H1104)	16000201	80755	60
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)	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
Hepart	Vitamin C (H1104)	19001003	81195	40
Hepart	Vitamin C (H1104)	19001004	81196	40
Hepart	Vitamin C (H1104)	19001005	81197	40
Hepart	Vitamin C (H1104)	19001006	81198	40
Hepart	Vitamin C (H1104)	19000134	81199	40

- 19954 spectra from a total of 430 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 58 spectra from 11 *Apo-Ident* customers from 26 batches from the substance/substance group *Vitamin C (H1104)*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Vitamin C (H1104)	44502	1
Falceto	Vitamin C (H1104)	44602	1
HCK	Vitamin C (H1104)	16000203/0	2
Hepart	Vitamin C (H1104)	170009150	1
Hepart	Vitamin C (H1104)	16000231/0	1
Hepart / Unisan	Vitamin C (H1104)	170009170	1
Hepart AG	Vitamin C (H1104)	1084025020	3
Hepart AG	Vitamin C (H1104)	1085025020	1
Hepart AG	Vitamin C (H1104)	44501	3
Hepart AG	Vitamin C (H1104)	44502	3
Hepart AG	Vitamin C (H1104)	44601	2
Hepart AG	Vitamin C (H1104)	73901	3
Hepart AG	Vitamin C (H1104)	74201	2
Hepart AG	Vitamin C (H1104)	16000197/0	1

continued on the next page

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Supplier	Substance	Batch	Spectra
Hepart AG	Vitamin C (H1104)	16000198	1
Hepart AG	Vitamin C (H1104)	17000915/0	2
Hepart AG	Vitamin C (H1104)	16000231/0	1
Hepart AG	Vitamin C (H1104)	17000917/0	1
Hepart AG, CH-8280 Kreu...	Vitamin C (H1104)	1084025019	1
unisan	Vitamin C (H1104)	14001794	1
Unisan	Vitamin C (H1104)	1085025020	3
Unisan	Vitamin C (H1104)	1084025020	1
Unisan	Vitamin C (H1104)	25020	1
Unisan	Vitamin C (H1104)	44501	3
Unisan	Vitamin C (H1104)	44502	1
Unisan	Vitamin C (H1104)	73901	3
Unisan	Vitamin C (H1104)	74001	1
Unisan	Vitamin C (H1104)	14001780/0	1
Unisan	Vitamin C (H1104)	14001788	1
Unisan	Vitamin C (H1104)	14001797	1
Unisan	Vitamin C (H1104)	16000198	1
Unisan	Vitamin C (H1104)	16000200	1
Unisan	Vitamin C (H1104)	16000203/0	1
Unisan	Vitamin C (H1104)	16000203	1
Unisan	Vitamin C (H1104)	16000231	1
UNISAN	Vitamin C (H1104)	74001	1
Unisan GmbH, 78465 Kons...	Vitamin C (H1104)	25020	1
Unisan/Hepart AG	Vitamin C (H1104)	44602	2
Unisan/Hepart AG	Vitamin C (H1104)	44501	1

- 1829 spectra from 19 *Apo-Ident* customers from a total of 833 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 *Vitamin C (H1104)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin C (H1104)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	758	0	22 093
Type B	0	800	0	19 954
Type C	0	51	7	1829

The substance/substance group *Vitamin C (H1104)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9307 %)	100.0000 % (> 99.2084 %)
Type B	100.0000 % (> 99.8801 %)	100.0000 % (> 99.2500 %)
Type C	100.0000 % (> 98.7203 %)	87.9310 % (> 82.7586 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Vitamin C (H1104)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	28.04	—
Ginkgo (H1024)	33.08	—
Flavour orange (H1405)	33.34	—
Calcium (H1008)	39.40	—
PET basis (H1503)	43.44	—
Green coffee extract (H1433)	43.59	—
Potassium (H1030)	43.87	—
Antibiosis forte complex (H1115)	45.93	—
Yeast organic (H1007)	46.37	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vitamin C (H1104)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80394	80394	0.00	33.77
80395	80395	0.00	31.97
80397	80397	0.00	30.62
80418	80418	0.00	46.43
80499	80499	0.00	30.62
80500	80500	0.00	32.72
80501	80501	0.00	35.51
80363	80363	0.00	54.17
80438	80438	0.00	53.84
80751	80751	0.00	51.17
80753	80753	0.00	55.10
80756	80756	0.00	51.86
80760	80760	0.00	51.42
80502	80502	0.00	50.32
80396	80396	0.00	47.71

