

Validation documentation
HCK

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*.

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*. 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*) and *narcotics - solid medicinal substances*. If, for individual substance classes, variations are required, they are depicted in the section [Particularities of individual substance classes](#).

1. Collecting the reference spectra (calibration sample)

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

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

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

2. Generating the chemometric models (calibration)

- a) Determination of the transformation matrix from the reference spectra using variance maximisation [8, 9]. (All reference spectra are always included, even if only a few spectra are added for an update.) All reference spectra receive the same data pre-treatment, which is also later applied to all measurement spectra in the field (in the pharmacies).
- b) Checking that the number of principal components used is still sufficient.
- c) Calculating the limits for each substance from the spread of the reference spectra. The calculation regulation is identical for each substance in a substance class.
- d) Checking the distances between the limits of the separable substances: The distance matrix contains the *Mahalanobis distances* from each substance to each other. The values in a bidirectional manner are different in each case because the spread of the initial substance is included. If a distance is smaller than the minimal distance, the substances are not considered to be reliably separable. The minimal distance is set at 9. The developer of the model may specify a larger minimal distance (one value for the entire *chemometric model*), to increase the selectivity.
- e) Verification of the model using the reference spectra. No *false-positive* results are permitted.
- f) If one of the criteria is violated (d) *Minimum distance between two substances undershot* or (e) *One substance is identified as another*, the database developers decide which of the following options to apply:

- They remove both substances from the database. (The spectra remain in the validation and may also be included when generating the model. However, they are not offered for testing.)
 - They form a substance group of several substances which cannot be reliably separated. The result is then ambiguous: The chemometric model determines that the sample is one of the substances in the group and not another substance. However, it cannot determine which of the group members it is. In order to determine the clear identity, the user must carry out a suitable additional analysis.
 - They create another *chemometric model* with a smaller scope, in which at least all substances of the non-separable substance group are included (second-stage model). Second-stage models are only called up if the first stage has established that only one of the substances included in the second-stage model can be involved.
- g) If *chemometric models* that fulfil both criteria (distance matrix and no *false positives*), are available for all substance classes, they are combined with the evaluation algorithms to form an *IdentModule* and encoded. This unit can no longer be changed. Its overall function is checked by the validation.

3. Set of validation spectra (validation samples)

The following is provided for validation:

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

All manufacturers’ batches from which spectra are used for the validation are listed by substance in this document: for substances included in the substance class *HCK* in the respective validation reports; otherwise in attachments *A*, *B* and *C*.

Furthermore remains valid: validation spectra may only be removed if an 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)** and **Narcotic substances, liquid/semi-solid**. 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.

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 HCK micro-nutrients from the Swiss company *Hepart AG*.

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, *Angelica root oil* of the substance class *APIs & excipients, liquid/semi-solid (with analysis certificate)* neither needs to be delimited from *Angelica root oil* of the substance class *APIs & excipients, liquid/semi-solid (other)* 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 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 $\mathbf{X}$.

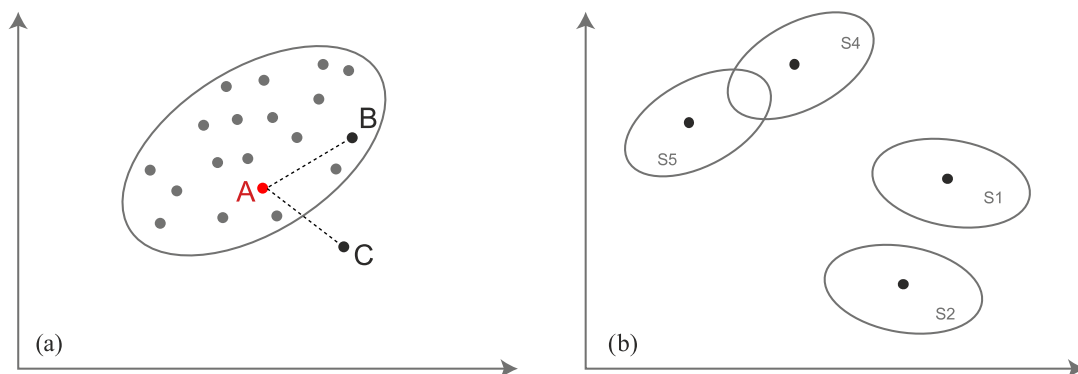


Figure 1: (a) The *Mahalanobis distance* from *A* to *B* is less than from *A* to *C*. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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 53 925 spectra from 2267 different batches for a total of 136 substances were used to validate the substance class *HCK*.

Validation samples

The validation samples can be categorised as follows:

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

Substance class	Substances	Batches	Spectra
HCK	131	574	28 276

From category *A* a total of 28 276 spectra from 574 batches for a total of 131 substances were taken into account for validation.

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

Substance class	Substances	Batches	Spectra
HCK	80	496	22 679

From category *B* a total of 22 679 spectra from 496 batches for a total of 80 substances were taken into account for validation.

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

Substance class	Substances	Batches	Spectra
HCK	63	1468	2970

From category *C* a total of 2970 spectra from 1468 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* 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* 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	28 276	0	2 290 356
Type B	0	22 013	226	1 837 237
Type C	0	2703	258	240 579

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

	Specificity	Recognition rate
Type A	100.000 00 % (> 99.999 17 %)	100.000 00 % (> 99.932 40 %)
Type B	100.000 00 % (> 99.998 40 %)	98.419 05 % (> 98.350 26 %)
Type C	100.000 00 % (> 99.986 12 %)	87.193 85 % (> 86.700 43 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 2.8-2024-04

Validated substance/substance group **Acerola (H1516)**
Substance class HCK
Report date 25/11/2024
Report number 10006322-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Acerola (H1516)

Special notes

When selecting the *Acerola (H1516)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Acerola (H1516)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Acerola (H1516)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Acerola (H1516)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Ginkgo Extrakt (H1024)	15,82	—
Aroma Orange (H1405)	16,53	—
Rhodiola (H1064)	18,80	—
PET Basis (H1503)	19,03	—
Antioxidantien NAT Komplex (H1004)	20,35	—
Calcium L-(+) -Lactat Komplex (H1008)	23,17	—
Vitamin C (H1104)	24,35	—
PET Well-Aging (H1500)	30,64	—
Vitamin B1 (H1101)	31,21	—
L-Arginin (H1036)	39,11	—
Grüner Kaffee Extrakt (H1433)	39,97	—
Sanddorn (H1523)	41,80	—
Catechin-Extrakt (H1010)	43,33	—
PET Gelenke (H1501)	43,72	—
Bioflavonoide Komplex (H1006)	45,68	—
Pathogene Komplex (H1803)	48,23	—
L-Carnitin (H1038)	48,34	—
Walnussblatt Extrakt (H1114)	48,91	—
Kupfer (H1032)	50,34	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Acerola (H1516)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Acerola (H1516)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Acerola (H1516)	23002135	81526	40	from supplier

Validation samples

A total of 53 925 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 *Acerola (H1516)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Acerola (H1516)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Acerola (H1516)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Acerola (H1516)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Acerola (H1516)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Acerola (H1516)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81526	81526	0,00	16,66

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 2.8-2024-04

Validated substance/substance group **a-Liponsäure (H1000)**
Substance class HCK
Report date 25/11/2024
Report number 80022-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

a-Liponsäure (H1000)

Special notes

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

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
a-Liponsäure (H1000)	10	6	23

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *a-Liponsäure (H1000)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Vitamin E NAT (H1107)	26,60	—
Coenzym Q10 (H1013)	36,89	—
Aminomix NAC (H1002)	39,21	—
Antibiose forte Komplex (H1115)	52,46	—

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Liponsäure (H1000)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	a-Liponsäure (H1000)	054301	80321	58	from supplier
Hepart	a-Liponsäure (H1000)	14001420	80482	60	from supplier
Hepart	a-Liponsäure (H1000)	14001726	80491	60	from supplier
Hepart	a-Liponsäure (H1000)	15001526 (B1.2)	80681	60	from supplier
Hepart	a-Liponsäure (H1000)	14000497	80682	60	from supplier
Hepart	a-Liponsäure (H1000)	20001859	81281	40	from supplier
Hepart	a-Liponsäure (H1000)	20002669	81309	40	from supplier
Hepart	a-Liponsäure (H1000)	22000274	81424	40	from supplier
Hepart	a-Liponsäure (H1000)	22001329	81445	40	from supplier
Hepart	a-Liponsäure (H1000)	22001766	81464	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 498 spectra of 10 reference samples from the substance/substance group *a-Liponsäure (H1000)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 27 778 spectra from a total of 562 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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-Liponsäure (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-Liponsäure (H1000)	066601	80369	40
Hepart	a-Liponsäure (H1000)	15001526 (B1.1)	80680	60
Hepart	a-Liponsäure (H1000)	14000497 (F1)	80683	60
Hepart	a-Liponsäure (H1000)	14000497 (F2)	80684	60
Hepart	a-Liponsäure (H1000)	15001526 (MM)	80685	60
Hepart	a-Liponsäure (H1000)	18000250	81017	40

- 22 359 spectra from a total of 490 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 52 spectra from 18 *Apo-Ident* customers from 26 batches from the substance/substance group *a-Liponsäure (H1000)*.
- 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	a-Liponsäure (H1000)	14000497/0	1
HCK	a-Liponsäure (H1000)	14000497-2	1
Hepart / Unisan	a-Liponsäure (H1000)	150015262	1
Hepart ag/Unisan	a-Liponsäure (H1000)	20001859	1
Hepart AG/Unisan	a-Liponsäure (H1000)	20001859/1	1
Hepart AG	a-Liponsäure (H1000)	1313025701	2
Hepart AG	a-Liponsäure (H1000)	14000497/1	1
Hepart AG	a-Liponsäure (H1000)	150001526/2	1
Hepart AG	a-Liponsäure (H1000)	15001526/2	3
Hepart AG	a-Liponsäure (H1000)	18000250/1	1
Hepart AG	a-Liponsäure (H1000)	25701	1
Hepart AG	a-Liponsäure (H1000)	54301	1
Hepart	a-Liponsäure (H1000)	15001526/3	1
Hepart	a-Liponsäure (H1000)	15001526-2	2
Hepart	a-Liponsäure (H1000)	18000250	2
Hepart	a-Liponsäure (H1000)	18000250/0	5
Hepart	a-Liponsäure (H1000)	18000250/1	2
Hepart	a-Liponsäure (H1000)	18000250/2	1
Hepart	a-Liponsäure (H1000)	18000250/3	1
Hepart	a-Liponsäure (H1000)	20001859/0	1
Hepart	a-Liponsäure (H1000)	66601	2
Th. Geyer	a-Liponsäure (H1000)	15001526/0	1
Unisan GmbH, 78465 K...	a-Liponsäure (H1000)	25701	2
Unisan/Hepart AG	a-Liponsäure (H1000)	25701	1
Unisan/Hepart AG	a-Liponsäure (H1000)	54301	1
Unisan	a-Liponsäure (H1000)	1312993101	1
Unisan	a-Liponsäure (H1000)	14000497	1
UNISAN	a-Liponsäure (H1000)	14001726	2
Unisan	a-Liponsäure (H1000)	25701	6
unisan	a-Liponsäure (H1000)	66601	1
Unisan	a-Liponsäure (H1000)	66601	1
Unisan	a-Liponsäure (H1000)	993101	2
unisan	a-Liponsäure (H1000)	H100031	1

- 2918 spectra from 26 *Apo-Ident* customers from a total of 1434 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-Liponsäure (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-Liponsäure (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	498	0	27 778
Type B	0	320	0	22 359
Type C	0	52	0	2918

The substance/substance group *a-Liponsäure (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 % (> 98.7952 %)
Type B	100.0000 % (> 99.8666 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 98.8280 %)	100.0000 % (> 88.4615 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80321	80321	0,00	60,19
80482	80482	0,00	80,92
80491	80491	0,00	60,23
80681	80681	0,00	61,49
80682	80682	0,00	60,95
81281	81281	0,00	54,38
81309	81309	0,00	53,40
81424	81424	0,00	35,61
81445	81445	0,00	51,75
81464	81464	0,00	67,89

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 2.8-2024-04

Validated substance/substance group **Aminomix NAC (H1002)**
Substance class HCK
Report date 25/11/2024
Report number 80003-2024-11-25
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

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Aminomix NAC (H1002)	10	16	33

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Aminomix NAC (H1002)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Kürbiskernprotein (H1509)	20,80	—
Isoflavone Extrakt (H1025)	23,27	—
Coenzym Q10 (H1013)	24,99	—
Amino V Komplex (H1400)	26,62	—
Antibiose forte Komplex (H1115)	30,04	—
L-Glutamin (H1043)	31,22	—
Lupinenprotein BCAA Komplex (H1510)	31,65	—
Haferkleie beta-Glucan (H1529)	32,50	—
PET Haut und Haare (H1504)	33,89	—
Glutathion (H1020)	34,26	—
Vitamin E NAT (H1107)	36,25	—
Antioxidantien NAT Komplex (H1004)	37,45	—
Calcium L-(+) -Lactat Komplex (H1008)	38,76	—
Hanfprotein (H1406)	39,01	—
a-Liponsäure (H1000)	39,70	—
Vitamin B1 (H1101)	40,73	—
Kollagenpeptide-MTC (H1125)	41,07	—
L-Carnitin (H1038)	43,43	—
PET Basis (H1503)	45,48	—
Aroma Orange (H1405)	49,22	—
PET Gelenke (H1501)	49,86	—
Ginkgo Extrakt (H1024)	51,17	—

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.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 (H1002)	041401	80312	40	from supplier
Hepart	Aminomix NAC (H1002)	041402	80314	60	from supplier
Hepart	Aminomix NAC (H1002)	14000258	80407	40	from supplier
Hepart	Aminomix NAC (H1002)	14000258	80444	40	from supplier
Hepart	Aminomix NAC (H1002)	14000259	80447	40	from supplier
Hepart	Aminomix NAC (H1002)	15000295 (B1)	80538	60	from supplier
Hepart	Aminomix NAC (H1002)	15000297 (F2)	80544	60	from supplier
Hepart	Aminomix NAC (H1002)	15000320	80545	60	from supplier
Hepart	Aminomix NAC (H1002)	15000321	80546	60	from supplier
Hepart	Aminomix NAC (H1002)	15000319 (F2)	80549	60	from supplier
Hepart	Aminomix NAC (H1002)	210008-03-02	81348	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 560 spectra of 11 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 10 different batches.
- 27 716 spectra from a total of 562 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 880 spectra of 18 reference samples from the substance/substance group *Aminomix NAC (H1002)*.
- Among them are spectra of independent samples from 16 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

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Supplier	Substance	Batch	Sample ID	Spectra
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)	20001550	81285	40
Hepart	Aminomix NAC (H1002)	14000259	80408	40
Hepart	Aminomix NAC (H1002)	041401	80457	40

- 21 799 spectra from a total of 478 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 72 spectra from 18 *Apo-Ident* customers from 37 batches from the substance/substance group *Aminomix NAC (H1002)*.
- Among them are spectra of independent samples from 33 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)	15000297/0	1
HCK	Aminomix NAC (H1002)	15000320-0	1
HCK	Aminomix NAC (H1002)	16001453	1
Hepart / Unisan	Aminomix NAC (H1002)	19000543/0	1
Hepart / Unisan	Aminomix NAC (H1002)	19002356/0	1
Hepart AG, CH-8280 K...	Aminomix NAC (H1002)	1054019101	1
Hepart ag/Unisan	Aminomix NAC (H1002)	19002356/0	1
Hepart AG/Unisan	Aminomix NAC (H1002)	20000735/0	1
Hepart AG/Unisan	Aminomix NAC (H1002)	20001550/0	1
Hepart AG	Aminomix NAC (H1002)	1054019101	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	1
Hepart AG	Aminomix NAC (H1002)	17000766/0	1
Hepart AG	Aminomix NAC (H1002)	19000543/0	1
Hepart AG	Aminomix NAC (H1002)	41401	2
Hepart AG	Aminomix NAC (H1002)	41402	2
Hepart	Aminomix NAC (H1002)	16001452	1
Hepart	Aminomix NAC (H1002)	16001452-0	1
Hepart	Aminomix NAC (H1002)	16001453/0	1
Hepart	Aminomix NAC (H1002)	16001453-1	1
Hepart	Aminomix NAC (H1002)	17000766	2
Hepart	Aminomix NAC (H1002)	17000766/0	2
Hepart	Aminomix NAC (H1002)	18001998	1
Hepart	Aminomix NAC (H1002)	18001998/0	3

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Supplier	Substance	Batch	Spectra
Hepart	Aminomix NAC (H1002)	19000543/0	2
Hepart	Aminomix NAC (H1002)	19000543/3	1
Hepart	Aminomix NAC (H1002)	19002356/0	2
Hepart	Aminomix NAC (H1002)	20000735/0	1
Hepart	Aminomix NAC (H1002)	21000802/0	1
Hepart	Aminomix NAC (H1002)	21000803	1
Hepart	Aminomix NAC (H1002)	21000803/0	1
Hepart	Aminomix NAC (H1002)	21002331	1
Unisan 02.04.2016	Aminomix NAC (H1002)	15000320/0	1
Unisan/Hepart AG	Aminomix NAC (H1002)	41402	1
unisan	Aminomix NAC (H1002)		1
Unisan	Aminomix NAC (H1002)	140000259	1
Unisan	Aminomix NAC (H1002)	14000258	3
Unisan	Aminomix NAC (H1002)	14000259	1
Unisan	Aminomix NAC (H1002)	15000295/0	3
unisan	Aminomix NAC (H1002)	15000297	1
Unisan	Aminomix NAC (H1002)	15000298/0	1
Unisan	Aminomix NAC (H1002)	15000320	1
Unisan	Aminomix NAC (H1002)	15000320/0	2
Unisan	Aminomix NAC (H1002)	16001017/0	1
Unisan	Aminomix NAC (H1002)	16001453/0	1
Unisan	Aminomix NAC (H1002)	165001017/0	1
Unisan	Aminomix NAC (H1002)	17000766	2
Unisan	Aminomix NAC (H1002)	19101	1
Unisan	Aminomix NAC (H1002)	41401	1
Unisan	Aminomix NAC (H1002)	41402	4
Unisan	Aminomix NAC (H1002)	971701	1

- 2898 spectra from 26 *Apo-Ident* customers from a total of 1424 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	560	0	27 716
Type B	0	880	0	21 799
Type C	0	69	3	2898

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 % (> 99.9309 %)	100.0000 % (> 98.9286 %)
Type B	100.0000 % (> 99.8662 %)	100.0000 % (> 99.3182 %)
Type C	100.0000 % (> 98.8260 %)	95.8333 % (> 91.6667 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80312	80312	0,00	35,94
80314	80314	0,00	32,90
80407	80407	0,00	32,71
80444	80444	0,00	26,62
80447	80447	0,00	27,59
80538	80538	0,00	33,34
80544	80544	0,00	31,65
80545	80545	0,00	32,29
80546	80546	0,00	33,55
80549	80549	0,00	32,17
81348	81348	0,00	23,27

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 2.8-2024-04

Validated substance/substance group **Argentum (H1116)**
Substance class HCK
Report date 25/11/2024
Report number 80674-2024-11-25
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

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	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

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Argentum (H1116)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Eisen (H1015)	11,44	—
Kupfer (H1032)	20,17	—
Spurenelemente SE Komplex (H1082)	52,01	—

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.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 53 925 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.
- 28 176 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples

are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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	28 176
Type B	0	0	0	22 679
Type C	0	0	0	2970

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 % (> 99.9316 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80674	80674	0,00	11,44
80890	80890	0,00	15,96

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 2.8-2024-04

Validated substance/substance group **Artemisia annua Extrakt (H1118)**
Substance class HCK
Report date 25/11/2024
Report number 80665-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Artemisia annua Extrakt (H1118)

Special notes

When selecting the *Artemisia annua Extrakt (H1118)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Artemisia annua Extrakt (H1118)	3	1	0

Second-stage model

For differentiation of the substance/substance group *Artemisia annua Extrakt (H1118)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Artemisia annua Extrakt (H1118)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Garcinia Cambogia (H1017)	12,87	—
Silicium (H1070)	18,21	—
Ginseng (H1018)	18,83	—
Óleo de zimbro (H1112)	19,22	—
Eibisch Extrakt (H1439)	21,05	—
Artischocke Extrakt (H1440)	21,50	—
Safran Blüten (H1435)	21,88	—
Kupfer (H1032)	22,92	—
Orthovimin Neutral Komplex (H1403)	23,20	—
Safran Griffel (H1434)	23,86	—
Coenzym Q10 (H1013)	33,42	—
Vitamin K2 (75µg Mono) (H1108)	34,57	—
Ashwagandha (H1132)	36,36	—
Walnussblatt Extrakt (H1114)	37,51	—
Pathogene Komplex (H1803)	37,90	—
Vitamin B12 (H1102)	37,94	—
Vitamin B1 (H1101)	38,00	—
Magnesium (H1060)	38,47	—
Detox Komplex (H1111)	38,72	—
Vitamin E NAT (H1107)	38,74	—
Lycopen (H1058)	38,75	—
Enzian Extrakt (H1438)	39,02	—
Eisen (H1015)	40,04	—
Leaky Gut Komplex (H1802)	40,44	—
Ingwer Extrakt (H1437)	40,80	—
Zink (H1110)	41,69	—
Calcium L-(+) -Lactat Komplex (H1008)	42,16	—
Aroma Orange (H1405)	42,55	—
Biotin (H1007)	43,11	—
Antioxidantien NAT Komplex (H1004)	45,37	—
Rhodiola (H1064)	46,36	—
Glutathion (H1020)	47,24	—
Aminomix NAC (H1002)	47,85	—
Argentum (H1116)	50,84	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the sub-

stance/substance group *Artemisia annua Extrakt (H1118)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Artemisia annua Extrakt (...)	15001134	80665	60	from supplier
Hepart	Artemisia annua Extrakt (...)	19002655	81291	40	from supplier
Hepart	Artemisia annua Extrakt (...)	21000173	81332	40	from supplier

Validation samples

A total of 53 925 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 *Artemisia annua Extrakt (H1118)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 136 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Artemisia annua Extrakt (H1118)*.
- 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	Artemisia annua Extrakt (...)	20000169	81292	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were

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

Type C Spectra of independent samples not included in the database structure. *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 *Artemisia annua Extrakt (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Artemisia annua Extrakt (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 *Artemisia annua Extrakt (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	140	0	28 136
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Artemisia annua Extrakt (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 % (> 99.9314 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80665	80665	0,00	21,88
81291	81291	0,00	19,22
81332	81332	0,00	21,31

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 2.8-2024-04

Validated substance/substance group **Artischocke Extrakt (H1440)**
Substance class **HCK**
Report date **25/11/2024**
Report number **81088-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Artischocke Extrakt (H1440)

Special notes

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

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Artischocke Extrakt (H1440)	5	1	0

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Artischocke Extrakt (H1440)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Eibisch Extrakt (H1439)	12,68	—
Óleo de zimbro (H1112)	15,71	—
Enzian Extrakt (H1438)	16,20	—
Selenhefe (H1068)	17,19	—
Detox Komplex (H1111)	18,50	—
Safran Griffel (H1434)	19,14	—
Silicium (H1070)	21,44	—
Bor (H1005)	21,96	—
Rhodiola (H1064)	22,22	—
Garcinia Cambogia (H1017)	22,70	—
Artemisia annua Extrakt (H1118)	24,15	—
Ginseng (H1018)	24,15	—
Orthovimin Neutral Komplex (H1403)	25,98	—
Leaky Gut Komplex (H1802)	26,10	—
Lycopen (H1058)	26,90	—
Flohsamenschalen (H1527)	29,27	—
Ingwer Extrakt (H1437)	30,07	—
Baobab (H1410)	30,54	—
Biotin (H1007)	31,25	—
Magnesium (H1060)	31,63	—
Grüner Kaffee Extrakt (H1433)	32,01	—
Coenzym Q10 (H1013)	33,51	—
Glutathion (H1020)	34,02	—
Vitamin B1 (H1101)	34,33	—
Orthocolon Komplex (H1800)	34,90	—
Ashwagandha (H1132)	35,18	—
Zink (H1110)	35,19	—
Vitamin K2 (75µg Mono) (H1108)	35,71	—
L-Arginin (H1036)	36,01	—
Aroma Orange (H1405)	36,42	—
Kupfer (H1032)	37,22	—
Vitamin B12 (H1102)	38,23	—
Calcium L-(+) -Lactat Komplex (H1008)	40,15	—
Selen (H1067)	40,28	—
Karotte (H1513)	41,25	—
Safran Blüten (H1435)	42,31	—
PET Coenzym Q10 (H1505)	44,69	—
Chrom (H1012)	45,47	—

continued on the next page

continued from previous page

Substanz	Distance in main model	Distance in second-stage model
Eisen (H1015)	45,77	–
Vitamin D3 (H1105)	50,56	–

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Artischocke Extrakt (H1440)	18001094	81088	40	from supplier
Hepart	Artischocke Extrakt (H1440)	20001312	81278	40	from supplier
Hepart	Artischocke Extrakt (H1440)	21001670	81372	50	from supplier
Hepart	Artischocke Extrakt (H1440)	22002406	81466	40	from supplier
Hepart	Artischocke Extrakt (H1440)	24001301	81550	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 210 spectra of 5 reference samples from the substance/substance group *Artischocke Extrakt (H1440)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 28 066 spectra from a total of 567 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Artischocke Extrakt (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	Artischocke Extrakt (H1440)	20000368	81234	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Artischocke Extrakt (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Artischocke Extrakt (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 *Artischocke Extrakt (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	210	0	28 066
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Artischocke Extrakt (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 % (> 99.9312 %)	100.0000 % (> 97.1429 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81088	81088	0,00	17,54
81278	81278	0,00	24,69
81372	81372	0,00	22,69
81466	81466	0,00	15,71
81550	81550	0,00	15,70

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 2.8-2024-04

Validated substance/substance group **Ashwagandha (H1132)**
Substance class HCK
Report date 25/11/2024
Report number 10006006-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ashwagandha (H1132)

Special notes

When selecting the *Ashwagandha (H1132)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Ashwagandha (H1132)	3	0	0

Second-stage model

For differentiation of the substance/substance group *Ashwagandha* (H1132) the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Ashwagandha* (H1132) in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Detox Komplex (H1111)	13,07	—
Ginseng (H1018)	13,45	—
Eibisch Extrakt (H1439)	14,25	—
Safran Griffel (H1434)	17,34	—
Bor (H1005)	19,53	—
Vitamin K2 (75µg Mono) (H1108)	20,20	—
Enzian Extrakt (H1438)	20,76	—
Óleo de zimbro (H1112)	21,48	—
Baobab (H1410)	23,49	—
Silicium (H1070)	24,64	—
Artemisia annua Extrakt (H1118)	25,22	—
Selenhefe (H1068)	25,29	—
Grüner Kaffee Extrakt (H1433)	25,31	—
Artischocke Extrakt (H1440)	25,34	—
Leaky Gut Komplex (H1802)	26,53	—
Ingwer Extrakt (H1437)	26,86	—
Biotin (H1007)	26,94	—
Zink (H1110)	29,73	—
Orthovimin Neutral Komplex (H1403)	32,27	—
Garcinia Cambogia (H1017)	32,44	—
Vitamin E NAT (H1107)	32,75	—
Selen (H1067)	33,08	—
PET Coenzym Q10 (H1505)	33,42	—
Coenzym Q10 (H1013)	34,01	—
Chrom (H1012)	34,31	—
Vitamin B12 (H1102)	34,36	—
Lycopen (H1058)	35,88	—
Safran Blüten (H1435)	36,03	—
Aroma Orange (H1405)	38,17	—
Rhodiola (H1064)	38,53	—
Glutathion (H1020)	38,63	—
Vitamin B1 (H1101)	39,49	—
Magnesium (H1060)	39,52	—
Acacia Gum (H1526)	40,59	—
Flohsamenschalen (H1527)	42,74	—
Chondroitinsulfat (H1065)	45,56	—
Konjak Glucomannan (H1530)	48,41	—
Aminomix NAC (H1002)	49,16	—

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Substanz	Distance in main model	Distance in second-stage model
L-Arginin (H1036)	49,33	–
Calcium L-(+) -Lactat Komplex (H1008)	50,90	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ashwagandha (H1132)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ashwagandha (H1132)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Ashwagandha (H1132)	22000710	81441	40	from supplier
Hepart	Ashwagandha (H1132)	23001779	81513	40	from supplier
Hepart	Ashwagandha (H1132)	24001335	81551	40	from supplier

Validation samples

A total of 53 925 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 *Ashwagandha (H1132)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 156 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Ashwagandha (H1132)*.
- 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.

- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Ashwagandha (H1132)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Ashwagandha (H1132)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ashwagandha (H1132)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 156
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Ashwagandha (H1132)* can be clearly distinguished from all other substances. In order to make these figures comparable, 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 % (> 95.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81441	81441	0,00	17,34
81513	81513	0,00	13,45
81551	81551	0,00	13,07

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 2.8-2024-04

Validated substance/substance group **Betain Hydrochlorid (H1119)**
Substance class HCK
Report date 25/11/2024
Report number 80926-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Betain Hydrochlorid (H1119)

Special notes

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

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Betain Hydrochlorid (H1119)	4	2	0

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Betain Hydrochlorid (H1119)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Calcium L-(+)-Lactat Komplex (H1008)	21,69	—
L-Arginin (H1036)	23,20	—
Silymarin (H1071)	24,76	—
Vitamin B1 (H1101)	25,99	—
Coenzym Q10 (H1013)	29,88	—
OPC Proanthocyanidine (Pine Bark) (...)	30,60	—
L-Carnitin (H1038)	31,04	—
Aroma Orange (H1405)	35,22	—
Rhodiola (H1064)	37,11	—
Bioflavonoide Komplex (H1006)	38,93	—
Glutathion (H1020)	39,80	—
Orthocolon Komplex (H1800)	40,55	—
Antioxidantien NAT Komplex (H1004)	42,89	—
Garcinia Cambogia (H1017)	43,22	—
Orthovimin Neutral Komplex (H1403)	46,28	—
Artischocke Extrakt (H1440)	50,84	—

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Betain Hydrochlorid (H1119)	17000829	80926	40	from supplier
Hepart	Betain Hydrochlorid (H1119)	19000533	81169	40	from supplier
Hepart	Betain Hydrochlorid (H1119)	21002227/1	81440	40	from supplier
Hepart	Betain Hydrochlorid (H1119)	23002237	81518	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Betain Hydrochlorid (H1119)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 28 116 spectra from a total of 568 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Betain Hydrochlorid (H1119)*.
- 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	Betain Hydrochlorid (H1119)	19001723	81203	40
Hepart	Betain Hydrochlorid (H1119)	22002247	81458	40

- 22 599 spectra from a total of 494 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Betain Hydrochlorid (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 *Betain Hydrochlorid (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	160	0	28 116
Type B	0	80	0	22 599
Type C	0	0	0	2970

The substance/substance group *Betain Hydrochlorid (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 % (> 99.9313 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8684 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80926	80926	0,00	52,24
81169	81169	0,00	46,94
81440	81440	0,00	24,76
81518	81518	0,00	26,91

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 2.8-2024-04

Validated substance/substance group **Brokkoli (H1512)**
Substance class HCK
Report date 25/11/2024
Report number 10006321-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Brokkoli (H1512)

Special notes

When selecting the *Brokkoli (H1512)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Brokkoli (H1512)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Brokkoli (H1512)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Brokkoli (H1512)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Aroma Orange (H1405)	13,98	—
Calcium L-(+) -Lactat Komplex (H1008)	17,65	—
Grünkohl (H1126)	19,71	—
Rhodiola (H1064)	21,31	—
L-Arginin (H1036)	26,41	—
Antioxidantien NAT Komplex (H1004)	27,09	—
Vitamin B1 (H1101)	28,63	—
Karotte (H1513)	29,48	—
Orthocolon Komplex (H1800)	35,63	—
PET Basis (H1503)	36,20	—
Sanddorn (H1523)	37,88	—
Glutathion (H1020)	38,98	—
Vitamin C (H1104)	39,12	—
Kohlmix (H1514)	40,28	—
Rote Bete (H1515)	45,35	—
Catechin-Extrakt (H1010)	46,84	—
L-Carnitin (H1038)	46,84	—
Cranberry (H1519)	48,04	—
PET Gelenke (H1501)	48,26	—
Bioflavonoide Komplex (H1006)	48,34	—
Coenzym Q10 (H1013)	48,57	—
PET Well-Aging (H1500)	49,09	—
Garcinia Cambogia (H1017)	50,23	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Brokkoli (H1512)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Brokkoli (H1512)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Brokkoli (H1512)	23002194	81525	40	from supplier

Validation samples

A total of 53 925 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 *Brokkoli (H1512)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Brokkoli (H1512)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Brokkoli (H1512)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Brokkoli (H1512)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Brokkoli (H1512)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Brokkoli (H1512)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81525	81525	0,00	19,71

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 2.8-2024-04

Validated substance/substance group **Catechin-Extrakt (H1010)**
Substance class HCK
Report date 25/11/2024
Report number 80031-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Catechin-Extrakt (H1010)

Special notes

When selecting the *Catechin-Extrakt (H1010)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Catechin-Extrakt (H1010)	9	0	18

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Catechin-Extrakt (H1010)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Calcium L-(+)-Lactat Komplex (H1008)	12,21	—
L-Carnitin (H1038)	14,89	—
Rhodiola (H1064)	17,04	—
Griffonia (H1035)	19,05	—
Ginkgo Extrakt (H1024)	19,12	—
Grüner Kaffee Extrakt (H1433)	20,74	—
Bioflavonoide Komplex (H1006)	21,58	—
Vitamine Komplex (H1100)	23,86	—
OPC Proanthocyanidine (Pine Bark) (...)	25,03	—
Silymarin (H1071)	35,76	—
PET Immunsystem (H1502)	36,39	—
Coenzym Q10 (H1013)	39,40	—
Antibiose forte Komplex (H1115)	39,96	—
Aroma Orange (H1405)	40,01	—
Vitamin B1 (H1101)	41,38	—
Vitamin B6 (Pyridoxal-5-phosphat) (...)	42,44	—
L-Arginin (H1036)	42,77	—
PET Basis (H1503)	45,05	—
Betain Hydrochlorid (H1119)	45,13	—
Antioxidantien NAT Komplex (H1004)	46,25	—
Vitamin C (H1104)	49,13	—
Kreatin (H1031)	50,23	—

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Extrakt (H1010)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Catechin-Extrakt (H1010)	062901	80338	40	from supplier
Hepart	Catechin-Extrakt (H1010)	062701	80339	40	from supplier
Hepart	Catechin-Extrakt (H1010)	062801	80340	40	from supplier
Hepart	Catechin-Extrakt (H1010)	15000206	80555	60	from supplier
Hepart	Catechin-Extrakt (H1010)	15000206/4	80849	40	from supplier
Hepart	Catechin-Extrakt (H1010)	17000409/0	80880	40	from supplier
Hepart	Catechin-Extrakt (H1010)	18001420	81144	40	from supplier
Hepart	Catechin-Extrakt (H1010)	22000151	81404	40	from supplier
Hepart	Catechin-Extrakt (H1010)	22000851	81427	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 380 spectra of 9 reference samples from the substance/substance group *Catechin-Extrakt (H1010)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 27 896 spectra from a total of 563 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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-Extrakt (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-Extrakt (H1010)	15000206	80872	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 15 *Apo-Ident* customers from 19 batches from the substance/substance group *Catechin-Extrakt (H1010)*.
- Among them are spectra of independent samples from 18 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	Catechin-Extrakt (H1010)	62901	1
Heaprt AG	Catechin-Extrakt (H1010)	17000409/2	1
Hepart / Unisan	Catechin-Extrakt (H1010)	170004092	1
Hepart AG, CH-8280 K...	Catechin-Extrakt (H1010)	1571025702	1
Hepart AG, CH-8280 K...	Catechin-Extrakt (H1010)	18601	1
Hepart AG, CH-8280 K...	Catechin-Extrakt (H1010)	62901	1
Hepart AG/Unisan	Catechin-Extrakt (H1010)	18001420/0	1
Hepart AG/Unisan	Catechin-Extrakt (H1010)	18001420/1	1
Hepart AG	Catechin-Extrakt (H1010)	130208020	1
Hepart AG	Catechin-Extrakt (H1010)	15000206/2	1
Hepart AG	Catechin-Extrakt (H1010)	1574018601	1
Hepart AG	Catechin-Extrakt (H1010)	17000409/2	1
Hepart AG	Catechin-Extrakt (H1010)	18601	2
Hepart	Catechin-Extrakt (H1010)	115000206/5	1
Hepart	Catechin-Extrakt (H1010)	17000409	1
Hepart	Catechin-Extrakt (H1010)	17000409/0	1
Hepart	Catechin-Extrakt (H1010)	17000409/2	3
Hepart	Catechin-Extrakt (H1010)	17000409/3	5
Hepart	Catechin-Extrakt (H1010)	17000409/4	1
Hepart	Catechin-Extrakt (H1010)	18001420/0	1
Unisan/Hepart AG	Catechin-Extrakt (H1010)	18601	1
Unisan	Catechin-Extrakt (H1010)	130208020	1
Unisan	Catechin-Extrakt (H1010)	15000206/2	1
Unisan	Catechin-Extrakt (H1010)	1571025702	1
Unisan	Catechin-Extrakt (H1010)	1571681501	1
Unisan	Catechin-Extrakt (H1010)	17000409	1
Unisan	Catechin-Extrakt (H1010)	25702	1
Unisan	Catechin-Extrakt (H1010)	62801	1
Unisan	Catechin-Extrakt (H1010)	62901	1
Unisan	Catechin-Extrakt (H1010)	681501	1

- 2933 spectra from 26 *Apo-Ident* customers from a total of 1441 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-Extrakt (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-Extrakt (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	380	0	27 896
Type B	0	40	0	22 639
Type C	0	24	13	2933

The substance/substance group *Catechin-Extrakt (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 % (> 99.9310 %)	100.0000 % (> 98.4211 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8309 %)	64.8649 % (> 56.7568 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80338	80338	0,00	31,77
80339	80339	0,00	43,25
80340	80340	0,00	20,74
80555	80555	0,00	32,18
80849	80849	0,00	29,96
80880	80880	0,00	25,89
81144	81144	0,00	42,91
81404	81404	0,00	17,60
81427	81427	0,00	33,40

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 2.8-2024-04

Validated substance/substance group **Chaga (H1011)**
Substance class HCK
Report date 25/11/2024
Report number 80032-2024-11-25
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

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Chaga (H1011)	6	1	7

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Chaga (H1011)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Kupfer (H1032)	14,96	—
Garcinia Cambogia (H1017)	16,61	—
Spurenelemente SE Komplex (H1082)	17,50	—
Walnussblatt Extrakt (H1114)	24,35	—
Eisen (H1015)	32,64	—
Artemisia annua Extrakt (H1118)	38,18	—
Magnesium (H1060)	39,04	—
Argentum (H1116)	40,78	—
Antibiose mite Komplex (H1113)	41,89	—
Pathogene Komplex (H1803)	47,03	—
PET Basis (H1503)	49,73	—

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.

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Hepart	Chaga (H1011)	21002785/0	81423	40	from supplier
Hepart	Chaga (H1011)	23000051	81465	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Chaga (H1011)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 28016 spectra from a total of 566 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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

- 22619 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 4 *Apo-Ident* customers from 8 batches from the substance/substance group *Chaga (H1011)*.
- 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	Chaga (H1011)	14001688/5	1
Hepart	Chaga (H1011)	16000235-1	3
Hepart	Chaga (H1011)	17001560/1	1
Purren Apotheke	Chaga (H1011)	1514675601	1
Unisan/Hepart AG	Chaga (H1011)	46701	1

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Supplier	Substance	Batch	Spectra
Unisan	Chaga (H1011)	14001688	1
Unisan	Chaga (H1011)	16000235	1
Unisan	Chaga (H1011)	64001	2

- 2959 spectra from 26 *Apo-Ident* customers from a total of 1452 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	260	0	28 016
Type B	0	60	0	22 619
Type C	0	11	0	2959

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 % (> 97.6923 %)
Type B	100.0000 % (> 99.8693 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8549 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80466	80466	0,00	72,11
80493	80493	0,00	40,48

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80825	80825	0,00	33,01
80952	80952	0,00	32,25
81423	81423	0,00	25,00
81465	81465	0,00	33,71

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 2.8-2024-04

Validated substance/substance group **Chiasamenprotein (H1506)**
Substance class HCK
Report date 25/11/2024
Report number 10006319-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chiasamenprotein (H1506)

Special notes

When selecting the *Chiasamenprotein (H1506)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Chiasamenprotein (H1506)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Chiasamenprotein (H1506)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Chiasamenprotein (H1506)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
PET Immunsystem (H1502)	25,11	—
Kakao (H1521)	42,02	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chiasamenprotein (H1506)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Chiasamenprotein (H1506)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Chiasamenprotein (H1506)	23002137	81522	40	from supplier

Validation samples

A total of 53 925 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 *Chiasamenprotein (H1506)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with

the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Chiasamenprotein (H1506)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Chiasamenprotein (H1506)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Chiasamenprotein (H1506)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chiasamenprotein (H1506)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Chiasamenprotein (H1506)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81522	81522	0,00	25,11

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 2.8-2024-04

Validated substance/substance group **Chondroitinsulfat (H1065)**
Substance class HCK
Report date 25/11/2024
Report number 10005853-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chondroitinsulfat (H1065)

Special notes

When selecting the *Chondroitinsulfat (H1065)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Chondroitinsulfat (H1065)	6	3	14

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Chondroitinsulfat (H1065)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Coenzym Q10 (H1013)	19,74	—
Vitamin E NAT (H1107)	39,12	—
Silicium (H1070)	41,13	—
PET Coenzym Q10 (H1505)	42,14	—
Ginseng (H1018)	46,05	—
Magnesium (H1060)	55,25	—

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Chondroitinsulfat (H1065)	14001991	80533	60	from supplier
Hepart	Chondroitinsulfat (H1065)	031801	80584	60	from supplier
Hepart	Chondroitinsulfat (H1065)	14001985/2	80779	60	from supplier
Hepart	Chondroitinsulfat (H1065)	17000211	80871	40	from supplier
Hepart	Chondroitinsulfat (H1065)	20002086/0	81393	50	from supplier
Hepart	Chondroitinsulfat (H1065)	21002683	81462	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 310 spectra of 6 reference samples from the substance/substance group *Chondroitinsulfat (H1065)*. These samples are listed above in the [calibration samples](#) section. The reference

samples come from 6 different batches.

- 27 966 spectra from a total of 566 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Chondroitinsulfat (H1065)*.
- 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	Chondroitinsulfat (H1065)	14001985	80532	60
Hepart	Chondroitinsulfat (H1065)	19000780	81180	40
Hepart	Chondroitinsulfat (H1065)	23000663	81490	40

- 22 539 spectra from a total of 493 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 40 spectra from 15 *Apo-Ident* customers from 16 batches from the substance/substance group *Chondroitinsulfat (H1065)*.
- 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
Fagron	Chondroitinsulfat (H1065)	1821031801	1
Hepart AG, CH-8280 K...	Chondroitinsulfat (H1065)	1820031801	1
Hepart AG, CH-8280 K...	Chondroitinsulfat (H1065)	31801	1
Hepart AG	Chondroitinsulfat (H1065)	17000211/1	1
Hepart AG	Chondroitinsulfat (H1065)	19000780/0	1
hepart ag	Chondroitinsulfat (H1065)	31801	1

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Supplier	Substance	Batch	Spectra
Hepart AG	Chondroitinsulfat (H1065)	31801	1
Hepart AG	Chondroitinsulfat (H1065)	31801/1	1
Hepart/Unisan	Chondroitinsulfat (H1065)	19000780/1	1
Hepart	Chondroitinsulfat (H1065)		1
Hepart	Chondroitinsulfat (H1065)	14001985/5	1
Hepart	Chondroitinsulfat (H1065)	14001985-7	5
Hepart	Chondroitinsulfat (H1065)	17000211	1
Hepart	Chondroitinsulfat (H1065)	17000211/0	1
Hepart	Chondroitinsulfat (H1065)	17000211/1	1
Hepart	Chondroitinsulfat (H1065)	19000780	1
Hepart	Chondroitinsulfat (H1065)	19000780/0	6
Hepart	Chondroitinsulfat (H1065)	19000780/1	2
Purren Apotheke	Chondroitinsulfat (H1065)	1821964101	1
Unisan/Hepart AG	Chondroitinsulfat (H1065)	31801	2
Unisan	Chondroitinsulfat (H1065)	1801	2
Unisan	Chondroitinsulfat (H1065)	1820001801	2
Unisan	Chondroitinsulfat (H1065)	1821964101	1
Unisan	Chondroitinsulfat (H1065)	31801	4

- 2930 spectra from 26 *Apo-Ident* customers from a total of 1444 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 *Chondroitinsulfat (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 *Chondroitinsulfat (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	310	0	27 966
Type B	0	140	0	22 539
Type C	0	33	7	2930

The substance/substance group *Chondroitinsulfat (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 % (> 98.0645 %)
Type B	100.0000 % (> 99.8674 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 98.8302 %)	82.5000 % (> 75.0000 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80533	80533	0,00	49,02
80584	80584	0,00	67,08
80779	80779	0,00	54,72
80871	80871	0,00	65,14
81393	81393	0,00	66,18
81462	81462	0,00	42,14

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 2.8-2024-04

Validated substance/substance group	Classificação I HCK
Substance class	HCK
Report date	25/11/2024
Report number	80331-2024-11-25
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Classificação I HCK; Acacia Gum (H1526); Baobab (H1410); Biotin (H1007); Bor (H1005); Chrom (H1012); Detox Komplex (H1111); Eibisch Extrakt (H1439); Enzian Extrakt (H1438); Folat (L-5-MTHF) (H1128); Ginseng (H1018); Guar-Granulat (H1023); Ingwer Extrakt (H1437); Iod (H1044); Lycoplen (H1058); Óleo de zimbro (H1112); Safran Blüten (H1435); Safran Griffel (H1434); Selen (H1067); Selenhefe (H1068); Silicium (H1070); Vitamin B12 (H1102); Vitamin D3 (H1105); Vitamin K2 (75µg Mono) (H1108)

Special notes

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

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Classificação I HCK	73	35	170

Second-stage model

For differentiation of the substance/substance group *Classificação I HCK* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Classificação I HCK* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
PET Coenzym Q10 (H1505)	11,84	—
Artischocke Extrakt (H1440)	13,31	—
Leaky Gut Komplex (H1802)	13,73	—
Artemisia annua Extrakt (H1118)	14,65	—
Aroma Orange (H1405)	14,79	—
Flohsamenschalen (H1527)	17,28	—
Garcinia Cambogia (H1017)	17,43	—
Vitamin E NAT (H1107)	17,56	—
Grüner Kaffee Extrakt (H1433)	18,40	—
Orthovimin Neutral Komplex (H1403)	18,64	—
Zink (H1110)	19,40	—
Glutathion (H1020)	19,85	—
Vitamin B1 (H1101)	21,85	—
Coenzym Q10 (H1013)	21,97	—
Ashwagandha (H1132)	22,20	—
Chondroitinsulfat (H1065)	24,34	—
Konjak Glucomannan (H1530)	27,52	—
Haferkleie beta-Glucan (H1529)	29,64	—
Spurenelemente BAG (H1078)	30,80	—
Rhodiola (H1064)	31,00	—
Orthocolon Komplex (H1800)	31,71	—
Magnesium (H1060)	34,54	—
L-Arginin (H1036)	34,80	—
Aminomix NAC (H1002)	35,27	—
Kupfer (H1032)	35,52	—
Antioxidantien NAT Komplex (H1004)	36,23	—
Eisen (H1015)	37,14	—
Calcium L-(+) -Lactat Komplex (H1008)	37,15	—
Lutein-Zeaxanthin-Astaxanthin (H1129)	38,77	—
Ginkgo Extrakt (H1024)	42,99	—
Betain Hydrochlorid (H1119)	46,60	—
Spurenelemente JK Komplex (H1080)	47,32	—

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Substanz	Distance in main model	Distance in second-stage model
L-Carnitin (H1038)	49,38	—
Vitamine BAG Komplex (H1091)	49,42	—
PET Gelenke (H1501)	49,81	—
OPC Proanthocyanidine (Pine Bark) (...)	49,83	—

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Acacia Gum (H1526)	23000659	81493	40	from supplier
Hepart	Baobab (H1410)	16001158	80921	40	from supplier
Hepart	Baobab (H1410)	18000501/0	81158	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	Bor (H1005)	17000827/1	81119	40	from supplier
Hepart	Bor (H1005)	23002123	81515	40	from supplier
Hepart	Chrom (H1012)	16000520/0	80791	40	from supplier
Hepart	Chrom (H1012)	16000520/4	80792	40	from supplier
Hepart	Chrom (H1012)	23000555	81470	40	from supplier
Hepart	Detox Komplex (H1111)	16001075 (MM)	80894	40	from supplier
Hepart	Detox Komplex (H1111)	16001076	80895	40	from supplier
Hepart	Eibisch Extrakt (H1439)	18001095	81091	40	from supplier
Hepart	Eibisch Extrakt (H1439)	21003061/0	81422	40	from supplier
Hepart	Enzian Extrakt (H1438)	18001096	81092	40	from supplier
Hepart	Enzian Extrakt (H1438)	21001723	81368	50	from supplier
Hepart	Folat (L-5-MTHF) (H1128)	22000772	81447	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	Ginseng (H1018)	22002234/0	81480	40	from supplier
Hepart	Ginseng (H1018)	23001439	81500	40	from supplier
Hepart	Guar-Granulat (H1023)	20002454	81310	40	from supplier
Hepart	Guar-Granulat (H1023)	24000935	81547	30	from supplier
Hepart	Ingwer Extrakt (H1437)	18001115	81089	40	from supplier
Hepart	Ingwer Extrakt (H1437)	21001131	81377	50	from supplier
Hepart	Iod (H1044)	22002410	81509	40	from supplier
Hepart	Lycopen (H1058)	053501	80335	40	from supplier
Hepart	Lycopen (H1058)	17000619	80913	40	from supplier
Hepart	Lycopen (H1058)	17000619/0	81024	40	from supplier
Hepart	Óleo de zimbro (H1112)	15001004	80702	60	from supplier
Hepart	Óleo de zimbro (H1112)	16000683	80891	40	from supplier
Hepart	Safran Blüten (H1435)	18000806	81056	40	from supplier
Hepart	Safran Blüten (H1435)	19000801	81204	40	from supplier
Hepart	Safran Griffel (H1434)	18001093	81090	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Safran Griffel (H1434)	21001804	81370	50	from supplier
Hepart	Safran Griffel (H1434)	23001375/3	81546	30	from supplier
Hepart	Selen (H1067)	065601	80361	40	from supplier
Hepart	Selen (H1067)	065501	80364	40	from supplier
Hepart	Selen (H1067)	065701	80366	40	from supplier
Hepart	Selen (H1067)	15000157	80530	60	from supplier
Hepart	Selen (H1067)	15000158	80531	60	from supplier
Hepart	Selen (H1067)	15000159	80535	60	from supplier
Hepart	Selen (H1067)	065501	80706	60	from supplier
Hepart	Selen (H1067)	16001349	80822	40	from supplier
Hepart	Selen (H1067)	18000578	81025	40	from supplier
Hepart	Selenhefe (H1068)	16001450/1	81014	40	from supplier
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
Hepart	Silicium (H1070)	20002801	81306	40	from supplier
Hepart	Silicium (H1070)	210021-29-30	81400	50	from supplier
Hepart	Silicium (H1070)	23000181	81471	40	from supplier
Hepart	Silicium (H1070)	23000336	81473	40	from supplier
Hepart	Silicium (H1070)	23000337/1	81507	40	from supplier
Hepart	Vitamin B12 (H1102)	025017	80353	40	from supplier
Hepart	Vitamin B12 (H1102)	15000993	80603	60	from supplier
Hepart	Vitamin B12 (H1102)	15000993(B1)	80604	60	from supplier
Hepart	Vitamin B12 (H1102)	17000277	80910	40	from supplier
Hepart	Vitamin B12 (H1102)	19001114	81201	40	from supplier
Hepart	Vitamin B12 (H1102)	23000507	81489	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 Mono) (H1108)	16001559	80874	40	from supplier
Hepart	Vitamin K2 (75µg Mono) (H1108)	18001656	81126	60	from supplier
Hepart	Vitamin K2 (75µg Mono) (H1108)	20000422	81282	40	from supplier
Hepart	Vitamin K2 (75µg Mono) (H1108)	21000562	81328	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 3310 spectra of 76 reference samples from the substance/substance group *Classificação I HCK*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 73 different batches.
- 24 966 spectra from a total of 500 batches from further 108 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 1530 spectra of 38 reference samples from the substance/substance group *Classificação I HCK*.
- Among them are spectra of independent samples from 35 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
Hepart	Baobab (H1410)	20001258	81280	40
Hepart	Baobab (H1410)	21002191	81402	50
Hepart	Biotin (H1007)	20002313	81324	40
Hepart	Biotin (H1007)	21000967	81385	50
Hepart	Biotin (H1007)	22001540	81437	40
Hepart	Chrom (H1012)	977201	80033	15
Hepart	Chrom (H1012)	16000520/2	80793	40
Hepart	Chrom (H1012)	18002076	81148	40
Hepart	Detox Komplex (H1111)	16001075(Nr. 5-7)	80892	40
Hepart	Detox Komplex (H1111)	16001075(Nr. 1-4)	80893	40
Hepart	Ginseng (H1018)	17000285	80873	40
Hepart	Selen (H1067)	16001350	80823	40
Hepart	Selen (H1067)	16001351	80824	40
Hepart	Selen (H1067)	18000422	81026	40
Hepart	Selen (H1067)	18001021	81078	40
Hepart	Selen (H1067)	18001022	81079	40
Hepart	Selen (H1067)	21001836	81365	50
Hepart	Selen (H1067)	21001761	81383	50
Hepart	Selen (H1067)	22000058	81409	40
Hepart	Selen (H1067)	23000482	81479	40
Hepart	Silicium (H1070)	17000326	80906	40
Hepart	Silicium (H1070)	19000534	81184	40
Hepart	Silicium (H1070)	20001082	81265	40
Hepart	Vitamin B12 (H1102)	15000993(F2)	80605	60
Hepart	Vitamin B12 (H1102)	17000276	80911	40
Hepart	Vitamin B12 (H1102)	21000708	81335	40
Hepart	Vitamin D3 (H1105)	17000874	80959	40
Hepart	Vitamin D3 (H1105)	19001583	81224	40
Hepart	Vitamin D3 (H1105)	20000338	81266	40
Hepart	Vitamin D3 (H1105)	20001988	81311	40
Hepart	Vitamin D3 (H1105)	20001952	81312	40
Hepart	Vitamin D3 (H1105)	21000024	81349	40
Hepart	Vitamin D3 (H1105)	210012-40-41	81389	45
Hepart	Vitamin D3 (H1105)	23001560	81503	40
Hepart	Ginseng (H1018)	067801	80403	40
Hepart	Ginseng (H1018)	17000285	81103	40
Hepart	Silicium (H1070)	18000448	81022 [†]	10