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Vitamin complex (H1100)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80073-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Vitamin complex (H1100)	20	22	34

Second-stage model

For differentiation of the substance/substance group *Vitamin complex (H1100)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Vitamin complex ...	14001589	80486	60	from supplier
Hepart	Vitamin complex ...	14001591	80487	60	from supplier
Hepart	Vitamin complex ...	15001276(B1)	80637	60	from supplier
Hepart	Vitamin complex ...	15001277(F2)	80638	60	from supplier
Hepart	Vitamin complex ...	15001274(B1)	80640	60	from supplier
Hepart	Vitamin complex ...	15001275(F2)	80642	60	from supplier
Hepart	Vitamin complex ...	15001277	80643	60	from supplier
Hepart	Vitamin complex ...	15001276(F2)	80646	60	from supplier
Hepart	Vitamin complex ...	15001274	80647	60	from supplier
Hepart	Vitamin complex ...	15001275	80648	60	from supplier
Hepart	Vitamin complex ...	16000957	80827	40	from supplier
Hepart	Vitamin complex ...	17001751/0	80990	40	from supplier
Hepart	Vitamin complex ...	19001423/0	81171	40	from supplier
Hepart	Vitamin complex ...	19001424/0	81172	40	from supplier
Hepart	Vitamin complex ...	19001023	81251	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 1020 spectra of 20 reference samples from the substance/substance group *Vitamin complex (H1100)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 20 different batches.
- 21 831 spectra from a total of 420 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied

Type B spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 960 spectra of 22 reference samples from the substance/substance group *Vitamin complex (H1100)*.
- Among them are spectra of independent samples from 22 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin complex (H1100)	15001275 (B1)	80639	60
Hepart	Vitamin complex (H1100)	15001277 (B1)	80641	60
Hepart	Vitamin complex (H1100)	15001274 (F2)	80644	60
Hepart	Vitamin complex (H1100)	15001276	80645	60
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
Hepart	Vitamin complex (H1100)	19000433	81173	40
Hepart	Vitamin complex (H1100)	19000544	81174	40
Hepart	Vitamin complex (H1100)	19002512	81218	40
Hepart	Vitamin complex (H1100)	20000144/0	81226	40
Hepart	Vitamin complex (H1100)	20000836	81248	40
Hepart	Vitamin complex (H1100)	19001582	81249	40
Hepart	Vitamin complex (H1100)	19002234	81250	40
Hepart	Vitamin complex (H1100)	19001581	81252	40

- 19 794 spectra from a total of 425 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 81 spectra from 14 *Apo-Ident* customers from 37 batches from the substance/substance group *Vitamin complex (H1100)*.
- Among them are spectra of independent samples from 34 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hepart	Vitamin complex (H1100)	16000958	1
Hepart	Vitamin complex (H1100)	17000880	1

continued on the next page

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Supplier	Substance	Batch	Spectra
Hepart	Vitamin complex (H1100)	17001750	1
Hepart	Vitamin complex (H1100)	17001750/0	1
Hepart	Vitamin complex (H1100)	17001654	1
hepart ag	Vitamin complex (H1100)	1015954801	1
hepart ag	Vitamin complex (H1100)	10159548011	1
Hepart AG	Vitamin complex (H1100)	1014025101	1
Hepart AG	Vitamin complex (H1100)	1014025301	1
Hepart AG	Vitamin complex (H1100)	49201	4
Hepart AG	Vitamin complex (H1100)	49301	7
Hepart AG	Vitamin complex (H1100)	49202	5
Hepart AG	Vitamin complex (H1100)	77201	3
Hepart AG	Vitamin complex (H1100)	14001589	2
Hepart AG	Vitamin complex (H1100)	15001275/1	1
Hepart AG	Vitamin complex (H1100)	H110031	1
Hepart AG	Vitamin complex (H1100)	15001277	1
Hepart AG	Vitamin complex (H1100)	16000957/0	1
Hepart AG	Vitamin complex (H1100)	17000880/0	4
Hepart AG	Vitamin complex (H1100)	17001750/0	1
Hepart AG	Vitamin complex (H1100)	17001751/0	1
Hepart AG, CH-8280 Kreu...	Vitamin complex (H1100)	1014025101	1
Hepart AG, CH-8280 Kreu...	Vitamin complex (H1100)	49301	5
Hepart/Unisan	Vitamin complex (H1100)	15001275/0	1
unisan	Vitamin complex (H1100)	49302	1
Unisan	Vitamin complex (H1100)	1014009901	1
Unisan	Vitamin complex (H1100)	25201	1
Unisan	Vitamin complex (H1100)	25101	1
Unisan	Vitamin complex (H1100)	49301	2
Unisan	Vitamin complex (H1100)	49302	2
Unisan	Vitamin complex (H1100)	H110031	2
Unisan	Vitamin complex (H1100)	49202	1
Unisan	Vitamin complex (H1100)	904006	1
Unisan	Vitamin complex (H1100)	77201	3
Unisan	Vitamin complex (H1100)	77001	2
Unisan	Vitamin complex (H1100)	74101	1
Unisan	Vitamin complex (H1100)	1400159/0	1
Unisan	Vitamin complex (H1100)	14001590/0	1
Unisan	Vitamin complex (H1100)	14001589	1
Unisan	Vitamin complex (H1100)	14001590/1	1
Unisan	Vitamin complex (H1100)	15001275/0	1
Unisan	Vitamin complex (H1100)	15001276/0	1
Unisan	Vitamin complex (H1100)	15001277/0	1
Unisan	Vitamin complex (H1100)	16000958/0	2
Unisan	Vitamin complex (H1100)	16000962	2
Unisan	Vitamin complex (H1100)	17001750	1
Unisan	Vitamin complex (H1100)	1014025401	1
Unisan/Hepart AG	Vitamin complex (H1100)	49201	1
Unisan/Hepart AG	Vitamin complex (H1100)	48301	1
Hepart	Vitamin complex (H1100)	17001751/0	1

- 1806 spectra from 19 *Apo-Ident* customers from a total of 822 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 *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	1020	0	21 831
Type B	0	960	0	19 794
Type C	0	80	1	1806

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 % (> 99.9306 %)	100.0000 % (> 99.4118 %)
Type B	100.0000 % (> 99.8801 %)	100.0000 % (> 99.3750 %)
Type C	100.0000 % (> 98.7188 %)	98.7654 % (> 95.0617 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Vitamin complex (H1100)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium (H1008)	28.78	—
Antibiosis forte complex (H1115)	31.08	—
Carnitine (L-) (H1038)	35.97	—
Creatine (H1031)	38.06	—
Curcumin and piperine (H1014)	43.43	—
Silymarin (H1071)	47.96	—
Caffeine guarana extract (H1425)	49.18	—
Flavour orange (H1405)	49.26	—
Antioxidants NAT complex (H1004)	51.29	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vitamin complex (H1100)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81251	81251	0.00	31.08
80349	80349	0.00	44.30
81171	81171	0.00	47.87
81172	81172	0.00	52.11
80486	80486	0.00	45.17
80487	80487	0.00	43.95
80638	80638	0.00	46.29
80642	80642	0.00	44.65
80647	80647	0.00	46.16
80648	80648	0.00	44.45
80411	80411	0.00	41.91
80431	80431	0.00	43.14
80432	80432	0.00	40.83
80485	80485	0.00	41.86
80637	80637	0.00	45.08
80640	80640	0.00	45.98
80643	80643	0.00	44.80
80646	80646	0.00	44.61
80827	80827	0.00	46.37
80990	80990	0.00	42.35

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Vitamin E NAT (H1107)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80010-2020-06-25
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

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Vitamin E NAT (H1107)	11	21	23