- 21 149 spectra from a total of 459 batches from further 71 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

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

- 513 spectra from 22 *Apo-Ident* customers from 221 batches from the substance/substance group *Classificação I HCK*.
- Among them are spectra of independent samples from 198 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Selen (H1067)	1144010201	1
Euro OTC	Ginseng (H1018)	15001047/0	1
Fagron	Chrom (H1012)	1582977201	3
Fagron	Vitamin D3 (H1105)	63701	1
Falcento	Chrom (H1012)	16000520	4
Flaigg Ag CH-4147 Ae...	Vitamin K2 (75µg Mono) (H1108)	18001656/5	1
HCK	Vitamin B12 (H1102)	1000993-0	1
HCK	Chrom (H1012)	14000429	1
HCK	Chrom (H1012)	14000429/7	1
HCK	Ginseng (H1018)	14002047	1
HCK	Selen (H1067)	15000157/1	1
HCK	Selen (H1067)	15000157-1	1
HCK	Selen (H1067)	15000157-2	1
HCK	Selen (H1067)	15000158-0	1
HCK	Vitamin D3 (H1105)	15000490/1	1
HCK	Vitamin D3 (H1105)	15000490-4	1
HCK	Vitamin D3 (H1105)	15000490-5	1
HCK	Biotin (H1007)	15000735/2	2
HCK	Biotin (H1007)	15000735-2	1
HCK	Biotin (H1007)	15000735-5	3
HCK	Vitamin B12 (H1102)	15000993	1
HCK	Vitamin B12 (H1102)	15000993/0	1
HCK	Chrom (H1012)	16000520-0	2
HCK	Lycopen (H1058)	17000619	1
HCK	Lycopen (H1058)	17000619/0	1
HCK	Lycopen (H1058)	53501-8	2
HCK	Selen (H1067)	65501/2	1
HCK	Selenhefe (H1068)	71901	1
HCK	Vitamin B12 (H1102)	75301/4	1
HCK	Vitamin D3 (H1105)	8101	1
Hepart AG, CH-8280 K...	Selen (H1067)	10201	1
Hepart AG, CH-8280 K...	Vitamin B12 (H1102)	1064026401	1
Hepart AG, CH-8280 K...	Selen (H1067)	1144010201	1
Hepart AG, CH-8280 K...	Vitamin D3 (H1105)	1336008101	2
Hepart AG, CH-8280 K...	Biotin (H1007)	1592029603	1
Hepart AG, CH-8280 K...	Vitamin D3 (H1105)	64801	1
Hepart AG, CH-8280 K...	Chrom (H1012)	977201	2
Hepart ag/ Unisan	Vitamin D3 (H1105)	20001952/0	1
Hepart AG/Unisan	Vitamin B12 (H1102)	17000276/2	1
Hepart ag/Unisan	Vitamin B12 (H1102)	17000277	1
Hepart AG/Unisan	Vitamin B12 (H1102)	17000277/0	1
Hepart AG/Unisan	Vitamin B12 (H1102)	17000277/2	2

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

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Supplier	Substance	Batch	Spectra
Hepart ag/Unisan	Selen (H1067)	18000578/1	1
Hepart ag/Unisan	Selen (H1067)	18001021	1
Hepart AG/Unisan	Vitamin D3 (H1105)	19001097	1
Hepart AG/Unisan	Vitamin D3 (H1105)	20000338/2	1
Hepart AG	Selen (H1067)	10201	9
Hepart AG	Vitamin B12 (H1102)	1064025017	1
Hepart AG	Vitamin B12 (H1102)	1064026401	1
Hepart AG	Selen (H1067)	1144010201	3
Hepart AG	Vitamin D3 (H1105)	1335008101	1
Hepart AG	Chrom (H1012)	14000429/4	1
Hepart AG	Vitamin D3 (H1105)	14000481	3
Hepart AG	Selen (H1067)	15000157/1	1
Hepart AG	Selen (H1067)	15000158/0	1
Hepart AG	Vitamin D3 (H1105)	15000490/2	1
Hepart AG	Vitamin B12 (H1102)	15000993/0	1
Hepart AG	Ginseng (H1018)	15001047	1
Hepart AG	Biotin (H1007)	1592029603	3
Hepart AG	Chrom (H1012)	16000520/7	5
Hepart AG	Chrom (H1012)	16000520/8	5
Hepart AG	Vitamin D3 (H1105)	16000952/1	1
Hepart AG	Selen (H1067)	16001349/0	2
Hepart AG	Selen (H1067)	16001350/0	16
Hepart AG	Biotin (H1007)	16001396/5	1
Hepart AG	Vitamin B12 (H1102)	17000276/0	1
Hepart AG	Vitamin B12 (H1102)	170002796/0	1
Hepart AG	Ginseng (H1018)	17000285/0	1
Hepart AG	Lycopen (H1058)	17000619/1	1
Hepart AG	Bor (H1005)	17000827/3	1
Hepart AG	Selen (H1067)	18000422/2	1
Hepart AG	Vitamin B12 (H1102)	25017	4
Hepart AG	Biotin (H1007)	29601	2
Hepart AG	Biotin (H1007)	29603	3
Hepart AG	Ginseng (H1018)	38802	1
Hepart AG	Lycopen (H1058)	47301	1
Hepart AG	Lycopen (H1058)	53501	1
Hepart AG	Vitamin D3 (H1105)	63701	3
Hepart AG	Vitamin D3 (H1105)	64801	4
Hepart AG	Selen (H1067)	65701	3
Hepart AG	Vitamin D3 (H1105)	8101	1
Hepart AG	Selen (H1067)	933301	1
Hepart AG	Chrom (H1012)	977201	5
Hepart AG	Chrom (H1012)	H101221	1
Hepart/Unisan	Selen (H1067)	18001021/0	1
Hepart	Biotin (H1007)	14000862/4	2
Hepart	Selen (H1067)	15000157	1
Hepart	Selen (H1067)	15000158	1
Hepart	Selen (H1067)	15000158/1	1
Hepart	Selen (H1067)	15000158-1	2
Hepart	Selen (H1067)	15000159-0	1
Hepart	Selen (H1067)	15000159-1	2
Hepart	Vitamin B12 (H1102)	15000993/2	1
Hepart	Vitamin B12 (H1102)	15000993-1	1
Hepart	Chrom (H1012)	16000520	1
Hepart	Chrom (H1012)	16000520/3	4
Hepart	Chrom (H1012)	16000520/4	1
Hepart	Chrom (H1012)	16000520-1	3
Hepart	Chrom (H1012)	16000520-2	2
Hepart	Chrom (H1012)	160005203	1
Hepart	Vitamin D3 (H1105)	16000952	3
Hepart	Vitamin D3 (H1105)	16000952-0	1

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Supplier	Substance	Batch	Spectra
Hepart	Vitamin D3 (H1105)	16000952-1	2
Hepart	Vitamin D3 (H1105)	16001212/0	1
Hepart	Vitamin D3 (H1105)	16001212-0	1
Hepart	Vitamin D3 (H1105)	16001212-1	2
Hepart	Selen (H1067)	16001349/0	2
Hepart	Selen (H1067)	16001349-0	1
Hepart	Selen (H1067)	160013497/0	1
Hepart	Selen (H1067)	16001350	1
Hepart	Selen (H1067)	16001350/0	3
Hepart	Selen (H1067)	16001351/0	2
Hepart	Biotin (H1007)	16001396/0	1
Hepart	Biotin (H1007)	16001396/1	1
Hepart	Biotin (H1007)	16001396/4	2
Hepart	Biotin (H1007)	16001396-1	1
Hepart	Biotin (H1007)	16001396-2	2
Hepart	Vitamin B12 (H1102)	17000276	1
Hepart	Vitamin B12 (H1102)	17000276/0	1
Hepart	Vitamin B12 (H1102)	17000276/1	1
Hepart	Vitamin B12 (H1102)	17000276/2	1
Hepart	Vitamin B12 (H1102)	17000276-0	1
Hepart	Vitamin B12 (H1102)	17000277/0	4
Hepart	Vitamin B12 (H1102)	17000277/1	1
Hepart	Ginseng (H1018)	17000285	1
Hepart	Lycopene (H1058)	17000619	1
Hepart	Bor (H1005)	17000827/4	1
Hepart	Vitamin D3 (H1105)	17000874	2
Hepart	Vitamin D3 (H1105)	17000874/1	6
Hepart	Vitamin D3 (H1105)	17000874-0	4
Hepart	Silicium (H1070)	1700817/1	1
Hepart	Selen (H1067)	18000422/0	1
Hepart	Selen (H1067)	18000422/1	4
Hepart	Selen (H1067)	18000422/2	2
Hepart	Selen (H1067)	18000578	2
Hepart	Selen (H1067)	18000578/0	2
Hepart	Selen (H1067)	18000578/1	4
Hepart	Ginseng (H1018)	18000794/0	1
Hepart	Selen (H1067)	18001021/0	4
Hepart	Selen (H1067)	18001021/1	1
Hepart	Selen (H1067)	18001022/0	4
Hepart	Selen (H1067)	18001022/1	3
Hepart	Selen (H1067)	18001022/2	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	18001656	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	18001656/13	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	18001656/17	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	18001656/171	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	18001656/5	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	18001656/7	1
Hepart	Vitamin D3 (H1105)	18001771/0	3
Hepart	Vitamin D3 (H1105)	18001951/0	3
Hepart	Vitamin D3 (H1105)	18001951/1	2
Hepart	Vitamin D3 (H1105)	18001951/2	2
Hepart	Vitamin D3 (H1105)	18001951/4	1
Hepart	Chrom (H1012)	18002076	1
Hepart	Chrom (H1012)	18002076/0	1
Hepart	Chrom (H1012)	18002076/1	1
Hepart	Chrom (H1012)	18002076/2	1
Hepart	Chrom (H1012)	18002076/6	1
Hepart	Chrom (H1012)	18002076/7	4
Hepart	Biotin (H1007)	19000754/0	1
Hepart	Biotin (H1007)	19000754/1	2

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Supplier	Substance	Batch	Spectra
Hepart	Ginseng (H1018)	19000824/0	1
Hepart	Ginseng (H1018)	19000824/1	2
Hepart	Ginseng (H1018)	19000824/2	1
Hepart	Ginseng (H1018)	19000824/5	1
Hepart	Vitamin D3 (H1105)	19001097/0	2
Hepart	Silicium (H1070)	19001317/0	2
Hepart	Vitamin D3 (H1105)	19001583/0	2
Hepart	Biotin (H1007)	20000178	1
Hepart	Biotin (H1007)	20000178/0	3
Hepart	Vitamin D3 (H1105)	20000338/0	1
Hepart	Vitamin D3 (H1105)	20000338/1	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	20000422	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	20000422/0	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	20000422/1	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	20000422/2	3
Hepart	Lycopen (H1058)	20001766/0	1
Hepart	Vitamin D3 (H1105)	20001952/0	4
Hepart	Vitamin D3 (H1105)	20001988/0	1
Hepart	Biotin (H1007)	20002313	1
Hepart	Biotin (H1007)	20002313/1	2
Hepart	Biotin (H1007)	20002313/2	1
Hepart	Vitamin D3 (H1105)	21000024	1
Hepart	Vitamin D3 (H1105)	21000024/0	4
Hepart	Vitamin K2 (75µg Mono) (H1108)	21000562	1
Hepart	Vitamin K2 (75µg Mono) (H1108)	210005627/3	1
Hepart	Bor (H1005)	21000564/1	1
Hepart	Bor (H1005)	21000564/2	2
Hepart	Bor (H1005)	21000564/3	1
Hepart	Vitamin D3 (H1105)	21001240/0	1
Hepart	Vitamin B12 (H1102)	21001674	1
Hepart	Selen (H1067)	21001761/0	1
Hepart	Selen (H1067)	21001836/0	2
Hepart	Vitamin B12 (H1102)	21002290/0	2
Hepart	Vitamin K2 (75µg Mono) (H1108)	21002794	1
Hepart	Chrom (H1012)	21003059/0	1
Hepart	Silicium (H1070)	2101442/0	1
Hepart	Selen (H1067)	22000057/0	1
Hepart	Vitamin D3 (H1105)	22000391	1
Hepart	Vitamin D3 (H1105)	22000391/0	3
Hepart	Selenhefe (H1068)	71901	2
Hepart	Vitamin B12 (H1102)	75301	1
Ichthyol Gesellschaft...	Biotin (H1007)	1591983601	1
Unisan GmbH, 78465 K...	Vitamin D3 (H1105)	63701	1
Unisan/Hepart AG	Ginseng (H1018)	38802	1
Unisan/Hepart AG	Lycopen (H1058)	47301	1
Unisan/Hepart	Selen (H1067)	15000158/0	2
Unisan/Hepart	Vitamin D3 (H1105)	15000490/5	1
unisan	Chrom (H1012)		2
Unisan	Selen (H1067)	10201	10
Unisan	Vitamin B12 (H1102)	1061025017	1
Unisan	Vitamin B12 (H1102)	1064025017	3
Unisan	Selen (H1067)	1144010201	1
Unisan	Selen (H1067)	1144933301	1
Unisan	Vitamin D3 (H1105)	1335008101	2
Unisan	Vitamin D3 (H1105)	1335008108	1
Unisan	Vitamin D3 (H1105)	1335959601	1
Unisan	Chrom (H1012)	14000429	2
UNISAN	Chrom (H1012)	14000429	4
Unisan	Vitamin D3 (H1105)	14000481	1
Unisan	Vitamin D3 (H1105)	14000481/2	3

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Supplier	Substance	Batch	Spectra
Unisan	Lycopen (H1058)	14000803	1
Unisan	Biotin (H1007)	14000862	2
Unisan	Biotin (H1007)	14000862/2	2
Unisan	Ginseng (H1018)	14002047/1	1
Unisan	Ginseng (H1018)	14002047/2	1
Unisan	Selen (H1067)	15000157	3
Unisan	Selen (H1067)	15000158	1
Unisan	Selen (H1067)	15000158/0	1
Unisan	Selen (H1067)	15000159	1
Unisan	Vitamin D3 (H1105)	15000490	4
Unisan	Vitamin D3 (H1105)	15000490/0	2
Unisan	Vitamin D3 (H1105)	15000490/5	1
Unisan	Biotin (H1007)	15000735	2
Unisan	Biotin (H1007)	15000735/0	1
Unisan	Biotin (H1007)	15000735/5	1
Unisan	Vitamin B12 (H1102)	15000993	4
Unisan	Vitamin B12 (H1102)	15000993/3	1
Unisan	Chrom (H1012)	1581977201	1
Unisan	Chrom (H1012)	1582977201	1
Unisan	Biotin (H1007)	1591983601	1
Unisan	Chrom (H1012)	16000520/0	1
Unisan	Vitamin D3 (H1105)	16000952	2
Unisan	Vitamin D3 (H1105)	16001212	3
Unisan	Vitamin D3 (H1105)	16001212/1	1
Unisan	Selen (H1067)	16001349	1
Unisan	Biotin (H1007)	16001396	3
Unisan	Biotin (H1007)	16001396/0	1
Unisan	Selenhefe (H1068)	16001450/0	1
Unisan	Vitamin B12 (H1102)	17000276	2
Unisan	Ginseng (H1018)	17000285	2
Unisan	Lycopen (H1058)	17000619/0	1
Unisan	Vitamin B12 (H1102)	25017	5
Unisan	Selenhefe (H1068)	25709	1
Unisan	Vitamin B12 (H1102)	26401	1
Unisan	Biotin (H1007)	29601	2
Unisan	Biotin (H1007)	29603	3
Unisan	Vitamin B12 (H1102)	3441377	1
Unisan	Ginseng (H1018)	38802	2
Unisan	Lycopen (H1058)	4501	4
Unisan	Lycopen (H1058)	47301	2
Unisan	Lycopen (H1058)	53501	7
Unisan	Lycopen (H1058)	53501/7	1
UNISAN	Vitamin D3 (H1105)	63601	1
Unisan	Vitamin D3 (H1105)	63701	4
Unisan	Vitamin D3 (H1105)	64801	5
Unisan	Selen (H1067)	65501	1
UNISAN	Selen (H1067)	65501	1
Unisan	Selen (H1067)	65501/2	1
Unisan	Selen (H1067)	65601	3
UNISAN	Selen (H1067)	65601	3
Unisan	Selen (H1067)	65601/1	1
Unisan	Selen (H1067)	65601/2	1
Unisan	Selen (H1067)	65701	2
Unisan	Ginseng (H1018)	67801	2
UNISAN	Ginseng (H1018)	67801	1
Unisan	Vitamin B12 (H1102)	75301	5
Unisan	Vitamin B12 (H1102)	75301/2	1
Unisan	Vitamin D3 (H1105)	8101	7
Unisan	Selenhefe (H1068)	9001	1
Unisan	Chrom (H1012)	977201	3

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Supplier	Substance	Batch	Spectra
Unisan	Biotin (H1007)	983601	1
Unisan	Lycopen (H1058)	H105811	1

- 2457 spectra from 26 *Apo-Ident* customers from a total of 1241 batches from a further 52 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	3310	0	24 966
Type B	0	1490	40	21 143
Type C	0	484	29	2457

The substance/substance group *Classificação I HCK* can be clearly distinguished from all other substances. In order to make these figures comparable, 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 % (> 99.8187 %)
Type B	100.0000 % (> 99.8656 %)	97.3856 % (> 97.1895 %)
Type C	100.0000 % (> 98.8215 %)	94.3470 % (> 93.7622 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80335	80335	0,00	23,32
80353	80353	0,00	24,04
80361	80361	0,00	44,56

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80364	80364	0,00	43,52
80365	80365	0,00	29,78
80366	80366	0,00	44,39
80385	80385	0,00	27,26
80455	80455	0,00	16,93
80456	80456	0,00	20,28
80478	80478	0,00	27,52
80530	80530	0,00	29,05
80531	80531	0,00	30,05
80534	80534	0,00	12,01
80535	80535	0,00	26,42
80580	80580	0,00	34,15
80586	80586	0,00	27,06
80603	80603	0,00	25,24
80604	80604	0,00	25,12
80663	80663	0,00	24,63
80702	80702	0,00	26,76
80706	80706	0,00	35,56
80780	80780	0,00	21,29
80791	80791	0,00	30,38
80792	80792	0,00	33,84
80816	80816	0,00	32,10
80822	80822	0,00	22,92
80855	80855	0,00	26,99
80863	80863	0,00	27,70
80874	80874	0,00	23,35
80891	80891	0,00	25,87
80894	80894	0,00	18,40
80895	80895	0,00	19,23
80910	80910	0,00	25,32
80913	80913	0,00	17,28
80914	80914	0,00	26,60
80921	80921	0,00	24,40
81014	81014	0,00	20,06
81022	81022	0,00	30,39
81024	81024	0,00	21,57
81025	81025	0,00	26,22
81056	81056	0,00	14,65
81089	81089	0,00	25,51
81090	81090	0,00	27,31
81091	81091	0,00	28,94
81092	81092	0,00	23,33
81119	81119	0,00	24,01
81126	81126	0,00	24,76
81127	81127	0,00	27,26
81130	81130	0,00	28,48
81158	81158	0,00	22,17
81201	81201	0,00	30,41
81204	81204	0,00	24,45
81205	81205	0,00	19,41
81206	81206	0,00	28,99

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81282	81282	0,00	27,27
81306	81306	0,00	19,11
81310	81310	0,00	40,05
81328	81328	0,00	23,57
81368	81368	0,00	26,24
81370	81370	0,00	28,60
81377	81377	0,00	11,84
81400	81400	0,00	19,25
81422	81422	0,00	17,52
81447	81447	0,00	30,53
81470	81470	0,00	24,82
81471	81471	0,00	20,21
81473	81473	0,00	20,35
81480	81480	0,00	30,20
81489	81489	0,00	47,29
81493	81493	0,00	37,11
81500	81500	0,00	24,31
81507	81507	0,00	29,99
81509	81509	0,00	40,85
81515	81515	0,00	30,62
81546	81546	0,00	27,89
81547	81547	0,00	30,46

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 2.8-2024-04

Validated substance/substance group	Classificação II HCK
Substance class	HCK
Report date	25/11/2024
Report number	80311-2024-11-25
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Classificação II HCK; Antioxidantien NAT Komplex (H1004); Aroma Orange (H1405); Bioflavonoide Komplex (H1006); Calcium L-(+) -Lactat Komplex (H1008); Camu Camu (H1518); Cranberry (H1519); Garcinia Cambogia (H1017); Ginkgo Extrakt (H1024); Glutathion (H1020); Grünkohl (H1126); Isoflavone Extrakt (H1025); Kohlmix (H1514); OPC Proanthocyanidine (Pine Bark) (H1066); Orthocolon Komplex (H1800); PET Basis (H1503); Rhodiola (H1064); Sanddorn (H1523); Vitamin B1 (H1101); Vitamine Komplex (H1100); Waldbeere (H1524)

Special notes

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

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Classificação II HCK	145	165	349

Second-stage model

For differentiation of the substance/substance group *Classificação II HCK* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Classificação II HCK* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Orthovimin Neutral Komplex (H1403)	11,46	—
Silymarin (H1071)	13,24	—
Griffonia (H1035)	13,52	—
Leaky Gut Komplex (H1802)	13,73	—
Granatapfel (H1409)	15,20	—
Bor (H1005)	15,48	—
Silicium (H1070)	16,92	—
Karotte (H1513)	17,05	—
L-Carnitin (H1038)	17,43	—
Grüner Kaffee Extrakt (H1433)	17,44	—
Coenzym Q10 (H1013)	17,85	—
L-Arginin (H1036)	18,36	—
Baobab (H1410)	18,96	—
Haferkleie beta-Glucan (H1529)	19,55	—
PET Gelenke (H1501)	20,20	—
Aminomix NAC (H1002)	20,31	—
Pathogene Komplex (H1803)	20,36	—
Catechin-Extrakt (H1010)	21,09	—
Rote Bete (H1515)	21,42	—
Betain Hydrochlorid (H1119)	22,36	—
Kupfer (H1032)	22,65	—
Brokkoli (H1512)	23,53	—
Artischocke Extrakt (H1440)	23,69	—
Vitamin E NAT (H1107)	23,85	—
PET Well-Aging (H1500)	25,47	—
Óleo de zimbao (H1112)	26,59	—
Zink (H1110)	26,68	—
Sonnenblumenkernprotein (H1511)	28,28	—
Magnesium (H1060)	28,31	—
Detox Komplex (H1111)	28,91	—
PET Immunsystem (H1502)	29,45	—
Kokos (H1522)	29,51	—

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Substanz	Distance in main model	Distance in second-stage model
Vitamin B6 (Pyridoxal-5-phosphat) (...)	30,31	—
Artemisia annua Extrakt (H1118)	30,96	—
Eibisch Extrakt (H1439)	31,17	—
Eisen (H1015)	31,62	—
Antibiose forte Komplex (H1115)	31,78	—
Ginseng (H1018)	32,18	—
Kreatin (H1031)	32,21	—
Vitamin C (H1104)	32,76	—
Safran Blüten (H1435)	33,53	—
Safran Griffel (H1434)	34,17	—
Vitamine BAG Komplex (H1091)	37,93	—
Flohsamenschalen (H1527)	38,49	—
Curcumin und Piperin (H1014)	38,65	—
Histaminblock Komplex (H1117)	40,51	—
Konjak Glucomannan (H1530)	41,68	—
Chaga (H1011)	42,34	—
Acerola (H1516)	42,49	—
Hefe (H1525)	42,53	—
Koffein Guarana Extrakt (H1425)	43,34	—
Spurenelemente SE Komplex (H1082)	43,42	—
Chondroitinsulfat (H1065)	44,88	—
Enzian Extrakt (H1438)	46,79	—
Spurenelemente JK Komplex (H1080)	47,33	—
Kürbiskernprotein (H1509)	47,39	—
Ingwer Extrakt (H1437)	47,74	—
PET Coenzym Q10 (H1505)	48,40	—
α -Liponsäure (H1000)	49,02	—
L-Glutamin (H1043)	49,46	—
Selen (H1067)	49,48	—
Argentum (H1116)	49,80	—
Walnussblatt Extrakt (H1114)	50,19	—

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antioxidantien NAT Komple...	051901	80311	60	from supplier
Hepart	Antioxidantien NAT Komple...	052001	80313	60	from supplier
Hepart	Antioxidantien NAT Komple...	052201	80315	50	from supplier
Hepart	Antioxidantien NAT Komple...	052101	80317	50	from supplier
Hepart	Antioxidantien NAT Komple...	051902	80318	60	from supplier
Hepart	Antioxidantien NAT Komple...	067301	80404	40	from supplier
Hepart	Antioxidantien NAT Komple...	067201	80405	40	from supplier
Hepart	Antioxidantien NAT Komple...	14000044	80419	40	from supplier
Hepart	Antioxidantien NAT Komple...	14000965	80469	40	from supplier
Hepart	Antioxidantien NAT Komple...	14000964	80473	40	from supplier
Hepart	Antioxidantien NAT Komple...	14001849	80504	60	from supplier
Hepart	Antioxidantien NAT Komple...	14001850	80505	60	from supplier
Hepart	Antioxidantien NAT Komple...	14001851	80506	60	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antioxidantien NAT Komple...	14001846	80507	60	from supplier
Hepart	Antioxidantien NAT Komple...	14001848	80508	60	from supplier
Hepart	Antioxidantien NAT Komple...	14001847	80509	60	from supplier
Hepart	Antioxidantien NAT Komple...	15000875(B1)	80607	60	from supplier
Hepart	Antioxidantien NAT Komple...	15000880	80609	60	from supplier
Hepart	Antioxidantien NAT Komple...	15000877(B1)	80613	60	from supplier
Hepart	Antioxidantien NAT Komple...	15000878(B1)	80616	60	from supplier
Hepart	Antioxidantien NAT Komple...	15000874	80618	60	from supplier
Hepart	Antioxidantien NAT Komple...	15000874(B1)	80619	60	from supplier
Hepart	Antioxidantien NAT Komple...	15000879	80621	60	from supplier
Hepart	Antioxidantien NAT Komple...	15000876	80624	60	from supplier
Hepart	Antioxidantien NAT Komple...	16000378	80783	40	from supplier
Hepart	Antioxidantien NAT Komple...	17000260	80946	40	from supplier
Hepart	Antioxidantien NAT Komple...	17000261	80986	40	from supplier
Hepart	Antioxidantien NAT Komple...	17001756	80987	40	from supplier
Hepart	Antioxidantien NAT Komple...	21000112	81329	40	from supplier
Hepart	Antioxidantien NAT Komple...	21000123	81345	40	from supplier
Hepart	Antioxidantien NAT Komple...	21001616-1748-1747-1652	81388	50	from supplier
Hepart	Antioxidantien NAT Komple...	24000111/0	81533	40	from supplier
Hepart	Antioxidantien NAT Komple...	24000540/0	81535	40	from supplier
Hepart	Aroma Orange (H1405)	16000262	80768	60	from supplier
Hepart	Aroma Orange (H1405)	17000491/0	81016	40	from supplier
Hepart	Aroma Orange (H1405)	19000149	81151	40	from supplier
Hepart	Aroma Orange (H1405)	19000607/0	81170	40	from supplier
Hepart	Aroma Orange (H1405)	21000861	81334	40	from supplier
Hepart	Bioflavonoide Komplex (H1006)	068101	80342	40	from supplier
Hepart	Bioflavonoide Komplex (H1006)	14001675	80492	60	from supplier
Hepart	Bioflavonoide Komplex (H1006)	17000256	80878	40	from supplier
Hepart	Bioflavonoide Komplex (H1006)	20002413	81315	40	from supplier
Hepart	Bioflavonoide Komplex (H1006)	21002660	81412	40	from supplier
Hepart	Bioflavonoide Komplex (H1006)	22001793	81460	40	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	055201	80322	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	055001	80323	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	055101	80327	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	055601	80329	50	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	14000106	80422	40	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	14001933	80521	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	14001934	80522	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	14001937	80525	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	14001938	80526	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	14001939	80527	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001669	80707	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001672(B1)	80709	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001671	80711	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001673(MM)	80712	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001668(B1)	80715	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001667(MM)	80719	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001666(MM)	80722	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001665(B1)	80724	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001670(B2)	80729	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001675(B2)	80732	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001676(MM)	80734	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001677(B1)	80740	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	15001674(B2)	80741	60	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	21000180-80-81-82-83-84	81338	40	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	20020-12-13-14-16-18	81399	50	from supplier
Hepart	Calcium L-(+) -Lactat Kom...	22001301-03	81439	40	from supplier
Hepart	Camu Camu (H1518)	23000543	81476	40	from supplier
Hepart	Cranberry (H1519)	23000480	81482	40	from supplier
Hepart	Cranberry (H1519)	23002136	81512	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Garcinia Cambogia (H1017)	056601	80346	40	from supplier
Hepart	Garcinia Cambogia (H1017)	056601	80477	40	from supplier
Hepart	Garcinia Cambogia (H1017)	14001687	80490	60	from supplier
Hepart	Garcinia Cambogia (H1017)	15001048(F2)	80660	60	from supplier
Hepart	Garcinia Cambogia (H1017)	17000873	80956	40	from supplier
Hepart	Garcinia Cambogia (H1017)	18001849	81150	40	from supplier
Hepart	Garcinia Cambogia (H1017)	21001144	81378	50	from supplier
Hepart	Ginkgo Extrakt (H1024)	067901	80391	80	from supplier
Hepart	Ginkgo Extrakt (H1024)	067901	80476	40	from supplier
Hepart	Ginkgo Extrakt (H1024)	15001039	80656	60	from supplier
Hepart	Ginkgo Extrakt (H1024)	15001038(F3)	80657	60	from supplier
Hepart	Ginkgo Extrakt (H1024)	15001038	80658	60	from supplier
Hepart	Ginkgo Extrakt (H1024)	17001832	81005	40	from supplier
Hepart	Ginkgo Extrakt (H1024)	18001386	81133	40	from supplier
Hepart	Ginkgo Extrakt (H1024)	19002623	81215	40	from supplier
Hepart	Ginkgo Extrakt (H1024)	21002839	81435	40	from supplier
Hepart	Ginkgo Extrakt (H1024)	23001413/0	81529	40	from supplier
Hepart	Glutathion (H1020)	074901	80430	40	from supplier
Hepart	Glutathion (H1020)	15000478	80583	60	from supplier
Hepart	Glutathion (H1020)	18000508/0	81316	40	from supplier
Hepart	Glutathion (H1020)	23002184	81541	40	from supplier
Hepart	Grünkohl (H1126)	22000777	81450	40	from supplier
Hepart	Grünkohl (H1126)	23000479	81481	40	from supplier
Hepart	Isoflavone Extrakt (H1025)	056701	80345	40	from supplier
Hepart	Isoflavone Extrakt (H1025)	15000205/2	80815	40	from supplier
Hepart	Isoflavone Extrakt (H1025)	16001644/0	80853	40	from supplier
Hepart	Kohlmix (H1514)	23001164	81488	40	from supplier
Hepart	OPC Proanthocyanidine (Pi...	130208-77	80337	40	from supplier
Hepart	OPC Proanthocyanidine (Pi...	068301	80352	40	from supplier
Hepart	OPC Proanthocyanidine (Pi...	070401	80380	40	from supplier
Hepart	OPC Proanthocyanidine (Pi...	070401	80398	40	from supplier
Hepart	OPC Proanthocyanidine (Pi...	16001439	80864	40	from supplier
Hepart	OPC Proanthocyanidine (Pi...	17001805	81001	40	from supplier
Hepart	OPC Proanthocyanidine (Pi...	21001640	81390	40	from supplier
Hepart	OPC Proanthocyanidine (Pi...	22000705	81451	40	from supplier
Hepart	Orthocolon Komplex (H1800)	18000636	81041	40	from supplier
Hepart	Orthocolon Komplex (H1800)	18000641	81042	40	from supplier
Hepart	Orthocolon Komplex (H1800)	19000177	81202	40	from supplier
Hepart	PET Basis (H1503)	15000402	80566	60	from supplier
Hepart	PET Basis (H1503)	15000402	80636	60	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	60	from supplier
Hepart	Rhodiola (H1064)	21001642	81375	50	from supplier
Hepart	Rhodiola (H1064)	22001550	81461	40	from supplier
Hepart	Sanddorn (H1523)	24000627	81534	40	from supplier
Hepart	Vitamin B1 (H1101)	053301	80316	60	from supplier
Hepart	Vitamin B1 (H1101)	075001	80392	40	from supplier
Hepart	Vitamin B1 (H1101)	075001	80479	40	from supplier
Hepart	Vitamin B1 (H1101)	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	Vitamine Komplex (H1100)	049201	80349	40	from supplier
Hepart	Vitamine Komplex (H1100)	077201	80411	40	from supplier
Hepart	Vitamine Komplex (H1100)	077001	80431	40	from supplier
Hepart	Vitamine Komplex (H1100)	077101	80432	40	from supplier
Hepart	Vitamine Komplex (H1100)	14001590	80485	60	from supplier
Hepart	Vitamine Komplex (H1100)	14001589	80486	60	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamine Komplex (H1100)	14001591	80487	60	from supplier
Hepart	Vitamine Komplex (H1100)	15001276(B1)	80637	60	from supplier
Hepart	Vitamine Komplex (H1100)	15001277(F2)	80638	60	from supplier
Hepart	Vitamine Komplex (H1100)	15001274(B1)	80640	60	from supplier
Hepart	Vitamine Komplex (H1100)	15001275(F2)	80642	60	from supplier
Hepart	Vitamine Komplex (H1100)	15001277	80643	60	from supplier
Hepart	Vitamine Komplex (H1100)	15001276(F2)	80646	60	from supplier
Hepart	Vitamine Komplex (H1100)	15001274	80647	60	from supplier
Hepart	Vitamine Komplex (H1100)	15001275	80648	60	from supplier
Hepart	Vitamine Komplex (H1100)	16000957	80827	40	from supplier
Hepart	Vitamine Komplex (H1100)	17001751/0	80990	40	from supplier
Hepart	Vitamine Komplex (H1100)	19001423/0	81171	40	from supplier
Hepart	Vitamine Komplex (H1100)	19001424/0	81172	40	from supplier
Hepart	Vitamine Komplex (H1100)	19001023	81251	40	from supplier
Hepart	Vitamine Komplex (H1100)	20001890	81271	40	from supplier
Hepart	Vitamine Komplex (H1100)	2100-1518-1264	81357	50	from supplier
Hepart	Vitamine Komplex (H1100)	22000230-231	81415	40	from supplier
Hepart	Vitamine Komplex (H1100)	24000871	81539	40	from supplier
Hepart	Waldbeere (H1524)	21002226	81449	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 7460 spectra of 152 reference samples from the substance/substance group *Classificação II HCK*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 145 different batches.
- 20 816 spectra from a total of 427 batches from further 111 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 7629 spectra of 166 reference samples from the substance/substance group *Classificação II HCK*.
- Among them are spectra of independent samples from 165 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	Antioxydantien NAT Komple...	14000043	80424	40
Hepart	Antioxydantien NAT Komple...	14000042	80428	40
Hepart	Antioxydantien NAT Komple...	14000961	80470	40
Hepart	Antioxydantien NAT Komple...	14000962	80471	39
Hepart	Antioxydantien NAT Komple...	14000963	80472	40
Hepart	Antioxydantien NAT Komple...	14000966	80474	40
Hepart	Antioxydantien NAT Komple...	15000875	80606	60
Hepart	Antioxydantien NAT Komple...	15000875 (F2)	80608	60
Hepart	Antioxydantien NAT Komple...	15000880 (B1)	80610	60
Hepart	Antioxydantien NAT Komple...	15000880 (F2)	80611	60
Hepart	Antioxydantien NAT Komple...	15000877	80612	60
Hepart	Antioxydantien NAT Komple...	15000877 (F2)	80614	60
Hepart	Antioxydantien NAT Komple...	15000878	80615	60
Hepart	Antioxydantien NAT Komple...	15000878 (F2)	80617	60
Hepart	Antioxydantien NAT Komple...	15000874 (F2)	80620	60
Hepart	Antioxydantien NAT Komple...	15000879 (B1)	80622	60
Hepart	Antioxydantien NAT Komple...	15000879 (F2)	80623	60
Hepart	Antioxydantien NAT Komple...	15000876 (B1)	80625	60
Hepart	Antioxydantien NAT Komple...	15000876 (F2)	80626	60
Hepart	Antioxydantien NAT Komple...	16000380	80784	40
Hepart	Antioxydantien NAT Komple...	16000376	80785	40
Hepart	Antioxydantien NAT Komple...	16000377	80786	40
Hepart	Antioxydantien NAT Komple...	16000965	80834	40
Hepart	Antioxydantien NAT Komple...	16000966	80835	40
Hepart	Antioxydantien NAT Komple...	16000967	80836	40
Hepart	Antioxydantien NAT Komple...	16000968	80837	40
Hepart	Antioxydantien NAT Komple...	16000969	80838	40
Hepart	Antioxydantien NAT Komple...	16000970	80839	40
Hepart	Antioxydantien NAT Komple...	16000971	80840	40
Hepart	Antioxydantien NAT Komple...	16000972	80841	40
Hepart	Antioxydantien NAT Komple...	16000973	80842	40
Hepart	Antioxydantien NAT Komple...	16000974	80843	40
Hepart	Antioxydantien NAT Komple...	17000268	80938	40
Hepart	Antioxydantien NAT Komple...	17000269	80939	40
Hepart	Antioxydantien NAT Komple...	17000267	80940	40
Hepart	Antioxydantien NAT Komple...	17000266	80941	40
Hepart	Antioxydantien NAT Komple...	17000264	80942	40
Hepart	Antioxydantien NAT Komple...	17000263	80943	40
Hepart	Antioxydantien NAT Komple...	17000262	80944	40
Hepart	Antioxydantien NAT Komple...	17001754/0	80988	40
Hepart	Antioxydantien NAT Komple...	17001757	80989	40
Hepart	Antioxydantien NAT Komple...	17001758	81002	40
Hepart	Antioxydantien NAT Komple...	17001755	81021	40
Hepart	Antioxydantien NAT Komple...	18001181	81084	40
Hepart	Antioxydantien NAT Komple...	18001182	81085	40
Hepart	Antioxydantien NAT Komple...	18001812	81138	40
Hepart	Antioxydantien NAT Komple...	18001814	81139	40
Hepart	Antioxydantien NAT Komple...	18001815	81140	40
Hepart	Antioxydantien NAT Komple...	18001816	81141	40
Hepart	Antioxydantien NAT Komple...	18001817	81142	40
Hepart	Antioxydantien NAT Komple...	18001818	81143	40
Hepart	Antioxydantien NAT Komple...	19000449	81192	40
Hepart	Antioxydantien NAT Komple...	19000603	81193	40
Hepart	Antioxydantien NAT Komple...	19002532	81221	40
Hepart	Antioxydantien NAT Komple...	20000224	81232	40
Hepart	Antioxydantien NAT Komple...	20000225	81233	40
Hepart	Antioxydantien NAT Komple...	20000805	81244	40
Hepart	Antioxydantien NAT Komple...	20000806	81245	40
Hepart	Antioxydantien NAT Komple...	20000720	81246	40
Hepart	Antioxydantien NAT Komple...	20000722	81247	40

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Antioxidantien NAT Komple...	20002053	81298	40
Hepart	Antioxidantien NAT Komple...	20002054	81299	40
Hepart	Antioxidantien NAT Komple...	20002055	81300	40
Hepart	Antioxidantien NAT Komple...	21000122	81330	40
Hepart	Antioxidantien NAT Komple...	21002561	81419	40
Hepart	Antioxidantien NAT Komple...	24000541/0	81536	40
Hepart	Aroma Orange (H1405)	18000770	81064	40
Hepart	Aroma Orange (H1405)	18001327	81095	40
Hepart	Aroma Orange (H1405)	18001422/0	81096	40
Hepart	Bioflavonoide Komplex (H1006)	17000257	80879	40
Hepart	Calcium L-(+) -Lactat Kom...	055301	80324	60
Hepart	Calcium L-(+) -Lactat Kom...	055401	80325	60
Hepart	Calcium L-(+) -Lactat Kom...	055501	80326	60
Hepart	Calcium L-(+) -Lactat Kom...	14000110	80406	40
Hepart	Calcium L-(+) -Lactat Kom...	14000107	80412	40
Hepart	Calcium L-(+) -Lactat Kom...	14000111	80414	40
Hepart	Calcium L-(+) -Lactat Kom...	14000108	80415	40
Hepart	Calcium L-(+) -Lactat Kom...	14000109	80417	30
Hepart	Calcium L-(+) -Lactat Kom...	14001935	80523	60
Hepart	Calcium L-(+) -Lactat Kom...	14001936	80524	60
Hepart	Calcium L-(+) -Lactat Kom...	15001672(B2)	80708	60
Hepart	Calcium L-(+) -Lactat Kom...	15001672(MM)	80710	60
Hepart	Calcium L-(+) -Lactat Kom...	15001673(B2)	80713	60
Hepart	Calcium L-(+) -Lactat Kom...	15001673(B1)	80714	60
Hepart	Calcium L-(+) -Lactat Kom...	15001668(MM)	80716	60
Hepart	Calcium L-(+) -Lactat Kom...	15001667(F2)	80717	60
Hepart	Calcium L-(+) -Lactat Kom...	15001667(B1)	80718	60
Hepart	Calcium L-(+) -Lactat Kom...	15001666(B1)	80720	60
Hepart	Calcium L-(+) -Lactat Kom...	15001666(F2)	80721	60
Hepart	Calcium L-(+) -Lactat Kom...	15001670(B1)	80723	60
Hepart	Calcium L-(+) -Lactat Kom...	15001670(MM)	80725	60
Hepart	Calcium L-(+) -Lactat Kom...	15001665(F2)	80726	60
Hepart	Calcium L-(+) -Lactat Kom...	15001665(MM)	80727	60
Hepart	Calcium L-(+) -Lactat Kom...	15001668(F2)	80728	60
Hepart	Calcium L-(+) -Lactat Kom...	15001675(MM)	80730	60
Hepart	Calcium L-(+) -Lactat Kom...	15001675(B1)	80731	60
Hepart	Calcium L-(+) -Lactat Kom...	15001675/4	80733	60
Hepart	Calcium L-(+) -Lactat Kom...	15001676(B2)	80735	60
Hepart	Calcium L-(+) -Lactat Kom...	15001676/4	80736	60
Hepart	Calcium L-(+) -Lactat Kom...	15001676(B1)	80737	60
Hepart	Calcium L-(+) -Lactat Kom...	15001677(MM)	80738	60
Hepart	Calcium L-(+) -Lactat Kom...	15001677/4	80739	60
Hepart	Calcium L-(+) -Lactat Kom...	15001674(B1)	80742	60
Hepart	Calcium L-(+) -Lactat Kom...	15001674(MM)	80743	60
Hepart	Calcium L-(+) -Lactat Kom...	17000249MM	80971	40
Hepart	Calcium L-(+) -Lactat Kom...	17000250	80972	40
Hepart	Calcium L-(+) -Lactat Kom...	17000201MM	80973	40
Hepart	Calcium L-(+) -Lactat Kom...	17000202MM	80974	40
Hepart	Calcium L-(+) -Lactat Kom...	17000203	80975	40
Hepart	Calcium L-(+) -Lactat Kom...	17000204MM	80976	40
Hepart	Calcium L-(+) -Lactat Kom...	17000205	80977	40
Hepart	Calcium L-(+) -Lactat Kom...	17000206	80978	40
Hepart	Calcium L-(+) -Lactat Kom...	18001413	81105	40
Hepart	Calcium L-(+) -Lactat Kom...	18001414/0	81106	40
Hepart	Calcium L-(+) -Lactat Kom...	18001415/0	81107	40
Hepart	Calcium L-(+) -Lactat Kom...	18001416/0	81108	40
Hepart	Calcium L-(+) -Lactat Kom...	18001417/0	81109	40
Hepart	Calcium L-(+) -Lactat Kom...	18001418	81110	40
Hepart	Calcium L-(+) -Lactat Kom...	19001637	81238	40
Hepart	Calcium L-(+) -Lactat Kom...	19001638	81239	40

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Calcium L-(+) -Lactat Kom...	19001639	81240	40
Hepart	Calcium L-(+) -Lactat Kom...	19001640	81241	40
Hepart	Calcium L-(+) -Lactat Kom...	19001641	81242	40
Hepart	Calcium L-(+) -Lactat Kom...	19001167	81243	40
Hepart	Garcinia Cambogia (H1017)	15001048	80661	60
Hepart	Garcinia Cambogia (H1017)	15001048(B1)	80662	60
Hepart	Garcinia Cambogia (H1017)	22000028	81408	40
Hepart	Ginkgo Extrakt (H1024)	15001038(F1)	80659	60
Hepart	Ginkgo Extrakt (H1024)	18001110	81072	40
Hepart	Glutathion (H1020)	16000938	80813	40
Hepart	Isoflavone Extrakt (H1025)	15000205	80556	60
Hepart	OPC Proanthocyanidine (Pi...	16001439(B1)	80865	40
Hepart	OPC Proanthocyanidine (Pi...	16001439(F1)	80866	40
Hepart	OPC Proanthocyanidine (Pi...	20002632/0	81307	40
Hepart	OPC Proanthocyanidine (Pi...	23000867	81508	40
Hepart	Orthocolon Komplex (H1800)	18000640	81043	40
Hepart	Orthocolon Komplex (H1800)	19000937	81185	40
Hepart	Rhodiola (H1064)	17000278	80915	40
Hepart	Rhodiola (H1064)	20000088	81235	40
Hepart	Rhodiola (H1064)	20002070	81318	40
Hepart	Vitamin B1 (H1101)	14001112	80480	40
Hepart	Vitamin B1 (H1101)	14001113	80481	40
Hepart	Vitamine Komplex (H1100)	15001275(B1)	80639	60
Hepart	Vitamine Komplex (H1100)	15001277(B1)	80641	60
Hepart	Vitamine Komplex (H1100)	15001274(F2)	80644	60
Hepart	Vitamine Komplex (H1100)	15001276	80645	60
Hepart	Vitamine Komplex (H1100)	16000958	80828	40
Hepart	Vitamine Komplex (H1100)	16000959	80829	40
Hepart	Vitamine Komplex (H1100)	16000960	80830	40
Hepart	Vitamine Komplex (H1100)	16000961	80831	40
Hepart	Vitamine Komplex (H1100)	16000962	80832	40
Hepart	Vitamine Komplex (H1100)	17001654	80984	40
Hepart	Vitamine Komplex (H1100)	17001752/0	80991	40
Hepart	Vitamine Komplex (H1100)	17000880/0	80992	40
Hepart	Vitamine Komplex (H1100)	17001753/0	80993	40
Hepart	Vitamine Komplex (H1100)	17001750/0	80994	40
Hepart	Vitamine Komplex (H1100)	19000433	81173	40
Hepart	Vitamine Komplex (H1100)	19000544	81174	40
Hepart	Vitamine Komplex (H1100)	19002512	81218	40
Hepart	Vitamine Komplex (H1100)	20000144/0	81226	40
Hepart	Vitamine Komplex (H1100)	20000836	81248	40
Hepart	Vitamine Komplex (H1100)	19001582	81249	40
Hepart	Vitamine Komplex (H1100)	19002234	81250	40
Hepart	Vitamine Komplex (H1100)	19001581	81252	40
Hepart	Vitamine Komplex (H1100)	24000857	81542	40
Hepart	Antioxidantien NAT Komple...	17000261	80945	40

- 15 050 spectra from a total of 330 batches from further 67 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 678 spectra from 26 *Apo-Ident* customers from 374 batches from the substance/substance group *Classificação II HCK*.
- Among them are spectra of independent samples from 347 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	Antioxidantien NAT Komple...	16000970	1
Flaigg Ag CH-4147 Ae...	OPC Proanthocyanidine (Pi...	1700185	1
Flaigg Ag CH-4147 Ae...	Ginkgo Extrakt (H1024)	18001386	1
Flaigg Ag CH-4147 Ae...	Ginkgo Extrakt (H1024)	18001386/1	1
HCK	Vitamin B1 (H1101)	14001112/0	1
HCK	Garcinia Cambogia (H1017)	14001687/2	1
HCK	Calcium L-(+) -Lactat Kom...	14001938/1	1
HCK	Calcium L-(+) -Lactat Kom...	14001938-1	1
HCK	Glutathion (H1020)	15000478	1
HCK	Antioxidantien NAT Komple...	15000876/0	1
HCK	Antioxidantien NAT Komple...	15000878-0	1
HCK	Rhodiola (H1064)	1500104-3	1
HCK	Rhodiola (H1064)	15001045-3	2
HCK	Rhodiola (H1064)	15001045-4	3
HCK	Rhodiola (H1064)	15001045-5	3
HCK	Vitamine Komplex (H1100)	15001275/0	1
HCK	Vitamine Komplex (H1100)	15001275/1	2
HCK	Vitamine Komplex (H1100)	15001275-1	1
HCK	Vitamine Komplex (H1100)	15001276-0	3
HCK	Vitamin B1 (H1101)	15001620	1
HCK	Vitamin B1 (H1101)	15001622-0	1
HCK	Vitamin B1 (H1101)	15001622-1	2
HCK	Calcium L-(+) -Lactat Kom...	15001667-0	1
HCK	Calcium L-(+) -Lactat Kom...	15001672	2
HCK	Bioflavonoide Komplex (H1006)	17000256	1
HCK	Isoflavone Extrakt (H1025)	56701	1
HCK	Ginkgo Extrakt (H1024)	67901-11	1
HCK	Rhodiola (H1064)	70501/7	1
HCK	Glutathion (H1020)	74901	1
Hedinger	Antioxidantien NAT Komple...	51901	1
Hepart / Unisan	Calcium L-(+) -Lactat Kom...	17000250	1
Hepart / Unisan	Bioflavonoide Komplex (H1006)	17000256/3	2
Hepart / Unisan	Antioxidantien NAT Komple...	17000257	1
Hepart / Unisan	Antioxidantien NAT Komple...	19000421/0	1
Hepart / Unisan	Antioxidantien NAT Komple...	19000421/1	1
Hepart / Unisan	Vitamine Komplex (H1100)	19000544/1	1
Hepart / Unisan	Antioxidantien NAT Komple...	20000720/0	1
Hepart AG, CH-8280 K...	Vitamine Komplex (H1100)	1014025101	1
Hepart AG, CH-8280 K...	Antioxidantien NAT Komple...	1034019901	1
Hepart AG, CH-8280 K...	Antioxidantien NAT Komple...	1034030901	1
Hepart AG, CH-8280 K...	Calcium L-(+) -Lactat Kom...	1104008901	4
Hepart AG, CH-8280 K...	Glutathion (H1020)	1251019703	1
Hepart AG, CH-8280 K...	Glutathion (H1020)	1251025703	1
Hepart AG, CH-8280 K...	OPC Proanthocyanidine (Pi...	130208	1
Hepart AG, CH-8280 K...	Glutathion (H1020)	40201	1
Hepart AG, CH-8280 K...	Vitamine Komplex (H1100)	49301	5
Hepart AG, CH-8280 K...	Antioxidantien NAT Komple...	52101	1
Hepart AG, CH-8280 K...	Vitamin B1 (H1101)	53301	1
Hepart AG, CH-8280 K...	Calcium L-(+) -Lactat Kom...	55501	2
Hepart AG, CH-8280 K...	Bioflavonoide Komplex (H1006)	56001	1
Hepart AG, Unisan GmbH	Vitamin B1 (H1101)	15001622/0	1
Hepart ag/ Unisan	Vitamine Komplex (H1100)	19001023/0	1
Hepart AG/Unisan	Vitamine Komplex (H1100)	19000544/1	1
Hepart AG/Unisan	Vitamine Komplex (H1100)	19001581/0	1

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Supplier	Substance	Batch	Spectra
Hepart ag/Unisan	Calcium L-(+) -Lactat Kom. ...	19001637	1
Hepart AG/Unisan	Vitamine Komplex (H1100)	20000144/0	1
Hepart AG/Unisan	Antioxidantien NAT Komple. ...	20000224/0	1
Hepart AG/Unisan	Antioxidantien NAT Komple. ...	20000806/1	2
Hepart AG/Unisan	Vitamine Komplex (H1100)	20000835/0	1
Hepart ag/Unisan	Vitamine Komplex (H1100)	20000836	1
Hepart AG/Unisan	Vitamine Komplex (H1100)	20001899/0	1
Hepart AG/Unisan	Antioxidantien NAT Komple. ...	21000121/0	1
Hepart AG	Vitamine Komplex (H1100)	1014025101	1
Hepart AG	Vitamine Komplex (H1100)	1014025301	1
hepart ag	Vitamine Komplex (H1100)	1015954801	1
hepart ag	Vitamine Komplex (H1100)	10159548011	1
Hepart AG	Antioxidantien NAT Komple. ...	1034019901	1
Hepart AG	Antioxidantien NAT Komple. ...	1034030901	1
Hepart AG	Antioxidantien NAT Komple. ...	1034030902	1
Hepart AG	Antioxidantien NAT Komple. ...	1034030904	1
Hepart AG	Antioxidantien NAT Komple. ...	1037030904	1
Hepart AG	Calcium L-(+) -Lactat Kom. ...	1104008901	6
Hepart AG	Garcinia Cambogia (H1017)	1221007401	1
Hepart AG	Glutathion (H1020)	1254025703	1
Hepart AG	Glutathion (H1020)	1254040201	1
Hepart AG	Bioflavonoide Komplex (H1006)	1284019001	1
Hepart AG	Bioflavonoide Komplex (H1006)	1284042501	1
Hepart AG	Isoflavone Extrakt (H1025)	1314025704	1
Hepart AG	Isoflavone Extrakt (H1025)	1314038801	1
Hepart AG	Antioxidantien NAT Komple. ...	14000963	3
Hepart AG	Vitamin B1 (H1101)	14001112	1
Hepart AG	Vitamine Komplex (H1100)	14001589	2
Hepart AG	Bioflavonoide Komplex (H1006)	14001675/1	1
Hepart AG	Calcium L-(+) -Lactat Kom. ...	14001933	1
Hepart AG	Antioxidantien NAT Komple. ...	15000878/0	2
Hepart AG	Ginkgo Extrakt (H1024)	15001038	1
Hepart AG	Ginkgo Extrakt (H1024)	15001039/1	1
Hepart AG	Rhodiola (H1064)	15001045/4	1
Hepart AG	Vitamine Komplex (H1100)	15001275/1	1
Hepart AG	Vitamine Komplex (H1100)	15001277	1
Hepart AG	Vitamin B1 (H1101)	15001622/0	1
Hepart AG	Calcium L-(+) -Lactat Kom. ...	15001668/0	2
Hepart AG	OPC Proanthocyanidine (Pi. ...)	1504018401	2
Hepart AG	Antioxidantien NAT Komple. ...	16000376	1
Hepart AG	Antioxidantien NAT Komple. ...	16000378	1
Hepart AG	OPC Proanthocyanidine (Pi. ...)	16000637	1
Hepart AG	Vitamin B1 (H1101)	16000698/0	1
Hepart AG	Glutathion (H1020)	16000938/1	1
Hepart AG	Glutathion (H1020)	16000938/2	1
Hepart AG	Vitamine Komplex (H1100)	16000957/0	1
Hepart AG	Antioxidantien NAT Komple. ...	16000970/0	1
Hepart AG	Isoflavone Extrakt (H1025)	16001644/2	1
Hepart AG	Isoflavone Extrakt (H1025)	16001644/3	2
Hepart AG	Vitamin B1 (H1101)	1621030202	1
Hepart AG	Vitamin B1 (H1101)	1622030202	2
Hepart AG	Calcium L-(+) -Lactat Kom. ...	17000203/0	2
Hepart AG	Calcium L-(+) -Lactat Kom. ...	17000205/0	2
Hepart AG	Calcium L-(+) -Lactat Kom. ...	17000206/0	1
Hepart AG	Calcium L-(+) -Lactat Kom. ...	17000252/0	1
Hepart AG	Calcium L-(+) -Lactat Kom. ...	17000253/0	2
Hepart AG	Antioxidantien NAT Komple. ...	17000264/0	1
Hepart AG	Antioxidantien NAT Komple. ...	17000266/0	1
Hepart AG	Rhodiola (H1064)	17000278/4	2
Hepart AG	Vitamine Komplex (H1100)	17000880/0	4