Second-stage model

For differentiation of the substance/substance group *Vitamin E NAT (H1107)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *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	60	from supplier
Hepart	Vitamin E NAT (H...	14001821	80513	60	from supplier
Hepart	Vitamin E NAT (H...	14001822	80514	60	from supplier
Hepart	Vitamin E NAT (H...	15001558	80688	60	from supplier
Hepart	Vitamin E NAT (H...	15001559(F2)	80690	60	from supplier
Hepart	Vitamin E NAT (H...	15001561	80693	60	from supplier
Hepart	Vitamin E NAT (H...	15001560(B1)	80694	60	from supplier
Hepart	Vitamin E NAT (H...	15001557	80697	60	from supplier
Hepart	Vitamin E NAT (H...	16001246	80826	40	from supplier

Validation samples

A total of 45 492 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 595 spectra of 11 reference samples from the substance/substance group *Vitamin E NAT (H1107)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 11 different batches.
- 22 256 spectra from a total of 429 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1160 spectra of 24 reference samples from the substance/substance group *Vitamin E NAT (H1107)*.

- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin E NAT (H1107)	065001	80350	40
Hepart	Vitamin E NAT (H1107)	071501	80381	40
Hepart	Vitamin E NAT (H1107)	15001557(B1)	80686	60
Hepart	Vitamin E NAT (H1107)	15001558(F2)	80687	60
Hepart	Vitamin E NAT (H1107)	15001561(B1)	80689	60
Hepart	Vitamin E NAT (H1107)	15001559	80691	60
Hepart	Vitamin E NAT (H1107)	15001561(F2)	80692	60
Hepart	Vitamin E NAT (H1107)	15001560(F2)	80695	60
Hepart	Vitamin E NAT (H1107)	15001557(F2)	80696	60
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
Hepart	Vitamin E NAT (H1107)	18001024	81080	40
Hepart	Vitamin E NAT (H1107)	18001025	81081	40
Hepart	Vitamin E NAT (H1107)	18001026	81082	40
Hepart	Vitamin E NAT (H1107)	19001884	81209	40
Hepart	Vitamin E NAT (H1107)	19001496	81210	40
Hepart	Vitamin E NAT (H1107)	19001883	81211	40
Hepart	Vitamin E NAT (H1107)	071501	80382	40
Hepart	Vitamin E NAT (H1107)	071501	80383	40
Hepart	Vitamin E NAT (H1107)	071501	80384	40

- 19 594 spectra from a total of 426 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 49 spectra from 14 *Apo-Ident* customers from 27 batches from the substance/substance group *Vitamin E NAT (H1107)*.
- Among them are spectra of independent samples from 23 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
HCK	Vitamin E NAT (H1107)	14001822/0	1
Hepart	Vitamin E NAT (H1107)	160005910	1
Hepart	Vitamin E NAT (H1107)	16000591/0	1
Hepart	Vitamin E NAT (H1107)	17000890	1
Hepart	Vitamin E NAT (H1107)	17000892/0	1
Hepart AG	Vitamin E NAT (H1107)	1094025022	1
Hepart AG	Vitamin E NAT (H1107)	25022	2
Hepart AG	Vitamin E NAT (H1107)	65101	3
Hepart AG	Vitamin E NAT (H1107)	15001557	1

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Supplier	Substance	Batch	Spectra
Hepart AG	Vitamin E NAT (H1107)	15001557/0	2
Hepart AG	Vitamin E NAT (H1107)	17000890/0	3
Hepart AG	Vitamin E NAT (H1107)	16001246/0	1
Hepart AG, CH-8280 Kreu...	Vitamin E NAT (H1107)	1094017701	1
Hepart AG, CH-8280 Kreu...	Vitamin E NAT (H1107)	65001	1
Purren Apotheke	Vitamin E NAT (H1107)	945901	1
Unisan	Vitamin E NAT (H1107)	1095961301	1
Unisan	Vitamin E NAT (H1107)	1094017701	1
Unisan	Vitamin E NAT (H1107)	1094025021	1
Unisan	Vitamin E NAT (H1107)	25022	2
Unisan	Vitamin E NAT (H1107)	65001	3
Unisan	Vitamin E NAT (H1107)	71501	4
Unisan	Vitamin E NAT (H1107)	14001821/0	1
Unisan	Vitamin E NAT (H1107)	14001821	1
Unisan	Vitamin E NAT (H1107)	15001558	1
Unisan	Vitamin E NAT (H1107)	15001557/0	1
Unisan	Vitamin E NAT (H1107)	15001659/0	1
Unisan	Vitamin E NAT (H1107)	16000589/0	2
Unisan	Vitamin E NAT (H1107)	16000591	2
Unisan	Vitamin E NAT (H1107)	16000591/0	1
Unisan	Vitamin E NAT (H1107)	16001246	1
UNISAN	Vitamin E NAT (H1107)	71701	1
Unisan 02.04.2016	Vitamin E NAT (H1107)	15001558/0	1
Unisan 2.10.2015	Vitamin E NAT (H1107)	14001821/0	1
Hepart	Vitamin E NAT (H1107)	16001246	1
	Vitamin E NAT (H1107)	25022	1

- 1838 spectra from 19 *Apo-Ident* customers from a total of 832 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 *Vitamin E NAT (H1107)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamin E NAT (H1107)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	595	0	22 256
Type B	0	1160	0	19 594
Type C	0	48	1	1838

The substance/substance group *Vitamin E NAT (H1107)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9307 %)	100.0000 % (> 98.9916 %)
Type B	100.0000 % (> 99.8801 %)	100.0000 % (> 99.4828 %)
Type C	100.0000 % (> 98.7212 %)	97.9592 % (> 91.8367 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Vitamin E NAT (H1107)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Coenzyme Q10 (H1013)	19.00	—
PET coenzyme Q10 (H0022)	33.13	—
Ginseng (H1018)	35.76	—
Glutamine (L-) (H1043)	49.11	—
Flavour orange (H1405)	56.30	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vitamin E NAT (H1107)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80690	80690	0.00	27.36
80421	80421	0.00	19.00
80426	80426	0.00	20.14
80512	80512	0.00	22.18
80513	80513	0.00	23.19
80514	80514	0.00	20.65
80688	80688	0.00	28.33
80693	80693	0.00	29.25
80694	80694	0.00	27.19
80697	80697	0.00	29.61
80826	80826	0.00	20.14

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Vitamins BAG (H1090)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 10003701-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Vitamins BAG (H1090)

Special notes

When selecting the *Vitamins BAG (H1090)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Vitamins BAG (H1090)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Vitamins BAG (H1090)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Vitamins BAG (H1090)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamins BAG (H1...	20000156	81228	40	from supplier
Hepart	Vitamins BAG (H1...	19002541/0	81229	40	from supplier

Validation samples

A total of 45 492 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 *Vitamins BAG (H1090)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Vitamins BAG (H1090)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamins BAG (H1090)	19002481	81230	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Vitamins BAG (H1090)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Vitamins BAG (H1090)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamins BAG (H1090)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	0	40	20 714
Type C	0	0	0	1887

The substance/substance group *Vitamins BAG (H1090)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8834 %)	0.0000 % (≥ 0.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Vitamins BAG (H1090)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium (H1008)	9.02	—
PET basis (H1503)	10.97	—
Antioxidants NAT complex (H1004)	11.47	—
Ginkgo (H1024)	18.77	—
Rhodiola (H1064)	21.74	—
Seabuckthorn organic (H1412)	22.73	—
Broccoli (H1415)	24.79	—
PET well-aging (H1500)	26.47	—
Vitamin B1 (H1101)	27.93	—
Flavour orange (H1405)	29.43	—
PET joints (H1501)	30.49	—
Silymarin (H1071)	35.73	—
Beetroot (H1414)	37.90	—
Garcinia cambogia (H1017)	39.79	—
Iron (H1015)	40.19	—
Pathogene complex (H1803)	41.43	—
Betaine hydrochloride (H1119)	42.43	—
Bioflavonoid complex (H1006)	43.09	—
Copper (H1032)	45.91	—
Vitamin C (H1104)	49.20	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vitamins BAG (H1090)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81228	81228	0.00	10.97
81229	81229	0.00	10.53

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Walnut leaf (H1114)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80904-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Walnut leaf (H1114)

Special notes

When selecting the *Walnut leaf (H1114)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Walnut leaf (H1114)	3	0	0

Second-stage model

For differentiation of the substance/substance group *Walnut leaf (H1114)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Walnut leaf (H1114)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Walnut leaf (H11...	16001149	80904	40	from supplier
Hepart	Walnut leaf (H11...	15001009	80908	40	from supplier
Hepart	Walnut leaf (H11...	19000343/0	81162	40	from supplier