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Supplier	Substance	Batch	Spectra
Hepart AG	Vitamin B1 (H1101)	17000914/1	1
Hepart AG	Vitamine Komplex (H1100)	17001750/0	2
Hepart AG	Vitamine Komplex (H1100)	17001751/0	2
Hepart AG	Antioxidantien NAT Komple...	17001754/0	1
Hepart AG	Antioxidantien NAT Komple...	18001182/0	2
Hepart AG	Antioxidantien NAT Komple...	18001182/1	2
Hepart AG	Calcium L-(+) -Lactat Kom...	18001414	1
Hepart AG	Calcium L-(+) -Lactat Kom...	18001416/0	1
Hepart AG	Antioxidantien NAT Komple...	18001815/0	2
Hepart AG	Garcinia Cambogia (H1017)	18001849/0	2
Hepart AG	OPC Proanthocyanidine (Pi...	18401	1
Hepart AG	Vitamine Komplex (H1100)	19000364/0	1
Hepart AG	Vitamine Komplex (H1100)	19000433/0	2
hepart ag	Antioxidantien NAT Komple...	19901	1
Hepart AG	Vitamine Komplex (H1100)	20000144/0	1
Hepart AG	Isoflavone Extrakt (H1025)	38801	1
Hepart AG	Bioflavonoide Komplex (H1006)	42501	1
Hepart AG	Vitamine Komplex (H1100)	49201	4
Hepart AG	Vitamine Komplex (H1100)	49202	5
Hepart AG	Vitamine Komplex (H1100)	49301	7
Hepart AG	Antioxidantien NAT Komple...	51902	1
Hepart AG	Antioxidantien NAT Komple...	52101	3
Hepart AG	Antioxidantien NAT Komple...	52201	2
Hepart AG	Vitamin B1 (H1101)	53301	2
Hepart AG	Calcium L-(+) -Lactat Kom...	55001	1
Hepart AG	Calcium L-(+) -Lactat Kom...	55201	1
Hepart AG	Calcium L-(+) -Lactat Kom...	55301	2
Hepart AG	Calcium L-(+) -Lactat Kom...	55401	4
Hepart AG	Calcium L-(+) -Lactat Kom...	55501	5
Hepart AG	Bioflavonoide Komplex (H1006)	56001	2
Hepart AG	Isoflavone Extrakt (H1025)	56701	1
Hepart AG	Antioxidantien NAT Komple...	67201	1
Hepart AG	Antioxidantien NAT Komple...	67301	2
Hepart AG	Antioxidantien NAT Komple...	67501	1
Hepart AG	Bioflavonoide Komplex (H1006)	68101	1
Hepart AG	OPC Proanthocyanidine (Pi...	70401	2
Hepart AG	Rhodiola (H1064)	70501	1
Hepart AG	Garcinia Cambogia (H1017)	7401	2
Hepart AG	Vitamine Komplex (H1100)	77201	3
Hepart AG	Calcium L-(+) -Lactat Kom...	8901	2
Hepart AG	Vitamine Komplex (H1100)	H110031	1
Hepart/ unisan	OPC Proanthocyanidine (Pi...	20000179	1
Hepart/Hepart	Vitamine Komplex (H1100)	17000880/0	1
Hepart/Unisan	Calcium L-(+) -Lactat Kom...	14001938/1	1
Hepart/Unisan	Antioxidantien NAT Komple...	15000877/1	1
Hepart/Unisan	Vitamine Komplex (H1100)	15001275/0	1
Hepart/Unisan	Antioxidantien NAT Komple...	16000376/0	1
Hepart/Unisan	Antioxidantien NAT Komple...	16000967	1
Hepart/Unisan	Calcium L-(+) -Lactat Kom...	19001639/0	1
Hepart/Unisan	Antioxidantien NAT Komple...	20000805	1
Hepart/Unisan	Vitamine Komplex (H1100)	20000836	1
Hepart	Bioflavonoide Komplex (H1006)	14001675/5	1
Hepart	Bioflavonoide Komplex (H1006)	14001675-4	2
Hepart	Calcium L-(+) -Lactat Kom...	14001937	1
Hepart	Glutathion (H1020)	15000478	1
Hepart	Rhodiola (H1064)	150010145-6	1
Hepart	Ginkgo Extrakt (H1024)	15001038-2	2
Hepart	Ginkgo Extrakt (H1024)	150010391	1
Hepart	Rhodiola (H1064)	15001045	1
Hepart	Rhodiola (H1064)	15001045-6	2

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Supplier	Substance	Batch	Spectra
Hepart	Calcium L-(+) -Lactat Kom. ...	15001667/0	1
Hepart	Calcium L-(+) -Lactat Kom. ...	150016740	1
Hepart	OPC Proanthocyanidine (Pi. ...	16000637-2	1
Hepart	Vitamin B1 (H1101)	16000698-0	1
Hepart	Glutathion (H1020)	16000938/0	4
Hepart	Vitamine Komplex (H1100)	16000957	1
Hepart	Vitamine Komplex (H1100)	16000957-0	1
Hepart	Vitamine Komplex (H1100)	16000958	1
Hepart	Vitamine Komplex (H1100)	16000959-0	1
Hepart	Vitamine Komplex (H1100)	16000960-0	1
Hepart	Antioxidantien NAT Komple. ...	16000965-0	1
Hepart	Antioxidantien NAT Komple. ...	16000968	2
Hepart	Antioxidantien NAT Komple. ...	16000970	1
Hepart	Antioxidantien NAT Komple. ...	16000970-0	1
Hepart	Garcinia Cambogia (H1017)	16001252	1
Hepart	Garcinia Cambogia (H1017)	16001252/1	1
Hepart	OPC Proanthocyanidine (Pi. ...	16001439	1
Hepart	OPC Proanthocyanidine (Pi. ...	16001439-0	1
Hepart	Isoflavone Extrakt (H1025)	16001644	1
Hepart	Isoflavone Extrakt (H1025)	16001644/0	1
Hepart	Isoflavone Extrakt (H1025)	16001644/1	3
Hepart	Isoflavone Extrakt (H1025)	16001644/3	5
Hepart	Isoflavone Extrakt (H1025)	16001644/4	3
Hepart	Calcium L-(+) -Lactat Kom. ...	17000202/0	1
Hepart	Calcium L-(+) -Lactat Kom. ...	17000204	1
Hepart	Calcium L-(+) -Lactat Kom. ...	170002040	1
Hepart	Calcium L-(+) -Lactat Kom. ...	17000205	1
Hepart	Calcium L-(+) -Lactat Kom. ...	17000206	1
Hepart	Calcium L-(+) -Lactat Kom. ...	17000206/0	1
Hepart	Calcium L-(+) -Lactat Kom. ...	17000208/0	1
Hepart	Calcium L-(+) -Lactat Kom. ...	17000250/0	4
Hepart	Calcium L-(+) -Lactat Kom. ...	17000251/0	1
Hepart	Calcium L-(+) -Lactat Kom. ...	17000253	1
Hepart	Calcium L-(+) -Lactat Kom. ...	17000253/0	2
Hepart	Calcium L-(+) -Lactat Kom. ...	17000254/0	1
Hepart	Bioflavonoide Komplex (H1006)	17000256	1
Hepart	Bioflavonoide Komplex (H1006)	17000256/2	7
Hepart	Bioflavonoide Komplex (H1006)	17000256/3	1
Hepart	Bioflavonoide Komplex (H1006)	17000257	3
Hepart	Bioflavonoide Komplex (H1006)	17000257/0	1
Hepart	Bioflavonoide Komplex (H1006)	17000257/1	2
Hepart	Antioxidantien NAT Komple. ...	17000260	1
Hepart	Antioxidantien NAT Komple. ...	17000264	2
Hepart	Antioxidantien NAT Komple. ...	17000264-0	1
Hepart	Antioxidantien NAT Komple. ...	17000265	1
Hepart	Rhodiola (H1064)	17000278	1
Hepart	Rhodiola (H1064)	17000278/0	1
Hepart	Rhodiola (H1064)	17000278/2	1
Hepart	Rhodiola (H1064)	17000278/4	1
Hepart	Rhodiola (H1064)	17000278-0	1
Hepart	Rhodiola (H1064)	17000278-1	2
Hepart	Rhodiola (H1064)	17000278-2	1
Hepart	Vitamine Komplex (H1100)	17000880	1
Hepart	Vitamine Komplex (H1100)	17000880/0	2
Hepart	Vitamine Komplex (H1100)	17000880-0	1
Hepart	Vitamin B1 (H1101)	17000914	1
Hepart	Vitamin B1 (H1101)	17001075/0	1
Hepart	Vitamin B1 (H1101)	17001075-0	2
Hepart	Vitamine Komplex (H1100)	17001654	1
Hepart	Vitamine Komplex (H1100)	17001654/0	2

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Supplier	Substance	Batch	Spectra
Hepart	Vitamine Komplex (H1100)	17001750	1
Hepart	Vitamine Komplex (H1100)	17001750/0	2
Hepart	Vitamine Komplex (H1100)	17001751	1
Hepart	Vitamine Komplex (H1100)	17001751/0	2
Hepart	Antioxidantien NAT Komple...	17001754	1
Hepart	Antioxidantien NAT Komple...	17001755/0	2
Hepart	Antioxidantien NAT Komple...	17001756/0	1
Hepart	OPC Proanthocyanidine (Pi...	17001805	2
Hepart	OPC Proanthocyanidine (Pi...	17001805/0	1
Hepart	OPC Proanthocyanidine (Pi...	17001805/1	2
Hepart	OPC Proanthocyanidine (Pi...	17001805/2	2
Hepart	OPC Proanthocyanidine (Pi...	17001805/3	1
Hepart	OPC Proanthocyanidine (Pi...	17001805/4	1
Hepart	Ginkgo Extrakt (H1024)	17001832	1
Hepart	Ginkgo Extrakt (H1024)	17001832/0	2
Hepart	Bioflavonoide Komplex (H1006)	1700257/1	2
Hepart	Ginkgo Extrakt (H1024)	18001110	1
Hepart	Ginkgo Extrakt (H1024)	18001110/0	5
Hepart	Antioxidantien NAT Komple...	18001181/0	1
Hepart	Antioxidantien NAT Komple...	18001182	1
Hepart	Ginkgo Extrakt (H1024)	18001386/1	2
Hepart	Ginkgo Extrakt (H1024)	18001386/2	1
Hepart	Calcium L-(+) -Lactat Kom...	18001413	1
Hepart	Calcium L-(+) -Lactat Kom...	18001414/0	1
Hepart	Calcium L-(+) -Lactat Kom...	18001415/0	1
Hepart	Calcium L-(+) -Lactat Kom...	18001417/0	1
Hepart	Calcium L-(+) -Lactat Kom...	18001418/0	1
Hepart	Antioxidantien NAT Komple...	18001814/0	1
Hepart	Antioxidantien NAT Komple...	18001816/0	1
Hepart	Antioxidantien NAT Komple...	18001817/0	2
Hepart	Antioxidantien NAT Komple...	18001818/0	1
Hepart	Vitamin B1 (H1101)	19000216/1	1
Hepart	OPC Proanthocyanidine (Pi...	19000258	1
Hepart	OPC Proanthocyanidine (Pi...	19000258/1	2
Hepart	Vitamine Komplex (H1100)	19000364/0	3
Hepart	Antioxidantien NAT Komple...	19000420/0	1
Hepart	Vitamine Komplex (H1100)	19000433/0	2
Hepart	Vitamine Komplex (H1100)	19000544/0	1
Hepart	Antioxidantien NAT Komple...	19000603	2
Hepart	Vitamin B1 (H1101)	19000685/0	1
Hepart	Vitamin B1 (H1101)	19000685/1	1
Hepart	Vitamine Komplex (H1100)	19001023/0	2
Hepart	Vitamine Komplex (H1100)	19001581	1
Hepart	Vitamine Komplex (H1100)	19001581/0	1
Hepart	Calcium L-(+) -Lactat Kom...	19001638/0	1
Hepart	Calcium L-(+) -Lactat Kom...	19001639/0	1
Hepart	Calcium L-(+) -Lactat Kom...	19001640/0	1
Hepart	Calcium L-(+) -Lactat Kom...	19001641	1
Hepart	Calcium L-(+) -Lactat Kom...	19001641/0	1
Hepart	Ginkgo Extrakt (H1024)	19002623	2
Hepart	Ginkgo Extrakt (H1024)	19002623/0	5
Hepart	Ginkgo Extrakt (H1024)	19002623/1	1
Hepart	Ginkgo Extrakt (H1024)	19002623/2	1
Hepart	Vitamine Komplex (H1100)	20000144	1
Hepart	Vitamine Komplex (H1100)	20000144/0	1
Hepart	OPC Proanthocyanidine (Pi...	20000179/0	1
Hepart	Antioxidantien NAT Komple...	20000225/0	1
Hepart	Antioxidantien NAT Komple...	20000805/0	2
Hepart	Vitamine Komplex (H1100)	20000835/0	1
Hepart	Vitamine Komplex (H1100)	20000836/0	1

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Supplier	Substance	Batch	Spectra
Hepart	Vitamin B1 (H1101)	20001639	1
Hepart	Vitamin B1 (H1101)	20001639/0	3
Hepart	Vitamine Komplex (H1100)	20001890/0	1
Hepart	Vitamine Komplex (H1100)	20001899/0	2
Hepart	Antioxidantien NAT Komple...	20002055/0	1
Hepart	Glutathion (H1020)	20002265	1
Hepart	Glutathion (H1020)	20002265/0	2
Hepart	Glutathion (H1020)	20002265/1	1
Hepart	Bioflavonoide Komplex (H1006)	20002413	1
Hepart	Bioflavonoide Komplex (H1006)	20002413/0	3
Hepart	Bioflavonoide Komplex (H1006)	20002413/1	6
Hepart	Vitamin B1 (H1101)	20002435/0	1
Hepart	OPC Proanthocyanidine (Pi...	20002632	2
Hepart	OPC Proanthocyanidine (Pi...	20002632/4	1
Hepart	Antioxidantien NAT Komple...	21000112/0	2
Hepart	Calcium L-(+) -Lactat Kom...	21000181	1
Hepart	Calcium L-(+) -Lactat Kom...	21000181/0	1
Hepart	Calcium L-(+) -Lactat Kom...	21000182/0	1
Hepart	Calcium L-(+) -Lactat Kom...	21000183	1
Hepart	Calcium L-(+) -Lactat Kom...	21000183/0	2
Hepart	Isoflavone Extrakt (H1025)	21000565	1
Hepart	Isoflavone Extrakt (H1025)	21000565/1	2
Hepart	Vitamine Komplex (H1100)	21001518	1
Hepart	Antioxidantien NAT Komple...	21001652	1
Hepart	Antioxidantien NAT Komple...	21001652/0	2
Hepart	Antioxidantien NAT Komple...	21001747	1
Hepart	Antioxidantien NAT Komple...	21001747/0	1
Hepart	Calcium L-(+) -Lactat Kom...	21002012	1
Hepart	Calcium L-(+) -Lactat Kom...	21002012/0	1
Hepart	Calcium L-(+) -Lactat Kom...	21002013/0	1
Hepart	Calcium L-(+) -Lactat Kom...	21002014	1
Hepart	Calcium L-(+) -Lactat Kom...	21002014/0	1
Hepart	Calcium L-(+) -Lactat Kom...	21002016	1
Hepart	Vitamine Komplex (H1100)	21002294/0	1
Hepart	Vitamine Komplex (H1100)	21002821/0	1
Hepart	Vitamine Komplex (H1100)	21002978	1
Hepart	Vitamine Komplex (H1100)	21002980	1
Hepart	Antioxidantien NAT Komple...	21003089/0	1
Hepart	Vitamine Komplex (H1100)	22001108/0	1
Phönix	Antioxidantien NAT Komple...	16000376	1
Purren Apotheke	Glutathion (H1020)	1254955501	1
Purren Apotheke	Isoflavone Extrakt (H1025)	1314955701	1
Unisan 02.04.2016	Bioflavonoide Komplex (H1006)	14001675/2	1
Unisan 02.04.2016	Isoflavone Extrakt (H1025)	15000205/1	1
Unisan 02.04.2016	Antioxidantien NAT Komple...	15000874/0	2
Unisan 2.10.2015	Bioflavonoide Komplex (H1006)	14001675/1	1
Unisan Gmbh, 78465 K...	Antioxidantien NAT Komple...	52201	1
Unisan Gmbh, 78465 K...	Calcium L-(+) -Lactat Kom...	55401	1
Unisan Gmbh, 78465 K...	Antioxidantien NAT Komple...	67301	1
Unisan/Hepart AG	Isoflavone Extrakt (H1025)	38801	1
Unisan/Hepart AG	Vitamine Komplex (H1100)	48301	1
Unisan/Hepart AG	Vitamine Komplex (H1100)	49201	1
Unisan/Hepart AG	Vitamin B1 (H1101)	53301	1
Unisan/Hepart AG	Calcium L-(+) -Lactat Kom...	8901	1
Unisan	Antioxidantien NAT Komple...		3
Unisan	Vitamine Komplex (H1100)	1014009901	1
Unisan	Vitamine Komplex (H1100)	1014025401	1
Unisan	Antioxidantien NAT Komple...	1034030904	1
Unisan	Antioxidantien NAT Komple...	11001	1
Unisan	Calcium L-(+) -Lactat Kom...	1105008901	1

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Supplier	Substance	Batch	Spectra
Unisan	Garcinia Cambogia (H1017)	1221007401	1
Unisan	Glutathion (H1020)	1251019703	1
Unisan	Glutathion (H1020)	1254025703	1
Unisan	Bioflavonoide Komplex (H1006)	1281683901	1
Unisan	Bioflavonoide Komplex (H1006)	1284019001	1
Unisan	Bioflavonoide Komplex (H1006)	1284042501	1
Unisan	Bioflavonoide Komplex (H1006)	1284648802	1
UNISAN	Antioxidantien NAT Komple...	14000042	1
Unisan	Antioxidantien NAT Komple...	14000044	1
Unisan	Calcium L-(+) -Lactat Kom...	14000108	1
Unisan	Calcium L-(+) -Lactat Kom...	14000110	1
UNISAN	Calcium L-(+) -Lactat Kom...	14000110	1
Unisan	Antioxidantien NAT Komple...	1400042	1
Unisan	Antioxidantien NAT Komple...	14000961	1
UNISAN	Antioxidantien NAT Komple...	14000961	1
Unisan	Antioxidantien NAT Komple...	14000963	2
Unisan	Vitamin B1 (H1101)	14001112/0	1
Unisan	Vitamine Komplex (H1100)	14001589	1
Unisan	Vitamine Komplex (H1100)	1400159/0	1
Unisan	Vitamine Komplex (H1100)	14001590/0	1
Unisan	Vitamine Komplex (H1100)	14001590/1	1
Unisan	Bioflavonoide Komplex (H1006)	14001675	2
Unisan	Bioflavonoide Komplex (H1006)	14001675/4	1
Unisan	Antioxidantien NAT Komple...	14001847/0	2
Unisan	Antioxidantien NAT Komple...	14001847/1	1
Unisan	Antioxidantien NAT Komple...	14001848/0	1
Unisan	Antioxidantien NAT Komple...	14001851/0	1
Unisan	Calcium L-(+) -Lactat Kom...	14001934/0	1
Unisan	Calcium L-(+) -Lactat Kom...	14001938/0	1
Unisan	Isoflavone Extrakt (H1025)	15000205	1
Unisan	Isoflavone Extrakt (H1025)	15000205/0	3
Unisan	Isoflavone Extrakt (H1025)	15000205/3	1
unisan	Antioxidantien NAT Komple...	15000877	2
Unisan	Antioxidantien NAT Komple...	15000877/0	1
Unisan	Antioxidantien NAT Komple...	15000880	1
Unisan	Ginkgo Extrakt (H1024)	15001039/1	1
Unisan	Rhodiola (H1064)	15001045/8	1
Unisan	Vitamine Komplex (H1100)	15001275/0	1
Unisan	Vitamine Komplex (H1100)	15001276/0	1
Unisan	Vitamine Komplex (H1100)	15001277/0	1
Unisan	Vitamin B1 (H1101)	15001620/0	1
Unisan	Vitamin B1 (H1101)	15001622	1
Unisan	Vitamin B1 (H1101)	15001622/0	1
Unisan	Calcium L-(+) -Lactat Kom...	15001666	1
Unisan	Calcium L-(+) -Lactat Kom...	15001666/0	1
Unisan	Calcium L-(+) -Lactat Kom...	15001667	2
Unisan	Calcium L-(+) -Lactat Kom...	15001672	1
Unisan	Calcium L-(+) -Lactat Kom...	15001672/0	1
Unisan	Antioxidantien NAT Komple...	16000376	1
Unisan	Antioxidantien NAT Komple...	16000378	1
Unisan	OPC Proanthocyanidine (Pi...	16000637	1
Unisan	Vitamin B1 (H1101)	16000698	1
Unisan	Glutathion (H1020)	16000938	1
Unisan	Vitamine Komplex (H1100)	16000958/0	2
Unisan	Vitamine Komplex (H1100)	16000962	2
Unisan	Antioxidantien NAT Komple...	16000966	1
Unisan	Antioxidantien NAT Komple...	16000966/0	2
Unisan	Antioxidantien NAT Komple...	16000968/0	1
Unisan	Antioxidantien NAT Komple...	16000970	1
Unisan	Antioxidantien NAT Komple...	16000970/0	3

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Supplier	Substance	Batch	Spectra
Unisan	Garcinia Cambogia (H1017)	16001252/0	1
Unisan	OPC Proanthocyanidine (Pi...	16001439	2
Unisan	OPC Proanthocyanidine (Pi...	16001439/0	1
Unisan	Vitamin B1 (H1101)	1622977301	1
Unisan	Calcium L-(+) -Lactat Kom...	17000201	1
Unisan	Bioflavonoide Komplex (H1006)	17000256	1
Unisan	Antioxidantien NAT Komple...	17000260	2
Unisan	Antioxidantien NAT Komple...	17000264	1
Unisan	Garcinia Cambogia (H1017)	17000873	1
Unisan	Vitamin B1 (H1101)	17001075	1
Unisan	Vitamine Komplex (H1100)	17001750	1
Unisan	OPC Proanthocyanidine (Pi...	18401	1
Unisan	Antioxidantien NAT Komple...	1851	1
Unisan	Antioxidantien NAT Komple...	19901	2
Unisan	Vitamine Komplex (H1100)	25101	1
Unisan	Vitamine Komplex (H1100)	25201	1
Unisan	Glutathion (H1020)	25703	1
Unisan	Vitamin B1 (H1101)	30202	2
Unisan	Antioxidantien NAT Komple...	30903	3
Unisan	Antioxidantien NAT Komple...	30904	1
Unisan	Glutathion (H1020)	40201	3
Unisan	Bioflavonoide Komplex (H1006)	42501	1
Unisan	Vitamine Komplex (H1100)	49202	1
Unisan	Vitamine Komplex (H1100)	49301	2
unisan	Vitamine Komplex (H1100)	49302	1
Unisan	Vitamine Komplex (H1100)	49302	2
Unisan	Antioxidantien NAT Komple...	51901	2
Unisan	Antioxidantien NAT Komple...	51902	1
Unisan	Antioxidantien NAT Komple...	52001	2
unisan	Calcium L-(+) -Lactat Kom...	55001	1
Unisan	Calcium L-(+) -Lactat Kom...	55001	1
Unisan	Calcium L-(+) -Lactat Kom...	55101	3
Unisan	Calcium L-(+) -Lactat Kom...	55301	1
Unisan	Calcium L-(+) -Lactat Kom...	55401	1
Unisan	Calcium L-(+) -Lactat Kom...	55501	1
Unisan	Calcium L-(+) -Lactat Kom...	55601	2
Unisan	Garcinia Cambogia (H1017)	56601	1
Unisan	Isoflavone Extrakt (H1025)	56701	2
Unisan	Antioxidantien NAT Komple...	67201	4
Unisan	Antioxidantien NAT Komple...	67501	1
Unisan	Antioxidantien NAT Komple...	67601	2
Unisan	Bioflavonoide Komplex (H1006)	68101	1
Unisan	Antioxidantien NAT Komple...	68201	4
Unisan	OPC Proanthocyanidine (Pi...	68301	4
Unisan	OPC Proanthocyanidine (Pi...	70401	2
UNISAN	OPC Proanthocyanidine (Pi...	70401	1
Unisan	Vitamine Komplex (H1100)	74101	1
Unisan	Glutathion (H1020)	74901	3
UNISAN	Glutathion (H1020)	74901	1
UNISAN	Vitamin B1 (H1101)	75001	1
Unisan	Vitamine Komplex (H1100)	77001	2
Unisan	Vitamine Komplex (H1100)	77201	3
Unisan	Calcium L-(+) -Lactat Kom...	8901	5
Unisan	Vitamine Komplex (H1100)	904006	1
Unisan	Calcium L-(+) -Lactat Kom...	956001	1
Unisan	Vitamin B1 (H1101)	977301	2
Unisan	Vitamine Komplex (H1100)	H110031	2

- 2292 spectra from 24 *Apo-Ident* customers from a total of 1087 batches from a further 52 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	7460	0	20 816
Type B	0	7573	56	14 854
Type C	0	637	41	2292

The substance/substance group *Classificação II HCK* can be clearly distinguished from all other substances. In order to make these figures comparable, 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 % (> 99.9196 %)
Type B	100.0000 % (> 99.8643 %)	99.2660 % (> 99.2266 %)
Type C	100.0000 % (> 98.8214 %)	93.9528 % (> 93.5103 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80311	80311	0,00	37,92
80313	80313	0,00	32,65
80315	80315	0,00	39,61
80316	80316	0,00	33,50
80317	80317	0,00	40,94
80318	80318	0,00	34,80
80322	80322	0,00	39,59
80323	80323	0,00	43,29
80327	80327	0,00	43,07
80329	80329	0,00	34,60

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80337	80337	0,00	38,63
80342	80342	0,00	23,12
80345	80345	0,00	42,70
80346	80346	0,00	47,51
80349	80349	0,00	45,88
80352	80352	0,00	13,24
80380	80380	0,00	17,98
80390	80390	0,00	31,38
80391	80391	0,00	30,27
80392	80392	0,00	34,06
80398	80398	0,00	18,75
80404	80404	0,00	32,25
80405	80405	0,00	33,38
80411	80411	0,00	41,71
80419	80419	0,00	34,41
80422	80422	0,00	42,14
80430	80430	0,00	24,14
80431	80431	0,00	42,98
80432	80432	0,00	40,71
80469	80469	0,00	32,72
80473	80473	0,00	31,82
80476	80476	0,00	26,89
80477	80477	0,00	44,40
80479	80479	0,00	38,72
80485	80485	0,00	43,02
80486	80486	0,00	46,28
80487	80487	0,00	45,15
80490	80490	0,00	20,36
80492	80492	0,00	27,59
80504	80504	0,00	32,19
80505	80505	0,00	37,50
80506	80506	0,00	33,50
80507	80507	0,00	37,91
80508	80508	0,00	33,55
80509	80509	0,00	34,91
80521	80521	0,00	42,25
80522	80522	0,00	36,88
80525	80525	0,00	44,83
80526	80526	0,00	43,22
80527	80527	0,00	44,57
80529	80529	0,00	35,95
80566	80566	0,00	27,83
80583	80583	0,00	21,32
80607	80607	0,00	32,06
80609	80609	0,00	31,96
80613	80613	0,00	32,51
80616	80616	0,00	33,30
80618	80618	0,00	34,87
80619	80619	0,00	35,67
80621	80621	0,00	31,96
80624	80624	0,00	31,77

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80632	80632	0,00	30,71
80636	80636	0,00	20,20
80637	80637	0,00	46,25
80638	80638	0,00	47,39
80640	80640	0,00	46,98
80642	80642	0,00	45,74
80643	80643	0,00	45,92
80646	80646	0,00	45,76
80647	80647	0,00	47,16
80648	80648	0,00	45,56
80656	80656	0,00	30,76
80657	80657	0,00	29,94
80658	80658	0,00	29,45
80660	80660	0,00	23,83
80672	80672	0,00	31,75
80707	80707	0,00	47,41
80709	80709	0,00	45,90
80711	80711	0,00	44,38
80712	80712	0,00	47,11
80715	80715	0,00	45,56
80719	80719	0,00	40,14
80722	80722	0,00	44,87
80724	80724	0,00	45,18
80729	80729	0,00	47,00
80732	80732	0,00	44,67
80734	80734	0,00	46,58
80740	80740	0,00	44,05
80741	80741	0,00	46,89
80768	80768	0,00	39,13
80783	80783	0,00	35,45
80815	80815	0,00	39,07
80827	80827	0,00	47,06
80853	80853	0,00	28,76
80864	80864	0,00	17,92
80878	80878	0,00	34,40
80946	80946	0,00	25,13
80953	80953	0,00	39,51
80956	80956	0,00	16,92
80980	80980	0,00	43,56
80986	80986	0,00	28,11
80987	80987	0,00	27,09
80990	80990	0,00	41,97
81001	81001	0,00	18,37
81005	81005	0,00	31,70
81016	81016	0,00	41,24
81041	81041	0,00	28,64
81042	81042	0,00	28,26
81133	81133	0,00	17,43
81136	81136	0,00	30,17
81150	81150	0,00	28,77
81151	81151	0,00	76,98

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81170	81170	0,00	75,66
81171	81171	0,00	43,34
81172	81172	0,00	50,56
81183	81183	0,00	42,44
81202	81202	0,00	22,56
81215	81215	0,00	19,90
81251	81251	0,00	31,78
81271	81271	0,00	43,38
81315	81315	0,00	25,34
81316	81316	0,00	28,29
81329	81329	0,00	36,03
81334	81334	0,00	66,64
81338	81338	0,00	42,51
81345	81345	0,00	35,75
81357	81357	0,00	29,91
81375	81375	0,00	32,94
81378	81378	0,00	25,06
81388	81388	0,00	33,15
81390	81390	0,00	16,58
81399	81399	0,00	39,90
81412	81412	0,00	21,09
81415	81415	0,00	41,87
81435	81435	0,00	26,42
81439	81439	0,00	34,35
81449	81449	0,00	20,64
81450	81450	0,00	21,42
81451	81451	0,00	11,46
81460	81460	0,00	23,14
81461	81461	0,00	27,68
81476	81476	0,00	28,90
81481	81481	0,00	23,53
81482	81482	0,00	36,18
81488	81488	0,00	29,37
81512	81512	0,00	29,18
81529	81529	0,00	24,59
81533	81533	0,00	36,38
81534	81534	0,00	29,50
81535	81535	0,00	35,46
81539	81539	0,00	36,28
81541	81541	0,00	25,65

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 2.8-2024-04

Validated substance/substance group **Coenzym Q10 (H1013)**
Substance class HCK
Report date 25/11/2024
Report number 80015-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Coenzym Q10 (H1013)

Special notes

When selecting the *Coenzym Q10 (H1013)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Coenzym Q10 (H1013)	10	4	40

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Coenzym Q10 (H1013)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Vitamin E NAT (H1107)	17,25	—
Ginseng (H1018)	25,70	—
Aminomix NAC (H1002)	38,39	—
PET Coenzym Q10 (H1505)	40,69	—
Glutathion (H1020)	42,89	—
a-Liponsäure (H1000)	44,76	—
Vitamin B1 (H1101)	44,79	—
Vitamin K2 (75µg Mono) (H1108)	44,90	—
L-Glutamin (H1043)	45,13	—
Antibiose forte Komplex (H1115)	46,77	—
Chondroitinsulfat (H1065)	47,11	—
Ingwer Extrakt (H1437)	47,39	—

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

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Coenzym Q10 (H1013)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Coenzym Q10 (H1013)	130521-300	80354	40	from supplier
Hepart	Coenzym Q10 (H1013)	14001546	80484	60	from supplier
Hepart	Coenzym Q10 (H1013)	14001546	80587	60	from supplier
Hepart	Coenzym Q10 (H1013)	16000402/0	80794	40	from supplier
Hepart	Coenzym Q10 (H1013)	16000402/0	80850	40	from supplier
Hepart	Coenzym Q10 (H1013)	16001598/4	80854	40	from supplier
Hepart	Coenzym Q10 (H1013)	16001598	80881	40	from supplier
Hepart	Coenzym Q10 (H1013)	18000792/0	81048	40	from supplier
Hepart	Coenzym Q10 (H1013)	18000806	81049	40	from supplier
Hepart	Coenzym Q10 (H1013)	19002493/4	81213	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Coenzym Q10 (H1013)	20002171	81308	40	from supplier
Hepart	Coenzym Q10 (H1013)	20002839	81346	40	from supplier

Validation samples

A total of 53 925 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 *Coenzym Q10 (H1013)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 27 756 spectra from a total of 563 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 170 spectra of 4 reference samples from the substance/substance group *Coenzym Q10 (H1013)*.
- Among them are spectra of independent samples from 4 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	Coenzym Q10 (H1013)	16000402/4	80795	40
Hepart	Coenzym Q10 (H1013)	16000402	80882	40
Hepart	Coenzym Q10 (H1013)	20000802	81257	40
Hepart	Coenzym Q10 (H1013)	210015-36-37	81373	50

- 22 509 spectra from a total of 492 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

provided by the customer regarding manufacturer and batch number.

- 107 spectra from 22 *Apo-Ident* customers from 47 batches from the substance/substance group *Coenzym Q10 (H1013)*.
- Among them are spectra of independent samples from 40 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	Coenzym Q10 (H1013)	14001546/4	2
HCK	Coenzym Q10 (H1013)	14001546-2	1
HCK	Coenzym Q10 (H1013)	16001598/1	1
Hepart / Unisan	Coenzym Q10 (H1013)	160015991	1
Hepart AG, CH-8280 K...	Coenzym Q10 (H1013)	1194015601	1
Hepart AG, CH-8280 K...	Coenzym Q10 (H1013)	15601	1
Hepart AG/Unisan	Coenzym Q10 (H1013)	200002171/0	1
Hepart AG/Unisan	Coenzym Q10 (H1013)	200002171/1	1
Hepart ag/Unisan	Coenzym Q10 (H1013)	2000080	1
Hepart AG/Unisan	Coenzym Q10 (H1013)	20000802/0	3
Hepart ag/Unisan	Coenzym Q10 (H1013)	20002171	1
Hepart AG/Unisan	Coenzym Q10 (H1013)	20002839/1	1
Hepart AG	Coenzym Q10 (H1013)	1194015601	2
Hepart AG	Coenzym Q10 (H1013)	130521-300	5
Hepart AG	Coenzym Q10 (H1013)	15601	4
Hepart AG	Coenzym Q10 (H1013)	16000402/0	1
Hepart AG	Coenzym Q10 (H1013)	16001598/1	1
Hepart AG	Coenzym Q10 (H1013)	16001599/1	2
Hepart AG	Coenzym Q10 (H1013)	18000792/1	1
Hepart AG	Coenzym Q10 (H1013)	19002493/1	1
Hepart	Coenzym Q10 (H1013)	14001546	1
Hepart	Coenzym Q10 (H1013)	16000402/1	1
Hepart	Coenzym Q10 (H1013)	16000402-2	1
Hepart	Coenzym Q10 (H1013)	16000402-3	1
Hepart	Coenzym Q10 (H1013)	16000402-4	1
Hepart	Coenzym Q10 (H1013)	16001598	1
Hepart	Coenzym Q10 (H1013)	16001598/0	2
Hepart	Coenzym Q10 (H1013)	16001598/1	2
Hepart	Coenzym Q10 (H1013)	16001598/2	5
Hepart	Coenzym Q10 (H1013)	16001598/3	3
Hepart	Coenzym Q10 (H1013)	16001598-2	2
Hepart	Coenzym Q10 (H1013)	16001599	1
Hepart	Coenzym Q10 (H1013)	16001599/2	12
Hepart	Coenzym Q10 (H1013)	18000792/0	1
Hepart	Coenzym Q10 (H1013)	18000792/2	1
Hepart	Coenzym Q10 (H1013)	18001598	1
Hepart	Coenzym Q10 (H1013)	19002492	1
Hepart	Coenzym Q10 (H1013)	19002493/0	1
Hepart	Coenzym Q10 (H1013)	20000802/0	2
Hepart	Coenzym Q10 (H1013)	20002839	2
Hepart	Coenzym Q10 (H1013)	20002839/0	1
Hepart	Coenzym Q10 (H1013)	20002839/2	1
Hepart	Coenzym Q10 (H1013)	21001536	1
Hepart	Coenzym Q10 (H1013)	21001536/0	1
Hepart	Coenzym Q10 (H1013)	21001537	1
Hepart	Coenzym Q10 (H1013)	21001537/1	1
Unisan 02.04.2016	Coenzym Q10 (H1013)	14001546/3	1
Unisan 2.10.2015	Coenzym Q10 (H1013)	14001546/2	1
Unisan	Coenzym Q10 (H1013)	1194015601	2
Unisan	Coenzym Q10 (H1013)	130521-300	4
UNISAN	Coenzym Q10 (H1013)	130521-300	2
Unisan	Coenzym Q10 (H1013)	14001546	2

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Supplier	Substance	Batch	Spectra
UNISAN	Coenzym Q10 (H1013)	14001546	2
Unisan	Coenzym Q10 (H1013)	14001546/1	2
Unisan	Coenzym Q10 (H1013)	15601	4
Unisan	Coenzym Q10 (H1013)	16000402	1
Unisan	Coenzym Q10 (H1013)	16000402/0	2
Unisan	Coenzym Q10 (H1013)	16001598	1
Unisan	Coenzym Q10 (H1013)	16001599	1
Unisan	Coenzym Q10 (H1013)	992501	1
Unisan	Coenzym Q10 (H1013)	H101311	1

- 2863 spectra from 26 *Apo-Ident* customers from a total of 1413 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 *Coenzym 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 *Coenzym 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	520	0	27 756
Type B	0	170	0	22 509
Type C	0	91	16	2863

The substance/substance group *Coenzym 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 % (> 99.9309 %)	100.0000 % (> 98.8462 %)
Type B	100.0000 % (> 99.8671 %)	100.0000 % (> 96.4706 %)
Type C	100.0000 % (> 98.8243 %)	85.0467 % (> 82.2430 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	32,06
80484	80484	0,00	27,44
80587	80587	0,00	46,77
80794	80794	0,00	28,13
80850	80850	0,00	25,68
80854	80854	0,00	25,00
80881	80881	0,00	37,26
81048	81048	0,00	31,35
81049	81049	0,00	40,69
81213	81213	0,00	37,93
81308	81308	0,00	37,31
81346	81346	0,00	43,63

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 2.8-2024-04

Validated substance/substance group	Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (H1803)
Substance class	HCK
Report date	25/11/2024
Report number	80675-2024-11-25
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (H1803); Antibiose forte Komplex (H1115); Antibiose mite Komplex (H1113); Pathogene Komplex (H1803)

Special notes

When selecting the *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (H1803)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (H1803)	5	6	0

Second-stage model

For differentiation of the substance/substance group *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (H1803)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (H1803)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Garcinia Cambogia (H1017)	16,85	—
Kupfer (H1032)	20,33	—
Walnussblatt Extrakt (H1114)	20,35	—
Chaga (H1011)	25,71	—
Histaminblock Komplex (H1117)	25,84	—
Antioxidantien NAT Komplex (H1004)	30,01	—
Aroma Orange (H1405)	31,99	—
Ginkgo Extrakt (H1024)	32,06	—
Artemisia annua Extrakt (H1118)	34,44	—
Calcium L-(+) -Lactat Komplex (H1008)	34,59	—
PET Basis (H1503)	34,78	—
Eisen (H1015)	36,77	—
Spurenelemente SE Komplex (H1082)	37,78	—
PET Gelenke (H1501)	40,85	—
Potássio (H1030)	42,84	—
Rhodiola (H1064)	47,59	—
Vitamin C (H1104)	47,78	—
Magnesium (H1060)	49,40	—
Amino V Komplex (H1400)	80,31	—

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Antibiose forte Komplex (...)	15001169	80675	60	from supplier
Hepart	Antibiose forte Komplex (...)	17001137	80912	40	from supplier
Hepart	Antibiose mite Komplex (H1113)	16001074	80900	40	from supplier
Hepart	Antibiose mite Komplex (H1113)	16001073	80903	40	from supplier
Hepart	Pathogene Komplex (H1803)	18000637	81038	40	from supplier

Validation samples

A total of 53 925 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 *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (H1803)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 28 056 spectra from a total of 567 batches from further 128 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (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	Antibiose forte Komplex (...)	17001151	81019	40
Hepart	Antibiose forte Komplex (...)	19000078	81152	40
Hepart	Antibiose mite Komplex (H1113)	16001073(B2)	80898	40
Hepart	Antibiose mite Komplex (H1113)	16001074(B2)	80899	40
Hepart	Antibiose mite Komplex (H1113)	16001074(B1)	80901	40
Hepart	Antibiose mite Komplex (H1113)	16001073(B1)	80902	40

- 22 439 spectra from a total of 490 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

Type C Spectra of independent samples not included in the database structure. *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 *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (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 *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (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	28 056
Type B	0	199	41	22 439
Type C	0	0	0	2970

The substance/substance group *Complexo antibiose forte (H1115) / Complexo antibiose ácaro (H1113) / Complexo patogênico (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 % (> 99.9311 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.8668 %)	82.9167 % (> 81.6667 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80675	80675	0,00	111,02
80900	80900	0,00	20,35
80903	80903	0,00	29,76
80912	80912	0,00	80,31
81038	81038	0,00	22,49

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 2.8-2024-04

Validated substance/substance group **Complexo de proteína de ervilha (H1428) / Complexo amino V**
Substance class **HCK**
Report date **25/11/2024**
Report number **80749-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Complexo de proteína de ervilha (H1428) / Complexo amino V (H1400); Amino V Komplex (H1400);
Erbсенprotein BCAA Komplex (H1507)

Special notes

When selecting the *Complexo de proteína de ervilha (H1428) / Complexo amino V (H1400)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Complexo de proteína de ervilha (H1428) / Complexo amino V (H1400)	11	20	1

Second-stage model

For differentiation of the substance/substance group *Complexo de proteína de ervilha (H1428)* / *Complexo amino V (H1400)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Complexo de proteína de ervilha (H1428)* / *Complexo amino V (H1400)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	19,54	—
Coenzym Q10 (H1013)	32,68	—
Kollagenpeptide-MTC (H1125)	37,96	—
Aminomix NAC (H1002)	44,60	—
Lupinenprotein BCAA Komplex (H1510)	48,36	—
L-Carnitin (H1038)	48,58	—
L-Glutamin (H1043)	49,09	—
PET Haut und Haare (H1504)	59,22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Complexo de proteína de ervilha (H1428)* / *Complexo amino V (H1400)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Complexo de proteína de ervilha (H1428)* / *Complexo amino V (H1400)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Amino V Komplex (H1400)	15001365(MM)	80749	60	from supplier
Hepart	Amino V Komplex (H1400)	15001366(B1)	80750	60	from supplier
Hepart	Amino V Komplex (H1400)	16001268	80820	40	from supplier
Hepart	Amino V Komplex (H1400)	16001229	80821	40	from supplier
Hepart	Amino V Komplex (H1400)	15001365	80862	40	from supplier
Hepart	Amino V Komplex (H1400)	17000382	80885	40	from supplier
Hepart	Amino V Komplex (H1400)	18000194	80995	40	from supplier
Hepart	Amino V Komplex (H1400)	18000803	81051	40	from supplier
Hepart	Amino V Komplex (H1400)	23001198	81486	40	from supplier
Hepart	Erbsenprotein BCAA Komple...	21001594	81446	40	from supplier
Hepart	Erbsenprotein BCAA Komple...	23000263	81483	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 480 spectra of 11 reference samples from the substance/substance group *Complexo de proteína de ervilha (H1428) / Complexo amino V (H1400)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 11 different batches.
- 27 796 spectra from a total of 561 batches from further 129 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 20 reference samples from the substance/substance group *Complexo de proteína de ervilha (H1428) / Complexo amino V (H1400)*.
- Among them are spectra of independent samples from 20 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 Komplex (H1400)	15001365(F2)	80745	60
Hepart	Amino V Komplex (H1400)	15001365(B1)	80746	60
Hepart	Amino V Komplex (H1400)	15001366(MM)	80747	60
Hepart	Amino V Komplex (H1400)	15001366(F2)	80748	60
Hepart	Amino V Komplex (H1400)	15001366	80884	40
Hepart	Amino V Komplex (H1400)	18000192	80996	40
Hepart	Amino V Komplex (H1400)	17001819	80997	40
Hepart	Amino V Komplex (H1400)	18000195	80998	40
Hepart	Amino V Komplex (H1400)	18000193	80999	40
Hepart	Amino V Komplex (H1400)	18000822	81052	40
Hepart	Amino V Komplex (H1400)	18000823	81053	40
Hepart	Amino V Komplex (H1400)	18000824	81054	40
Hepart	Amino V Komplex (H1400)	18000825	81066	40
Hepart	Amino V Komplex (H1400)	18000826	81067	40
Hepart	Amino V Komplex (H1400)	18001324	81100	40
Hepart	Amino V Komplex (H1400)	18001328	81101	40
Hepart	Amino V Komplex (H1400)	18001675	81122	60
Hepart	Amino V Komplex (H1400)	18001674	81123	60
Hepart	Amino V Komplex (H1400)	18001575	81124	60
Hepart	Amino V Komplex (H1400)	18001676	81125	60

- 21 719 spectra from a total of 476 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 1 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Complexo de proteína de ervilha (H1428) / Complexo amino V (H1400)*.
- Among them are spectra of independent samples from 1 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	Amino V Komplex (H1400)	16001229-0	1

- 2969 spectra from 26 *Apo-Ident* customers from a total of 1459 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 *Complexo de proteína de ervilha (H1428) / Complexo amino V (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 *Complexo de proteína de ervilha (H1428) / Complexo amino V (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	480	0	27 796
Type B	0	959	1	21 719
Type C	0	1	0	2969

The substance/substance group *Complexo de proteína de ervilha (H1428) / Complexo amino V (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 % (> 99.9309 %)	100.0000 % (> 98.7500 %)
Type B	100.0000 % (> 99.8662 %)	99.8958 % (> 99.5833 %)
Type C	100.0000 % (> 99.1958 %)	n/a (n/a)

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80749	80749	0,00	21,99
80750	80750	0,00	21,85
80820	80820	0,00	22,27
80821	80821	0,00	22,70
80862	80862	0,00	20,87
80885	80885	0,00	21,32
80995	80995	0,00	21,50
81051	81051	0,00	21,66
81446	81446	0,00	19,77
81483	81483	0,00	19,54
81486	81486	0,00	22,61

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 2.8-2024-04

Validated substance/substance group **Curcumin und Piperin (H1014)**
Substance class **HCK**
Report date **25/11/2024**
Report number **10005865-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Curcumin und Piperin (H1014)

Special notes

When selecting the *Curcumin und Piperin (H1014)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Curcumin und Piperin (H1014)	6	2	11

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Curcumin und Piperin (H1014)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	37,26	—
Betain Hydrochlorid (H1119)	71,92	—

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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 und Piperin (H1014)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Curcumin und Piperin (H1014)	14001017	80475	40	from supplier
Hepart	Curcumin und Piperin (H1014)	15001589	80705	60	from supplier
Hepart	Curcumin und Piperin (H1014)	16000369	80796	40	from supplier
Hepart	Curcumin und Piperin (H1014)	17000258	80883	40	from supplier
Hepart	Curcumin und Piperin (H1014)	21000433	81336	40	from supplier
Hepart	Curcumin und Piperin (H1014)	21000433	81406	40	from supplier
Hepart	Curcumin und Piperin (H1014)	22000029	81416	40	from supplier

Validation samples

A total of 53 925 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 *Curcumin und Piperin (H1014)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.

- 27976 spectra from a total of 566 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Curcumin und Piperin (H1014)*.
- 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	Curcumin und Piperin (H1014)	18001688	81128	40
Hepart	Curcumin und Piperin (H1014)	18001687	81129	40

- 22599 spectra from a total of 494 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 25 spectra from 10 *Apo-Ident* customers from 14 batches from the substance/substance group *Curcumin und Piperin (H1014)*.
- 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	Curcumin und Piperin (H1014)	14001017/6	1
HCK	Curcumin und Piperin (H1014)	16001002-1	1
Hepart AG, CH-8280 K...	Curcumin und Piperin (H1014)	13901	1
Hepart AG	Curcumin und Piperin (H1014)	13901	3
Hepart AG	Curcumin und Piperin (H1014)	15001589	1
Hepart AG	Curcumin und Piperin (H1014)	1534002201	1
Hepart AG	Curcumin und Piperin (H1014)	18001687/1	1
Hepart AG	Curcumin und Piperin (H1014)	72001	2
Hepart	Curcumin und Piperin (H1014)	1017	1

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Supplier	Substance	Batch	Spectra
Hepart	Curcumin und Piperin (H1014)	17000258	2
Hepart	Curcumin und Piperin (H1014)	17000258-0	1
Hepart	Curcumin und Piperin (H1014)	17000259/0	1
Hepart	Curcumin und Piperin (H1014)	180016870	1
Unisan	Curcumin und Piperin (H1014)	13901	1
Unisan	Curcumin und Piperin (H1014)	14001017	1
Unisan	Curcumin und Piperin (H1014)	14001017/6	1
Unisan	Curcumin und Piperin (H1014)	17000259	1
Unisan	Curcumin und Piperin (H1014)	72001	4

- 2945 spectra from 26 *Apo-Ident* customers from a total of 1446 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 und Piperin (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 und Piperin (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	300	0	27 976
Type B	0	80	0	22 599
Type C	0	23	2	2945

The substance/substance group *Curcumin und Piperin (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 % (> 99.9310 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.8684 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8358 %)	92.0000 % (> 80.0000 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80475	80475	0,00	38,90
80705	80705	0,00	38,82
80796	80796	0,00	43,15
80883	80883	0,00	37,26
81336	81336	0,00	41,93
81406	81406	0,00	42,26
81416	81416	0,00	45,73

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 2.8-2024-04

Validated substance/substance group **Ferro (H1015) / Cobre (H1032)**
Substance class HCK
Report date 25/11/2024
Report number 80341-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ferro (H1015) / Cobre (H1032); Eisen (H1015); Kupfer (H1032)

Special notes

When selecting the *Ferro (H1015) / Cobre (H1032)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Ferro (H1015) / Cobre (H1032)	14	11	50

Second-stage model

For differentiation of the substance/substance group *Ferro (H1015) / Cobre (H1032)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Ferro (H1015) / Cobre (H1032)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Argentum (H1116)	10,10	—
Spurenelemente SE Komplex (H1082)	19,29	—
Chaga (H1011)	37,40	—
Magnesium (H1060)	45,26	—
Garcinia Cambogia (H1017)	46,51	—
Walnussblatt Extrakt (H1114)	62,89	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ferro (H1015) / Cobre (H1032)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Eisen (H1015)	14000285	80510	60	from supplier
Hepart	Eisen (H1015)	040901	80511	60	from supplier
Hepart	Eisen (H1015)	040901	80568	60	from supplier
Hepart	Eisen (H1015)	14000285	80569	60	from supplier
Hepart	Eisen (H1015)	15001258	80650	60	from supplier
Hepart	Eisen (H1015)	15001259(B1)	80651	60	from supplier
Hepart	Eisen (H1015)	15001259	80653	60	from supplier
Hepart	Eisen (H1015)	20002186	81305	40	from supplier
Hepart	Eisen (H1015)	21000845	81367	50	from supplier
Hepart	Eisen (H1015)	23000509	81474	40	from supplier
Hepart	Eisen (H1015)	24000872	81540	40	from supplier
Hepart	Kupfer (H1032)	130415	80341	40	from supplier
Hepart	Kupfer (H1032)	15000211	80536	60	from supplier
Hepart	Kupfer (H1032)	19001347	81222	40	from supplier
Hepart	Kupfer (H1032)	20002434	81297	40	from supplier
Hepart	Kupfer (H1032)	21000943	81356	50	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 820 spectra of 16 reference samples from the substance/substance group *Ferro (H1015) / Cobre (H1032)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 14 different batches.
- 27 456 spectra from a total of 558 batches from further 129 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 560 spectra of 12 reference samples from the substance/substance group *Ferro (H1015) / Cobre (H1032)*.
- 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	Eisen (H1015)	15001259(F2)	80649	60
Hepart	Eisen (H1015)	15001258(F2)	80652	60
Hepart	Eisen (H1015)	15001258(B1)	80654	60
Hepart	Eisen (H1015)	17000279	80917	40
Hepart	Eisen (H1015)	20000399	81254	40
Hepart	Eisen (H1015)	20000089/0	81255	40
Hepart	Eisen (H1015)	20002902	81347	40
Hepart	Eisen (H1015)	21001399	81381	50
Hepart	Eisen (H1015)	21001967	81394	50
Hepart	Kupfer (H1032)	15000211/5	80875	40
Hepart	Kupfer (H1032)	23001418	81495	40
Hepart	Eisen (H1015)	14000285	80413	40