Validation samples

A total of 45 492 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 *Walnut leaf (H1114)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 731 spectra from a total of 437 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Walnut leaf (H1114)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Walnut leaf (H1114)	16001149	80907	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Walnut leaf (H1114)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Walnut leaf (H1114)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Walnut leaf (H1114)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	22 731
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Walnut leaf (H1114)* can be clearly distinguished from all other substances. In order 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 % (> 99.9313 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Walnut leaf (H1114)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Copper (H1032)	17.94	—
Chaga (H1011)	21.43	—
Iron (H1015)	30.27	—
Garcinia cambogia (H1017)	31.99	—
Pathogene complex (H1803)	32.77	—
Antibiosis mite complex (H1113)	37.90	—
Antioxidants NAT complex (H1004)	38.74	—
Argentum (H1116)	43.08	—
PET basis (H1503)	50.29	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Walnut leaf (H1114)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80908	80908	0.00	32.77
80904	80904	0.00	21.43
81162	81162	0.00	26.89

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-03

Validated substance/substance group **Yeast organic (H1007)**
Substance class HCK - nutritional supplements (Hepart)
Report date 25/06/2020
Report number 80925-2020-06-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yeast organic (H1007)

Special notes

When selecting the *Yeast organic (H1007)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yeast organic (H1007)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Yeast organic (H1007)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yeast organic (H1007)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Yeast organic (H...	16001157	80925	40	from supplier
Hepart	Yeast organic (H...	1900527	81194	40	from supplier

Validation samples

A total of 45 492 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 *Yeast organic (H1007)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 771 spectra from a total of 438 batches from further 117 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Yeast organic (H1007)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Yeast organic (H1007)	17001784/0	81004	40

- 20 714 spectra from a total of 446 batches from further 91 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Yeast organic (H1007)*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 1887 spectra from 19 *Apo-Ident* customers from a total of 859 batches from a further 63 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yeast organic (H1007)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yeast organic (H1007)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	22 771
Type B	0	40	0	20 714
Type C	0	0	0	1887

The substance/substance group *Yeast organic (H1007)* can be clearly distinguished from all other substances. In order 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 % (> 99.9317 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8834 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7704 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yeast organic (H1007)* in the substance class *HCK - nutritional supplements (Hepart)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Antioxidants NAT complex (H1004)	22.02	—
PET basis (H1503)	34.31	—
Antibiosis forte complex (H1115)	36.49	—
Vitamin B1 (H1101)	40.05	—
PET immune system (H1502)	47.55	—
Stomach complex (H1120)	48.76	—
Vitamin C (H1104)	50.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yeast organic (H1007)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80925	80925	0.00	33.24
81194	81194	0.00	33.53

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

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 7 batches. From these 380 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	Melatonin (H1061)	069101	40	from supplier
Hepart	Melatonin (H1061)	069101	60	from supplier
Hepart	Proline (-L) (H1051)	066401	40	from supplier
Hepart	TopFlora multi forte complex (H1119)	15001135	60	from supplier
Hepart	Vitamin K2-Ca-Mn-Si complex (osteocomplex) (H1109)	15000836	60	from supplier
Hepart	Vitamin K2-Ca-Mn-Si complex (osteocomplex) (H1109)	15000836	60	from supplier
Hepart	Vitamin K2-Ca-Mn-Si complex (osteocomplex) (H1109)	16000403	60	from supplier

Appendix C: Additional validation samples (*Type C*)

Spectra for substances from the field which cannot be identified with this model also enter the validation. In this manner, it is verified that the model also rejects unknown substances. The spectra for these samples were recorded by *Apo-Ident* customers. They belong to *Type C*. The information provided by the customer regarding the manufacturer and batch number is taken over by *HiperScan GmbH* to a large extent unchecked.

The samples originate from 5 batches. From these, 9 spectra were recorded. The spectra recorded on independent samples of substances from the field which can be identified with the model are listed respectively in the section *Type C* for the individual substances and do not appear again elsewhere in this list.

Supplier	Substance	Batch	Spectra
Hepart AG	Proline (-L) (H1051)	707801	2
Hepart AG	Proline (-L) (H1051)	25707	2
Unisan	Proline (-L) (H1051)	66401	2
Unisan	Vitamin K2-Ca-Mn comp...	69001	2
Hepart AG	Vitamin K2-Ca-Mn-Si c...	15000836/6	1

Appendix D: Requirements of validation

In order to ensure adherence to the safe scientific status, the individual methods for manufacturing and testing must be validated under certain circumstances (compare § 34 para. 1 no. 3, § 35 para. 1 no. 4 and para. 4 sentence 1 no. 2 b, para. 6 sentence 3 *ApoBetrO* [Pharmacies Rules and Regulations]). The *ApoBetrO* [Pharmacies Rules and Regulations] incorporates a legal definition in § 1 a para. 16 (quotation translated):

“Validation is the provision of documented proof which with a high degree of safety documents that, via a specific process or standard work process, a medicinal product is manufactured and tested, which is in accordance with previously determined quality features.”

Validation documentation can be used to prove that methods or devices which are not described in the Pharmacopoeia within the meaning of § 6 para. 1 sentence 3 *ApBetrO* [Pharmacies Rules and Regulations] achieve the same results as those in the Pharmacopoeia. On the other hand, with the requirements of the demanded validation it must be observed whether the respective testing method is already incorporated in the Pharmacopoeia.

NIR spectroscopy as a general testing method need not be validated in accordance with the express ruling in the *Ph. Eur. Section 1.1* [3], as it is already described in *Section 2.2.40* of the *Ph. Eur.* as an area of application for the identification of raw materials.

However, a special validation requirement exists for the reference database. This requirement is met with the existing document. Further requirements or rules as to how this proof must be furnished do not exist. It is required that the processes guarantee the same results as the methods and devices in the Pharmacopoeia [17].

Carrying out identity tests with *Apo-Ident* is therefore also possible if the NIR spectroscopy process is not required in the Pharmacopoeia monograph of the substance for identity testing. All NIR analyses with *Apo-Ident* prove several, often all molecule groups and are therefore comparable with a series of individual, targeted chemical proofs [4]. Therefore, the identity proof with *Apo-Ident* replaces the monograph test series (with two or more test combinations).

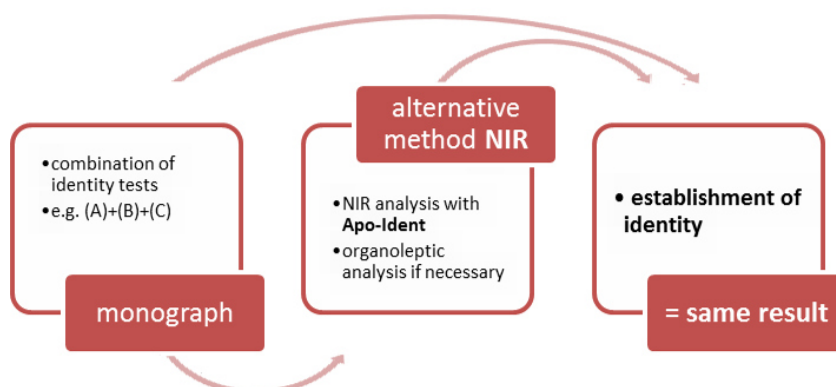


Figure 2: The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

With this validation documentation, proof is furnished that identical results are achieved with *Apo-Ident* and Pharmacopoeia methods, i.e. confirmation of the identity of the raw material [2].

Appendix E: Conformity of Apo-Ident with the European pharmacopeia

According to *Ph. Eur. Section 2.2.40*, NIR spectroscopy is basically suitable for: “Identification of agents, excipients, dosage forms, intermediate manufacturing products, chemical raw materials and packaging materials” ([3], quotation translated).

The fact that *Apo-Ident* meets the further criteria of the European Pharmacopoeia under the headings in *Section 2.2.40*

- Apparatus
- Measurement methods
- Sample preparation and presentation
- Testing the functionality of the instrument
- Identification and characterisation (qualitative analysis)
- Quantitative analysis
- Ongoing model evaluation
- Transfer of databases
- Data storage

can be proven based on the *HiperScan GmbH* documentation of “Meeting 2.2.40 *Ph. Eur.* by *Apo-Ident*” [4].

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