- 22 119 spectra from a total of 484 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 128 spectra from 20 *Apo-Ident* customers from 57 batches from the substance/substance group *Ferro (H1015) / Cobre (H1032)*.
- Among them are spectra of independent samples from 50 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	Kupfer (H1032)	933901	1
Flaigg Ag CH-4147 Ae...	Eisen (H1015)	15001259/2	2
HCK	Eisen (H1015)	1259	1
HCK	Eisen (H1015)	15001258/1	1
HCK	Eisen (H1015)	15001258-0	1
HCK	Eisen (H1015)	15001258-1	1
HCK	Eisen (H1015)	15001259-0	2
Hepart / Unisan	Eisen (H1015)	17000279/1	1
Hepart AG, CH-8280 K...	Eisen (H1015)	1114998701	1
Hepart ag/Unisan	Eisen (H1015)	20000399/0	1
Hepart ag/Unisan	Eisen (H1015)	20002186	1
Hepart AG	Eisen (H1015)	1114040901	2
Hepart AG	Eisen (H1015)	1114998701	1
Hepart AG	Kupfer (H1032)	13041501	1
Hepart AG	Kupfer (H1032)	130415-K1	1
Hepart AG	Kupfer (H1032)	15000211/4	2
Hepart AG	Eisen (H1015)	15001258/0	1
Hepart AG	Kupfer (H1032)	1544007901	1
Hepart AG	Kupfer (H1032)	1544046401	1
Hepart AG	Eisen (H1015)	40901	3
Hepart AG	Kupfer (H1032)	46401	1
Hepart/Unisan	Eisen (H1015)	15001258/1	1
Hepart/Unisan	Eisen (H1015)	20000399/0	1
Hepart	Kupfer (H1032)		1
Hepart	Kupfer (H1032)	15000211	1
Hepart	Kupfer (H1032)	15000211/5	1
Hepart	Kupfer (H1032)	15000211/8	2
Hepart	Kupfer (H1032)	150002117	1
Hepart	Eisen (H1015)	15001258	3
Hepart	Eisen (H1015)	15001258-4	1
Hepart	Eisen (H1015)	15001259/1	4
Hepart	Eisen (H1015)	15001259/2	3
Hepart	Eisen (H1015)	17000279	1
Hepart	Eisen (H1015)	17000279/0	3
Hepart	Eisen (H1015)	17000279/1	2
Hepart	Eisen (H1015)	17000279/2	1
Hepart	Kupfer (H1032)	19001221/0	1
Hepart	Kupfer (H1032)	19001347	1
Hepart	Kupfer (H1032)	19001347/0	6
Hepart	Kupfer (H1032)	19001347/1	2
Hepart	Kupfer (H1032)	19001347/2	1
Hepart	Eisen (H1015)	20000399/0	1
Hepart	Eisen (H1015)	20002186	1
Hepart	Eisen (H1015)	20002186/0	3
Hepart	Eisen (H1015)	20002186/1	1
Hepart	Eisen (H1015)	20002902	1
Hepart	Eisen (H1015)	2002186	1
Hepart	Kupfer (H1032)	21000943/0	2
Hepart	Kupfer (H1032)	21000943/3	1
Hepart	Eisen (H1015)	21001399/0	1

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Supplier	Substance	Batch	Spectra
Hepart	Eisen (H1015)	21001967/0	2
Unisan 02.04.2016	Eisen (H1015)	15001258/0	1
Unisan 11.08.2105	Eisen (H1015)	14000285/2	1
Unisan 2.10.2015	Eisen (H1015)	14000285/3	2
Unisan/Hepart AG	Kupfer (H1032)	13041501	1
Unisan/Hepart AG	Eisen (H1015)	40901	1
Unisan/Hepart	Eisen (H1015)	15001259/0	1
Unisan	Eisen (H1015)	1114040901	2
Unisan	Eisen (H1015)	1114603206	1
Unisan	Eisen (H1015)	1114998701	3
UNISAN	Kupfer (H1032)	13041501	5
Unisan	Eisen (H1015)	14000285	1
UNISAN	Eisen (H1015)	14000285	1
Unisan	Eisen (H1015)	14000285/1	2
Unisan	Eisen (H1015)	14000285/5	1
Unisan	Kupfer (H1032)	15000211	1
Unisan	Kupfer (H1032)	15000211/0	1
Unisan	Eisen (H1015)	15001258/0	1
Unisan	Eisen (H1015)	15001258/2	2
Unisan	Eisen (H1015)	15001259	2
Unisan	Kupfer (H1032)	1542933901	1
Unisan	Eisen (H1015)	40901	9
Unisan	Kupfer (H1032)	46401	2
Unisan	Kupfer (H1032)	7901	1
Unisan	Kupfer (H1032)	933901	1
Unisan	Eisen (H1015)	998701	6

- 2842 spectra from 26 *Apo-Ident* customers from a total of 1403 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 *Ferro (H1015) / Cobre (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 *Ferro (H1015) / Cobre (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	820	0	27 456
Type B	0	560	0	22 119
Type C	0	128	0	2842

The substance/substance group *Ferro (H1015) / Cobre (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 % (> 99.9308 %)	100.0000 % (> 99.2683 %)
Type B	100.0000 % (> 99.8663 %)	100.0000 % (> 98.9286 %)
Type C	100.0000 % (> 98.8237 %)	100.0000 % (> 95.3125 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80341	80341	0,00	27,09
80510	80510	0,00	19,79
80511	80511	0,00	20,68
80536	80536	0,00	38,56
80568	80568	0,00	18,13
80569	80569	0,00	20,04
80650	80650	0,00	12,47
80651	80651	0,00	12,07
80653	80653	0,00	12,27
81222	81222	0,00	24,58
81297	81297	0,00	21,48
81305	81305	0,00	10,10
81356	81356	0,00	26,93
81367	81367	0,00	17,48
81474	81474	0,00	103,89
81540	81540	0,00	139,29

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 2.8-2024-04

Validated substance/substance group **Flohsamenschalen (H1527)**
Substance class HCK
Report date 25/11/2024
Report number 10006097-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Flohsamenschalen (H1527)

Special notes

When selecting the *Flohsamenschalen (H1527)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Flohsamenschalen (H1527)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Flohsamenschalen* (H1527) the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Flohsamenschalen* (H1527) in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Safran Griffel (H1434)	19,97	—
Eibisch Extrakt (H1439)	23,79	—
Vitamin B1 (H1101)	24,67	—
Orthovimin Neutral Komplex (H1403)	25,18	—
Enzian Extrakt (H1438)	26,95	—
Lycopen (H1058)	28,16	—
Coenzym Q10 (H1013)	30,14	—
Silicium (H1070)	30,90	—
Selenhefe (H1068)	33,75	—
Ginseng (H1018)	34,17	—
Zink (H1110)	39,25	—
Óleo de zimbro (H1112)	40,06	—
Magnesium (H1060)	40,28	—
Baobab (H1410)	40,55	—
Bor (H1005)	40,69	—
L-Arginin (H1036)	41,21	—
Artischocke Extrakt (H1440)	41,97	—
Detox Komplex (H1111)	45,60	—
Safran Blüten (H1435)	46,78	—
Vitamin K2 (75µg Mono) (H1108)	46,94	—
Garcinia Cambogia (H1017)	47,83	—
Calcium L-(+) -Lactat Komplex (H1008)	48,01	—
Leaky Gut Komplex (H1802)	48,21	—
Glutathion (H1020)	48,67	—
Artemisia annua Extrakt (H1118)	48,71	—
Ingwer Extrakt (H1437)	49,91	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Flohsamenschalen* (H1527) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Flohsamenschalen* (H1527):

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Flohsamenschalen (H1527)	23000150	81468	40	from supplier

Validation samples

A total of 53 925 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 *Flohsamenschalen (H1527)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Flohsamenschalen (H1527)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Flohsamenschalen (H1527)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Flohsamenschalen (H1527)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Flohsamenschalen (H1527)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Flohsamenschalen (H1527)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81468	81468	0,00	20,93

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 2.8-2024-04

Validated substance/substance group **Glucosaminsulfat (H1019)**
Substance class HCK
Report date 25/11/2024
Report number 80094-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Glucosaminsulfat (H1019)

Special notes

When selecting the *Glucosaminsulfat (H1019)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Glucosaminsulfat (H1019)	3	7	15

Second-stage model

For differentiation of the substance/substance group *Glucosaminsulfat (H1019)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Glucosaminsulfat (H1019)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Aroma Orange (H1405)	28,22	—
Kreatin (H1031)	56,17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glucosaminsulfat (H1019)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Glucosaminsulfat (H1019)	038001	80319	60	from supplier
Hepart	Glucosaminsulfat (H1019)	038001	80362	40	from supplier
Hepart	Glucosaminsulfat (H1019)	075401	80402	40	from supplier
Hepart	Glucosaminsulfat (H1019)	16000948	80812	40	from supplier

Validation samples

A total of 53 925 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 *Glucosaminsulfat (H1019)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 096 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A*

section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 280 spectra of 7 reference samples from the substance/substance group *Glucosaminsulfat (H1019)*.
- 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	Glucosaminsulfat (H1019)	034001	80454	40
Hepart	Glucosaminsulfat (H1019)	17000073	80877	40
Hepart	Glucosaminsulfat (H1019)	17001387	80954	40
Hepart	Glucosaminsulfat (H1019)	17001245	80955	40
Hepart	Glucosaminsulfat (H1019)	19000775	81181	40
Hepart	Glucosaminsulfat (H1019)	20000494	81261	40
Hepart	Glucosaminsulfat (H1019)	20002248/0	81317	40

- 22 399 spectra from a total of 489 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 16 batches from the substance/substance group *Glucosaminsulfat (H1019)*.
- 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
Hepart AG	Glucosaminsulfat (H1019)	1822038001	1
Hepart AG	Glucosaminsulfat (H1019)	38001	2
Hepart/Unisan	Glucosaminsulfat (H1019)	20000494/0	1
Hepart	Glucosaminsulfat (H1019)	17000073	1
Hepart	Glucosaminsulfat (H1019)	17000073-0	1
Hepart	Glucosaminsulfat (H1019)	17000073-1	1
Hepart	Glucosaminsulfat (H1019)	17001245	2

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Supplier	Substance	Batch	Spectra
Hepart	Glucosaminsulfat (H1019)	17001387/0	9
Hepart	Glucosaminsulfat (H1019)	19000775	1
Hepart	Glucosaminsulfat (H1019)	19000775/0	1
Hepart	Glucosaminsulfat (H1019)	20000494	1
Hepart	Glucosaminsulfat (H1019)	20000494/0	1
Hepart	Glucosaminsulfat (H1019)	34001	1
Unisan GmbH, 78465 K...	Glucosaminsulfat (H1019)	38001	1
Unisan/Hepart AG	Glucosaminsulfat (H1019)	38001	1
Unisan	Glucosaminsulfat (H1019)	16000948	1
Unisan	Glucosaminsulfat (H1019)	17000073/0	1
Unisan	Glucosaminsulfat (H1019)	1823954901	2
UNISAN	Glucosaminsulfat (H1019)	34001	1
Unisan	Glucosaminsulfat (H1019)	38001	2
Unisan	Glucosaminsulfat (H1019)	75401	1

- 2937 spectra from 26 *Apo-Ident* customers from a total of 1444 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 *Glucosaminsulfat (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 *Glucosaminsulfat (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	28 096
Type B	0	240	40	22 399
Type C	0	22	11	2937

The substance/substance group *Glucosaminsulfat (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 % (> 99.9312 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8667 %)	85.7143 % (> 84.6429 %)
Type C	100.0000 % (> 98.8322 %)	66.6667 % (> 57.5758 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80319	80319	0,00	97,37
80362	80362	0,00	93,95
80402	80402	0,00	60,07
80812	80812	0,00	72,90

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 2.8-2024-04

Validated substance/substance group **Glycin (H1021)**
Substance class HCK
Report date 25/11/2024
Report number 80168-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Glycin (H1021)

Special notes

When selecting the *Glycin (H1021)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Glycin (H1021)	11	7	11

Second-stage model

For differentiation of the substance/substance group *Glycin (H1021)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Glycin (H1021)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
L-Lysin (H1047)	52,49	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glycin (H1021)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Glycin (H1021)	061801	80348	40	from supplier
Hepart	Glycin (H1021)	075501	80436	40	from supplier
Hepart	Glycin (H1021)	14001730	80494	60	from supplier
Hepart	Glycin (H1021)	16000239	80764	60	from supplier
Hepart	Glycin (H1021)	16000238	80765	60	from supplier
Hepart	Glycin (H1021)	16000933	80805	40	from supplier
Hepart	Glycin (H1021)	18000449	81027	40	from supplier
Hepart	Glycin (H1021)	20002705	81319	40	from supplier
Hepart	Glycin (H1021)	22000003	81411	40	from supplier
Hepart	Glycin (H1021)	22001472/1	81478	40	from supplier
Hepart	Glycin (H1021)	23001649	81497	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 500 spectra of 11 reference samples from the substance/substance group *Glycin (H1021)*. These

samples are listed above in the [calibration samples](#) section. The reference samples come from 11 different batches.

- 27 776 spectra from a total of 561 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Glycin (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	Glycin (H1021)	14001731	80495	60
Hepart	Glycin (H1021)	16000934	80806	40
Hepart	Glycin (H1021)	17001658	80981	40
Hepart	Glycin (H1021)	17001660	80982	40
Hepart	Glycin (H1021)	18000451/0	81028	40
Hepart	Glycin (H1021)	19001877	81216	40
Hepart	Glycin (H1021)	19001237	81217	40

- 22 379 spectra from a total of 489 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 23 spectra from 12 *Apo-Ident* customers from 14 batches from the substance/substance group *Glycin (H1021)*.
- Among them are spectra of independent samples from 10 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	Glycin (H1021)	16000239/0	1
HCK	Glycin (H1021)		1

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Supplier	Substance	Batch	Spectra
Hepart AG, CH-8280 K...	Glycin (H1021)	28101	1
Hepart AG	Glycin (H1021)	14001730/2	1
Hepart AG	Glycin (H1021)	16000239/0	1
Hepart AG	Glycin (H1021)	17001660/1	2
Hepart AG	Glycin (H1021)	18000449/0	1
Hepart AG	Glycin (H1021)	1803028101	1
Hepart AG	Glycin (H1021)	28101	3
Hepart AG	Glycin (H1021)	75501	1
Hepart	Glycin (H1021)	16000934	1
Hepart	Glycin (H1021)	17001660/0	1
Hepart	Glycin (H1021)	19001237	1
Hepart	Glycin (H1021)	20002705	1
Unisan/Hepart AG	Glycin (H1021)	28101	1
Unisan	Glycin (H1021)	14001730	1
Unisan	Glycin (H1021)	16000933	2
Unisan	Glycin (H1021)	28101	2

- 2947 spectra from 26 *Apo-Ident* customers from a total of 1446 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 *Glycin (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 *Glycin (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	500	0	27 776
Type B	0	300	0	22 379
Type C	0	23	0	2947

The substance/substance group *Glycin (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 % (> 99.9309 %)	100.0000 % (> 98.8000 %)
Type B	100.0000 % (> 99.8666 %)	100.0000 % (> 98.0000 %)
Type C	100.0000 % (> 98.8371 %)	100.0000 % (> 73.9130 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80348	80348	0,00	92,42
80436	80436	0,00	95,63
80494	80494	0,00	83,14
80764	80764	0,00	96,20
80765	80765	0,00	89,11
80805	80805	0,00	88,78
81027	81027	0,00	91,03
81319	81319	0,00	85,68
81411	81411	0,00	85,75
81478	81478	0,00	86,82
81497	81497	0,00	83,22

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 2.8-2024-04

Validated substance/substance group **Granatapfel (H1409)**
Substance class HCK
Report date 25/11/2024
Report number 81035-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Granatapfel (H1409)

Special notes

When selecting the *Granatapfel (H1409)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Granatapfel (H1409)	3	1	0

Second-stage model

For differentiation of the substance/substance group *Granatapfel (H1409)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Granatapfel (H1409)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Karotte (H1513)	20,90	—
Vitamin B1 (H1101)	21,30	—
Aroma Orange (H1405)	21,62	—
L-Arginin (H1036)	22,14	—
Rhodiola (H1064)	27,58	—
Kohlmix (H1514)	29,49	—
Artischocke Extrakt (H1440)	30,16	—
Glutathion (H1020)	31,10	—
Waldbeere (H1524)	31,94	—
Calcium L-(+) -Lactat Komplex (H1008)	31,98	—
Cranberry (H1519)	35,40	—
Leaky Gut Komplex (H1802)	35,69	—
Eibisch Extrakt (H1439)	37,30	—
Orthocolon Komplex (H1800)	37,84	—
Baobab (H1410)	38,23	—
Orthovimin Neutral Komplex (H1403)	38,39	—
Coenzym Q10 (H1013)	38,55	—
Enzian Extrakt (H1438)	41,54	—
Silymarin (H1071)	42,37	—
Vitamine Komplex (H1100)	43,95	—
Kreatin (H1031)	44,19	—
OPC Proanthocyanidine (Pine Bark) (...)	45,55	—
Ginseng (H1018)	48,85	—
Silicium (H1070)	48,87	—
L-Carnitin (H1038)	48,93	—
Bor (H1005)	49,56	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Granatapfel (H1409)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Granatapfel (H1409)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Granatapfel (H1409)	18000566/0	81035	40	from supplier
Hepart	Granatapfel (H1409)	20001374	81275	40	from supplier
Hepart	Granatapfel (H1409)	22000153	81405	40	from supplier

Validation samples

A total of 53 925 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 *Granatapfel (H1409)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 156 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Granatapfel (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	Granatapfel (H1409)	18001310	81086	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Granatapfel (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Granatapfel (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 *Granatapfel (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	120	0	28 156
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Granatapfel (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 % (> 99.9315 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81035	81035	0,00	27,36
81275	81275	0,00	28,48
81405	81405	0,00	23,51

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 2.8-2024-04

Validated substance/substance group **Griffonia (H1035)**
Substance class HCK
Report date 25/11/2024
Report number 10005948-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Griffonia (H1035)

Special notes

When selecting the *Griffonia (H1035)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Griffonia (H1035)	3	1	13

Second-stage model

For differentiation of the substance/substance group *Griffonia (H1035)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Griffonia (H1035)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Calcium L-(+) -Lactat Komplex (H1008)	12,29	—
Vitamine Komplex (H1100)	20,55	—
OPC Proanthocyanidine (Pine Bark) (...)	27,86	—
L-Carnitin (H1038)	28,79	—
Kreatin (H1031)	30,53	—
Silymarin (H1071)	36,12	—
Coenzym Q10 (H1013)	41,80	—
Bioflavonoide Komplex (H1006)	43,78	—
L-Arginin (H1036)	44,57	—
Rhodiola (H1064)	47,21	—
Antibiose forte Komplex (H1115)	49,02	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Griffonia (H1035)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Griffonia (H1035)	16000441	80797	40	from supplier
Hepart	Griffonia (H1035)	21002732	81403	40	from supplier
Hepart	Griffonia (H1035)	23002380	81520	40	from supplier

Validation samples

A total of 53 925 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 *Griffonia (H1035)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 156 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Griffonia (H1035)*.
- 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	Griffonia (H1035)	16000441/0	80851	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 19 spectra from 7 *Apo-Ident* customers from 14 batches from the substance/substance group *Griffonia (H1035)*.
- 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
HCK	Griffonia (H1035)	15001503/0	1
HCK	Griffonia (H1035)	15001503-5	1
HCK	Griffonia (H1035)	16000441	1
Hepart AG	Griffonia (H1035)	15001503	1
Hepart AG	Griffonia (H1035)	15001503/2	3
Hepart AG	Griffonia (H1035)	16000441/0	1
Hepart AG	Griffonia (H1035)	1837999801	1

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Supplier	Substance	Batch	Spectra
Hepart	Griffonia (H1035)	16000441/2	1
Hepart	Griffonia (H1035)	16000441-3	1
Hepart	Griffonia (H1035)	18000913	1
Unisan	Griffonia (H1035)	15001503/5	2
Unisan	Griffonia (H1035)	25006	3
Unisan	Griffonia (H1035)	25006/12	1
Unisan	Griffonia (H1035)	26102	1

- 2951 spectra from 26 *Apo-Ident* customers from a total of 1446 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 *Griffonia (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 *Griffonia (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	120	0	28 156
Type B	0	40	0	22 639
Type C	0	5	14	2951

The substance/substance group *Griffonia (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 % (> 99.9315 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8405 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80797	80797	0,00	29,60
81403	81403	0,00	33,08
81520	81520	0,00	36,83

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 2.8-2024-04

Validated substance/substance group **Grüner Kaffee Extrakt (H1433)**
Substance class HCK
Report date 25/11/2024
Report number 81037-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Grüner Kaffee Extrakt (H1433)

Special notes

When selecting the *Grüner Kaffee Extrakt (H1433)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Grüner Kaffee Extrakt (H1433)	4	0	0

Second-stage model

For differentiation of the substance/substance group *Grüner Kaffee Extrakt (H1433)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Grüner Kaffee Extrakt (H1433)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Detox Komplex (H1111)	14,37	—
Rhodiola (H1064)	17,31	—
Baobab (H1410)	17,35	—
Artischocke Extrakt (H1440)	18,86	—
Calcium L-(+) -Lactat Komplex (H1008)	18,98	—
Silicium (H1070)	19,38	—
Óleo de zimbro (H1112)	19,84	—
Ginkgo Extrakt (H1024)	20,01	—
Garcinia Cambogia (H1017)	21,03	—
Leaky Gut Komplex (H1802)	24,15	—
Eibisch Extrakt (H1439)	24,18	—
Antioxidantien NAT Komplex (H1004)	24,78	—
L-Carnitin (H1038)	25,27	—
Magen Komplex (H1120)	27,34	—
Aroma Orange (H1405)	27,87	—
Glutathion (H1020)	28,29	—
Ginseng (H1018)	28,73	—
PET Basis (H1503)	29,47	—
Orthocolon Komplex (H1800)	30,25	—
Safran Griffel (H1434)	30,71	—
Catechin-Extrakt (H1010)	31,55	—
Bor (H1005)	31,92	—
Coenzym Q10 (H1013)	32,08	—
PET Immunsystem (H1502)	33,39	—
Vitamin C (H1104)	34,98	—
Betain Hydrochlorid (H1119)	35,44	—
Ashwagandha (H1132)	35,95	—
Orthovimin Neutral Komplex (H1403)	36,83	—
Vitamin B1 (H1101)	36,94	—
Vitamin B6 (Pyridoxal-5-phosphat) (...)	37,80	—
Antibiose forte Komplex (H1115)	37,89	—
PET Well-Aging (H1500)	39,82	—
Lycopen (H1058)	40,09	—
Magnesium (H1060)	40,74	—
Bioflavonoide Komplex (H1006)	41,20	—
Silymarin (H1071)	42,24	—
Aminomix NAC (H1002)	42,39	—
Haferkleie beta-Glucan (H1529)	44,48	—

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Substanz	Distance in main model	Distance in second-stage model
L-Arginin (H1036)	44,82	—
Vitamin E NAT (H1107)	45,01	—
PET Gelenke (H1501)	45,38	—
Sanddorn (H1523)	48,27	—
Isoflavone Extrakt (H1025)	49,93	—
Artemisia annua Extrakt (H1118)	50,06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Grüner Kaffee Extrakt (H1433)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Grüner Kaffee Extrakt (H1433)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Grüner Kaffee Extrakt (H1433)	18000368	81037	40	from supplier
Hepart	Grüner Kaffee Extrakt (H1433)	20002440	81323	40	from supplier
Hepart	Grüner Kaffee Extrakt (H1433)	21000805	81331	40	from supplier
Hepart	Grüner Kaffee Extrakt (H1433)	23002216	81519	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Grüner Kaffee Extrakt (H1433)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 28 116 spectra from a total of 568 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Grüner Kaffee Extrakt (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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Grüner Kaffee Extrakt (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Grüner Kaffee Extrakt (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 *Grüner Kaffee Extrakt (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	160	0	28 116
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Grüner Kaffee Extrakt (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 % (> 99.9313 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81037	81037	0,00	25,41
81323	81323	0,00	27,34
81331	81331	0,00	14,37
81519	81519	0,00	21,65

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 2.8-2024-04

Validated substance/substance group **Haferkleie beta-Glucan (H1529)**
Substance class HCK
Report date 25/11/2024
Report number 10006062-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Haferkleie beta-Glucan (H1529)

Special notes

When selecting the *Haferkleie beta-Glucan (H1529)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Haferkleie beta-Glucan (H1529)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Haferkleie beta-Glucan (H1529)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Haferkleie beta-Glucan (H1529)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Leaky Gut Komplex (H1802)	11,51	—
Glutathion (H1020)	18,60	—
Aminomix NAC (H1002)	19,80	—
Coenzym Q10 (H1013)	21,00	—
Vitamin E NAT (H1107)	21,39	—
Aroma Orange (H1405)	21,40	—
Ginseng (H1018)	27,24	—
Calcium L-(+)-Lactat Komplex (H1008)	28,63	—
Antioxidantien NAT Komplex (H1004)	32,04	—
Isoflavone Extrakt (H1025)	33,21	—
Vitamin B1 (H1101)	34,97	—
Orthocolon Komplex (H1800)	37,23	—
Ginkgo Extrakt (H1024)	38,44	—
Camu Camu (H1518)	39,53	—
Garcinia Cambogia (H1017)	41,79	—
Baobab (H1410)	43,28	—
Sonnenblumenkernprotein (H1511)	43,62	—
PET Coenzym Q10 (H1505)	43,67	—
Ingwer Extrakt (H1437)	45,48	—
Kokos (H1522)	45,73	—
L-Arginin (H1036)	45,89	—
Chondroitinsulfat (H1065)	47,93	—
Bor (H1005)	48,93	—
Lutein-Zeaxanthin-Astaxanthin (H1129)	49,14	—
Orthovimin Neutral Komplex (H1403)	49,59	—
Detox Komplex (H1111)	50,17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Haferkleie beta-Glucan (H1529)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Haferkleie beta-Glucan (H1529)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Haferkleie beta-Glucan (H1529)	22001850	81452	40	from supplier
Hepart	Haferkleie beta-Glucan (H1529)	23002222	81516	40	from supplier

Validation samples

A total of 53 925 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 *Haferkleie beta-Glucan (H1529)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 28 196 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Haferkleie beta-Glucan (H1529)*.
- 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	Haferkleie beta-Glucan (H1529)	23002723/0	81531	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Haferkleie beta-Glucan (H1529)*.

- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Haferkleie beta-Glucan (H1529)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Haferkleie beta-Glucan (H1529)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 196
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Haferkleie beta-Glucan (H1529)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9319 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81452	81452	0,00	23,23
81516	81516	0,00	32,35

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 2.8-2024-04

Validated substance/substance group **Hanfprotein (H1406)**
Substance class HCK
Report date 25/11/2024
Report number 81099-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hanfprotein (H1406)

Special notes

When selecting the *Hanfprotein (H1406)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Hanfprotein (H1406)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Hanfprotein (H1406)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Hanfprotein (H1406)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	31,67	—
PET Haut und Haare (H1504)	39,94	—
Aminomix NAC (H1002)	41,73	—
Amino V Komplex (H1400)	42,87	—
Coenzym Q10 (H1013)	45,35	—
a-Liponsäure (H1000)	52,28	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hanfprotein (H1406)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hanfprotein (H1406)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Hanfprotein (H1406)	18001330	81099	40	from supplier
Hepart	Hanfprotein (H1406)	18001679	81134	40	from supplier

Validation samples

A total of 53 925 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 *Hanfprotein (H1406)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.

- 28 196 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Hanfprotein (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	Hanfprotein (H1406)	20000392	81256	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Hanfprotein (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Hanfprotein (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 *Hanfprotein (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	28 196
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Hanfprotein (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 % (> 99.9319 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81099	81099	0,00	31,67
81134	81134	0,00	33,59

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 2.8-2024-04

Validated substance/substance group **Hefe (H1525)**
Substance class HCK
Report date 25/11/2024
Report number 10006098-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hefe (H1525)

Special notes

When selecting the *Hefe (H1525)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Hefe (H1525)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Hefe* (H1525) the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Hefe* (H1525) in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antioxidantien NAT Komplex (H1004)	32,97	—
Antibiose forte Komplex (H1115)	34,03	—
PET Basis (H1503)	39,08	—
Aminomix NAC (H1002)	39,24	—
Coenzym Q10 (H1013)	42,76	—
a-Liponsäure (H1000)	48,02	—
Vitamin B1 (H1101)	49,13	—
Magen Komplex (H1120)	50,99	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hefe* (H1525) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hefe* (H1525):

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Hefe (H1525)	22002512	81469	40	from supplier

Validation samples

A total of 53 925 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 *Hefe* (H1525). These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.

- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Hefe (H1525)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Hefe (H1525)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Hefe (H1525)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hefe (H1525)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Hefe (H1525)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81469	81469	0,00	34,03

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 2.8-2024-04

Validated substance/substance group **Histaminblock Komplex (H1117)**
Substance class HCK
Report date 25/11/2024
Report number 80896-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Histaminblock Komplex (H1117)

Special notes

When selecting the *Histaminblock Komplex (H1117)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Histaminblock Komplex (H1117)	1	1	0

Second-stage model

For differentiation of the substance/substance group *Histaminblock Komplex (H1117)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Histaminblock Komplex (H1117)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Garcinia Cambogia (H1017)	19,49	—
Pathogene Komplex (H1803)	21,45	—
Kupfer (H1032)	22,06	—
Chaga (H1011)	30,42	—
Antibiose mite Komplex (H1113)	31,03	—
PET Basis (H1503)	35,34	—
Ginkgo Extrakt (H1024)	37,06	—
Antioxidantien NAT Komplex (H1004)	38,10	—
PET Gelenke (H1501)	40,10	—
Spurenelemente SE Komplex (H1082)	41,44	—
Aroma Orange (H1405)	46,39	—
Eisen (H1015)	46,82	—
Walnussblatt Extrakt (H1114)	47,07	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Histaminblock Komplex (H1117)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Histaminblock Komplex (H1117)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Histaminblock Komplex (H1117)	16001078	80896	40	from supplier

Validation samples

A total of 53 925 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 *Histaminblock Komplex (H1117)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Histaminblock Komplex (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	Histaminblock Komplex (H1117)	16001079	80897	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Histaminblock Komplex (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Histaminblock Komplex (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 *Histaminblock Komplex (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	28 236
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Histaminblock Komplex (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 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80896	80896	0,00	21,45

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 2.8-2024-04

Validated substance/substance group **Kakao (H1521)**
Substance class HCK
Report date 25/11/2024
Report number 10006306-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Kakao (H1521)

Special notes

When selecting the *Kakao (H1521)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Kakao (H1521)	3	0	0

Second-stage model

For differentiation of the substance/substance group *Kakao (H1521)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Kakao (H1521)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Moringa (H1131)	25,11	—
PET Immunsystem (H1502)	28,08	—
PET Basis (H1503)	33,76	—
Ginkgo Extrakt (H1024)	44,41	—
Vitamin C (H1104)	45,24	—
Kupfer (H1032)	47,28	—
PET Haut und Haare (H1504)	50,60	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Kakao (H1521)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Kakao (H1521)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Kakao (H1521)	23001438	81502	40	from supplier
Hepart	Kakao (H1521)	24000472	81548	30	from supplier
Hepart	Kakao (H1521)	24001271	81549	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 110 spectra of 3 reference samples from the substance/substance group *Kakao (H1521)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.

- 28 166 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Kakao (H1521)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Kakao (H1521)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Kakao (H1521)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Kakao (H1521)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	110	0	28 166
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Kakao (H1521)* can be clearly distinguished from all other substances. In order to make these figures comparable, 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 % (> 94.5455 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81502	81502	0,00	25,18
81548	81548	0,00	25,11
81549	81549	0,00	28,08

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 2.8-2024-04

Validated substance/substance group **Karotte (H1513)/Rote Bete (H1515)**
Substance class HCK
Report date 25/11/2024
Report number 10006064-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Karotte (H1513)/Rote Bete (H1515); Karotte (H1513); Rote Bete (H1515)

Special notes

When selecting the *Karotte (H1513)/Rote Bete (H1515)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Karotte (H1513)/Rote Bete (H1515)	5	0	0

Second-stage model

For differentiation of the substance/substance group *Karotte (H1513)/Rote Bete (H1515)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Karotte (H1513)/Rote Bete (H1515)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Aroma Orange (H1405)	11,22	—
Grünkohl (H1126)	21,89	—
Glutathion (H1020)	21,89	—
Orthocolon Komplex (H1800)	26,54	—
Kohlmix (H1514)	27,40	—
Eibisch Extrakt (H1439)	27,64	—
L-Arginin (H1036)	27,90	—
Calcium L-(+) -Lactat Komplex (H1008)	28,93	—
Artischocke Extrakt (H1440)	29,36	—
Vitamin B1 (H1101)	30,22	—
Brokkoli (H1512)	31,47	—
Rhodiola (H1064)	31,50	—
Leaky Gut Komplex (H1802)	33,64	—
Baobab (H1410)	35,51	—
Antioxidantien NAT Komplex (H1004)	37,00	—
Óleo de zimbro (H1112)	38,63	—
Detox Komplex (H1111)	38,68	—
Cranberry (H1519)	39,22	—
Granatapfel (H1409)	39,40	—
Coenzym Q10 (H1013)	39,66	—
Ginseng (H1018)	45,20	—
Eisen (H1015)	48,12	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Karotte (H1513)/Rote Bete (H1515)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Karotte (H1513)/Rote Bete (H1515)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Karotte (H1513)	21002986	81455	40	from supplier
Hepart	Karotte (H1513)	23001855	81499	40	from supplier
Hepart	Karotte (H1513)	23002234	81521	40	from supplier
Hepart	Rote Bete (H1515)	23000557	81475	40	from supplier
Hepart	Rote Bete (H1515)	24000573	81538	40	from supplier

Validation samples

A total of 53 925 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 *Karotte (H1513)/Rote Bete (H1515)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 28 076 spectra from a total of 567 batches from further 129 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Karotte (H1513)/Rote Bete (H1515)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Karotte (H1513)/Rote Bete (H1515)*.
- 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.

- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Karotte (H1513)/Rote Bete (H1515)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Karotte (H1513)/Rote Bete (H1515)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 076
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Karotte (H1513)/Rote Bete (H1515)* can be clearly distinguished from all other substances. In order to make these figures comparable, 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 % (> 97.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81455	81455	0,00	29,01
81475	81475	0,00	21,89
81499	81499	0,00	26,94
81521	81521	0,00	24,77
81538	81538	0,00	26,86

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 2.8-2024-04

Validated substance/substance group **Koffein Guarana Extrakt (H1425)**
Substance class **HCK**
Report date **25/11/2024**
Report number **10002191-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Koffein Guarana Extrakt (H1425)

Special notes

When selecting the *Koffein Guarana Extrakt (H1425)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Koffein Guarana Extrakt (H1425)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Koffein Guarana Extrakt (H1425)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Koffein Guarana Extrakt (H1425)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
L-Carnitin (H1038)	15,15	—
Calcium L-(+) -Lactat Komplex (H1008)	25,24	—
Coenzym Q10 (H1013)	25,75	—
OPC Proanthocyanidine (Pine Bark) (...)	27,02	—
Vitamine Komplex (H1100)	29,98	—
L-Arginin (H1036)	35,30	—
Silymarin (H1071)	39,99	—
Glutathion (H1020)	41,52	—
Bioflavonoide Komplex (H1006)	45,88	—
Vitamin B1 (H1101)	46,45	—
Leaky Gut Komplex (H1802)	47,94	—
Aroma Orange (H1405)	49,81	—

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Koffein Guarana Extrakt (...)	19000247/0	81212	40	from supplier
Hepart	Koffein Guarana Extrakt (...)	24001401	81553	40	from supplier

Validation samples

A total of 53 925 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 *Koffein Guarana Extrakt (H1425)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 28 196 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Koffein Guarana Extrakt (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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Koffein Guarana Extrakt (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Koffein Guarana Extrakt (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 *Koffein Guarana Extrakt (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	80	0	28 196
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Koffein Guarana Extrakt (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 % (> 99.9319 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81212	81212	0,00	29,18
81553	81553	0,00	30,03

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 2.8-2024-04

Validated substance/substance group **Kokos (H1522)**
Substance class HCK
Report date 25/11/2024
Report number 10006010-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Kokos (H1522)

Special notes

When selecting the *Kokos (H1522)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Kokos (H1522)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Kokos (H1522)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Kokos (H1522)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Glutathion (H1020)	13,51	—
Vitamin E NAT (H1107)	15,25	—
Coenzym Q10 (H1013)	19,80	—
Haferkleie beta-Glucan (H1529)	22,09	—
Aminomix NAC (H1002)	26,46	—
Aroma Orange (H1405)	31,09	—
Lutein-Zeaxanthin-Astaxanthin (H1129)	37,77	—
Isoflavone Extrakt (H1025)	41,04	—
Calcium L-(+) -Lactat Komplex (H1008)	41,27	—
Antioxidantien NAT Komplex (H1004)	41,67	—
Garcinia Cambogia (H1017)	42,75	—
Ginseng (H1018)	44,31	—
Leaky Gut Komplex (H1802)	46,00	—
Antibiose forte Komplex (H1115)	46,50	—
Ingwer Extrakt (H1437)	49,48	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Kokos (H1522)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Kokos (H1522)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Kokos (H1522)	21002574	81448	40	from supplier
Hepart	Kokos (H1522)	23000228	81463	40	from supplier

Validation samples

A total of 53 925 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 *Kokos (H1522)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 28 196 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Kokos (H1522)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Kokos (H1522)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Kokos (H1522)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Kokos (H1522)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 196
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Kokos (H1522)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9319 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81448	81448	0,00	24,04
81463	81463	0,00	26,12

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 2.8-2024-04

Validated substance/substance group **Kollagenpeptide-MTC (H1125)**
Substance class HCK
Report date 25/11/2024
Report number 10006002-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Kollagenpeptide-MTC (H1125)

Special notes

When selecting the *Kollagenpeptide-MTC (H1125)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Kollagenpeptide-MTC (H1125)	3	1	0

Second-stage model

For differentiation of the substance/substance group *Kollagenpeptide-MTC (H1125)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Kollagenpeptide-MTC (H1125)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model. A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Coenzym Q10 (H1013)	26,01	—
Antibiose forte Komplex (H1115)	30,81	—
Aminomix NAC (H1002)	36,02	—
PET Haut und Haare (H1504)	42,04	—
L-Glutamin (H1043)	48,66	—
Vitamin E NAT (H1107)	52,08	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Kollagenpeptide-MTC (H1125)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Kollagenpeptide-MTC (H1125)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Kollagenpeptide-MTC (H1125)	21001193	81432	40	from supplier
Hepart	Kollagenpeptide-MTC (H1125)	22002703	81496	40	from supplier
Hepart	Kollagenpeptide-MTC (H1125)	23002071	81510	40	from supplier

Validation samples

A total of 53 925 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 *Kollagenpeptide-MTC (H1125)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.

- 28 156 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Kollagenpeptide-MTC (H1125)*.
- 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	Kollagenpeptide-MTC (H1125)	24001329/0	81552	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Kollagenpeptide-MTC (H1125)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Kollagenpeptide-MTC (H1125)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Kollagenpeptide-MTC (H1125)* and it was evaluated how many matches (positive) and rejections (negative) were correct or

incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 156
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Kollagenpeptide-MTC (H1125)* can be clearly distinguished from all other substances. In order to make these figures comparable, 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 % (> 95.0000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81432	81432	0,00	31,73
81496	81496	0,00	31,92
81510	81510	0,00	30,81

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 2.8-2024-04

Validated substance/substance group **Konjak Glucomannan (H1530)**
Substance class HCK
Report date 25/11/2024
Report number 10006305-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Konjak Glucomannan (H1530)

Special notes

When selecting the *Konjak Glucomannan (H1530)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Konjak Glucomannan (H1530)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Konjak Glucomannan (H1530)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Konjak Glucomannan (H1530)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Ginseng (H1018)	9,65	—
Lycopen (H1058)	19,38	—
Safran Griffel (H1434)	19,42	—
Orthovimin Neutral Komplex (H1403)	20,53	—
Selenhefe (H1068)	25,04	—
Enzian Extrakt (H1438)	25,88	—
Zink (H1110)	28,02	—
Vitamin B12 (H1102)	28,56	—
Selen (H1067)	29,12	—
Flohsamenschalen (H1527)	31,46	—
Guar-Granulat (H1023)	32,00	—
Eibisch Extrakt (H1439)	32,63	—
L-Arginin (H1036)	33,66	—
Vitamin B1 (H1101)	34,02	—
Ashwagandha (H1132)	35,20	—
Vitamin D3 (H1105)	36,19	—
Silicium (H1070)	36,73	—
Coenzym Q10 (H1013)	38,39	—
Artischocke Extrakt (H1440)	38,40	—
Rhodiola (H1064)	39,80	—
Bor (H1005)	40,11	—
Biotin (H1007)	41,65	—
Artemisia annua Extrakt (H1118)	42,91	—
Baobab (H1410)	43,10	—
Magnesium (H1060)	43,17	—
Calcium L-(+) -Lactat Komplex (H1008)	44,06	—
Chrom (H1012)	44,33	—
OPC Proanthocyanidine (Pine Bark) (...)	45,59	—
Vitamin K2 (75µg Mono) (H1108)	45,65	—
Granatapfel (H1409)	49,06	—
Leaky Gut Komplex (H1802)	50,51	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Konjak Glucomannan (H1530)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Konjak Glucomannan (H1530)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Konjak Glucomannan (H1530)	23001630	81501	40	from supplier

Validation samples

A total of 53 925 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 *Konjak Glucomannan (H1530)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Konjak Glucomannan (H1530)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Konjak Glucomannan (H1530)*.

- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Konjak Glucomannan (H1530)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Konjak Glucomannan (H1530)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Konjak Glucomannan (H1530)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81501	81501	0,00	9,65

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 2.8-2024-04

Validated substance/substance group **Kreatin (H1031)**
Substance class HCK
Report date 25/11/2024
Report number 80149-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Kreatin (H1031)

Special notes

When selecting the *Kreatin (H1031)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Kreatin (H1031)	6	3	7

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Kreatin (H1031)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Vitamine Komplex (H1100)	29,27	—
Aroma Orange (H1405)	44,37	—
L-Carnitin (H1038)	50,33	—

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

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Kreatin (H1031)	025003	80440	40	from supplier
Hepart	Kreatin (H1031)	025004	80441	40	from supplier
Hepart	Kreatin (H1031)	15000749	80627	60	from supplier
Hepart	Kreatin (H1031)	15000750	80628	60	from supplier
Hepart	Kreatin (H1031)	20002161	81295	40	from supplier
Hepart	Kreatin (H1031)	24000700	81543	40	from supplier

Validation samples

A total of 53 925 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 *Kreatin (H1031)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.

- 27 996 spectra from a total of 566 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Kreatin (H1031)*.
- 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	Kreatin (H1031)	17001177	80918	40
Hepart	Kreatin (H1031)	18001411	81115	40
Hepart	Kreatin (H1031)	24001358	81554	40

- 22 559 spectra from a total of 493 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 5 *Apo-Ident* customers from 9 batches from the substance/substance group *Kreatin (H1031)*.
- 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	Kreatin (H1031)	15000749/1	1
HCK	Kreatin (H1031)	15000749-2	1
HCK	Kreatin (H1031)	17001177	2
Hepart AG	Kreatin (H1031)	15000749	1
Purren Apotheke	Kreatin (H1031)	965201	1
Unisan GmbH, 78465 K...	Kreatin (H1031)	1830025003	1
Unisan	Kreatin (H1031)	15000750	1
Unisan	Kreatin (H1031)	15000750/0	1
Unisan	Kreatin (H1031)	25003	2

- 2959 spectra from 26 *Apo-Ident* customers from a total of 1451 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 *Kreatin (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 *Kreatin (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	280	0	27 996
Type B	0	120	0	22 559
Type C	0	11	0	2959

The substance/substance group *Kreatin (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 % (> 97.8571 %)
Type B	100.0000 % (> 99.8676 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8549 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80440	80440	0,00	47,13
80441	80441	0,00	54,75
80627	80627	0,00	44,20
80628	80628	0,00	49,93
81295	81295	0,00	52,80
81543	81543	0,00	52,01

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 2.8-2024-04

Validated substance/substance group **Kürbiskernprotein (H1509)**
Substance class HCK
Report date 25/11/2024
Report number 10006065-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Kürbiskernprotein (H1509)

Special notes

When selecting the *Kürbiskernprotein (H1509)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Kürbiskernprotein (H1509)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Kürbiskernprotein (H1509)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Kürbiskernprotein (H1509)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Aminomix NAC (H1002)	14,44	—
L-Glutamin (H1043)	28,04	—
L-Carnitin (H1038)	28,53	—
Antibiose forte Komplex (H1115)	29,33	—
Coenzym Q10 (H1013)	32,70	—
Isoflavone Extrakt (H1025)	38,04	—
Vitamin B1 (H1101)	40,61	—
Lupinenprotein BCAA Komplex (H1510)	46,11	—
Amino V Komplex (H1400)	47,59	—
Glutathion (H1020)	48,91	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Kürbiskernprotein (H1509)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Kürbiskernprotein (H1509)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Kürbiskernprotein (H1509)	22002186	81456	40	from supplier
Hepart	Kürbiskernprotein (H1509)	23002724	81532	40	from supplier

Validation samples

A total of 53 925 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 *Kürbiskernprotein (H1509)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 28 196 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Kürbiskernprotein (H1509)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Kürbiskernprotein (H1509)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Kürbiskernprotein (H1509)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Kürbiskernprotein (H1509)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 196
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Kürbiskernprotein (H1509)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9319 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81456	81456	0,00	21,15
81532	81532	0,00	34,13

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 2.8-2024-04

Validated substance/substance group **L-Arginin (H1036)**
Substance class HCK
Report date 25/11/2024
Report number 80026-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Arginin (H1036)

Special notes

When selecting the *L-Arginin (H1036)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Arginin (H1036)	5	9	24

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Arginin (H1036)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Eisen (H1015)	39,46	—
Aminomix NAC (H1002)	45,51	—
Vitamin B1 (H1101)	46,50	—
Calcium L-(+) -Lactat Komplex (H1008)	47,04	—
Orthocolon Komplex (H1800)	48,90	—
Coenzym Q10 (H1013)	52,16	—

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

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Arginin (H1036)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Arginin (H1036)	066501	80373	40	from supplier
Hepart	L-Arginin (H1036)	16000949	80807	40	from supplier
Hepart	L-Arginin (H1036)	16000949	80867	40	from supplier
Hepart	L-Arginin (H1036)	16000950	80876	40	from supplier
Hepart	L-Arginin (H1036)	18001388	81113	40	from supplier
Hepart	L-Arginin (H1036)	210015-71-72	81371	50	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 250 spectra of 6 reference samples from the substance/substance group L-Arginin (H1036). These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 28 026 spectra from a total of 567 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 400 spectra of 10 reference samples from the substance/substance group L-Arginin (H1036).
- Among them are spectra of independent samples from 9 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	L-Arginin (H1036)	052401	80330	60
Hepart	L-Arginin (H1036)	14000563	80446	20
Hepart	L-Arginin (H1036)	14000564	80448	40
Hepart	L-Arginin (H1036)	17000878	80928	40
Hepart	L-Arginin (H1036)	17000877	80929	40
Hepart	L-Arginin (H1036)	18001443	81114	40
Hepart	L-Arginin (H1036)	19000626	81188	40
Hepart	L-Arginin (H1036)	19000689	81189	40
Hepart	L-Arginin (H1036)	22002215	81457	40
Hepart	L-Arginin (H1036)	16000950	80808	40

- 22 279 spectra from a total of 486 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 68 spectra from 17 *Apo-Ident* customers from 24 batches from the substance/substance group L-Arginin (H1036).
- Among them are spectra of independent samples from 24 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	L-Arginin (H1036)	1324044301	1
HCK	L-Arginin (H1036)	14000563/2	1
HCK	L-Arginin (H1036)	14000564	1
Hepart AG/Unisan	L-Arginin (H1036)	19000626	1
Hepart AG/Unisan	L-Arginin (H1036)	19000626/0	1
Hepart AG	L-Arginin (H1036)	14000563/2	1
Hepart AG	L-Arginin (H1036)	17000877/0	1
Hepart AG	L-Arginin (H1036)	17000878/0	9
Hepart AG	L-Arginin (H1036)	66501	1
Hepart	L-Arginin (H1036)	16000950/0	1
Hepart	L-Arginin (H1036)	17000877	1
Hepart	L-Arginin (H1036)	17000877/0	2
Hepart	L-Arginin (H1036)	17000877-0	2
Hepart	L-Arginin (H1036)	17000878	4
Hepart	L-Arginin (H1036)	17000878/0	4
Hepart	L-Arginin (H1036)	17000878/1	2
Hepart	L-Arginin (H1036)	17000878-0	1
Hepart	L-Arginin (H1036)	18001443/0	3
Hepart	L-Arginin (H1036)	19000626	2
Hepart	L-Arginin (H1036)	19000626/0	4
Hepart	L-Arginin (H1036)	19000689/0	2
Unisan Gmbh, 78465 K...	L-Arginin (H1036)	52401	2
Unisan/Hepart AG	L-Arginin (H1036)	1324044301	1
Unisan	L-Arginin (H1036)	1324950601	1
Unisan	L-Arginin (H1036)	14000563	1
Unisan	L-Arginin (H1036)	14000564/0	1
Unisan	L-Arginin (H1036)	14000564/2	1
Unisan	L-Arginin (H1036)	16000949/0	2
Unisan	L-Arginin (H1036)	17000877	3
Unisan	L-Arginin (H1036)	27802	1
Unisan	L-Arginin (H1036)	44301	2
unisan	L-Arginin (H1036)	52401	1
Unisan	L-Arginin (H1036)	52401	1
Unisan	L-Arginin (H1036)	66501	5
UNISAN	L-Arginin (H1036)	66501	1

- 2902 spectra from 26 *Apo-Ident* customers from a total of 1436 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-Arginin (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 *L-Arginin (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	250	0	28 026
Type B	0	400	0	22 279
Type C	0	67	1	2902

The substance/substance group *L-Arginin (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 % (> 99.9311 %)	100.0000 % (> 97.6000 %)
Type B	100.0000 % (> 99.8665 %)	100.0000 % (> 98.5000 %)
Type C	100.0000 % (> 98.8263 %)	98.5294 % (> 94.1176 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80373	80373	0,00	52,97
80807	80807	0,00	46,18
80867	80867	0,00	40,04
80876	80876	0,00	41,84
81113	81113	0,00	41,01
81371	81371	0,00	50,31

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 2.8-2024-04

Validated substance/substance group **L-Carnitin (H1038)**
Substance class HCK
Report date 25/11/2024
Report number 80013-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Carnitin (H1038)

Special notes

When selecting the *L-Carnitin (H1038)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Carnitin (H1038)	10	10	39

Second-stage model

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

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group L-Carnitin (H1038) in the substance class HCK. For Mahalanobis distances M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Calcium L-(+)-Lactat Komplex (H1008)	18,11	—
Koffein Guarana Extrakt (H1425)	23,74	—
Coenzym Q10 (H1013)	23,89	—
Ginkgo Extrakt (H1024)	24,28	—
Vitamin B1 (H1101)	26,08	—
Silymarin (H1071)	27,17	—
Orthocolon Komplex (H1800)	27,24	—
Antioxidantien NAT Komplex (H1004)	29,13	—
Sonnenblumenkernprotein (H1511)	33,04	—
Antibiose forte Komplex (H1115)	33,25	—
L-Arginin (H1036)	34,20	—
Aroma Orange (H1405)	37,56	—
Vitamine Komplex (H1100)	38,84	—
Aminomix NAC (H1002)	39,38	—
Glutathion (H1020)	43,16	—
OPC Proanthocyanidine (Pine Bark) (...)	44,13	—
Leaky Gut Komplex (H1802)	45,45	—
Rhodiola (H1064)	47,14	—
Kürbiskernprotein (H1509)	48,86	—
Isoflavone Extrakt (H1025)	48,95	—
Betain Hydrochlorid (H1119)	49,20	—

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

Calibration samples

Only spectra which have been recorded by HiperScan 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-Carnitin (H1038):

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Carnitin (H1038)	026010	80344	40	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Carnitin (H1038)	130605300	80371	40	from supplier
Hepart	L-Carnitin (H1038)	130605302	80483	60	from supplier
Hepart	L-Carnitin (H1038)	15000052	80557	60	from supplier
Hepart	L-Carnitin (H1038)	15000054	80559	60	from supplier
Hepart	L-Carnitin (H1038)	16000453	80787	40	from supplier
Hepart	L-Carnitin (H1038)	18000538	81045	40	from supplier
Hepart	L-Carnitin (H1038)	21000309	81350	40	from supplier
Hepart	L-Carnitin (H1038)	23000597	81472	40	from supplier
Hepart	L-Carnitin (H1038)	23000596	81487	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 460 spectra of 10 reference samples from the substance/substance group *L-Carnitin (H1038)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 27 816 spectra from a total of 562 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 440 spectra of 10 reference samples from the substance/substance group *L-Carnitin (H1038)*.
- Among them are spectra of independent samples from 10 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	L-Carnitin (H1038)	15000053	80558	60
Hepart	L-Carnitin (H1038)	15000055	80560	60
Hepart	L-Carnitin (H1038)	16000450	80788	40
Hepart	L-Carnitin (H1038)	16000451	80817	40
Hepart	L-Carnitin (H1038)	16000454	80818	40
Hepart	L-Carnitin (H1038)	18000539	81046	40
Hepart	L-Carnitin (H1038)	18000418	81047	40
Hepart	L-Carnitin (H1038)	20001491	81289	40
Hepart	L-Carnitin (H1038)	19001233	81290	40
Hepart	L-Carnitin (H1038)	20001492	81293	40

- 22 239 spectra from a total of 486 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 101 spectra from 18 *Apo-Ident* customers from 45 batches from the substance/substance group *L-Carnitin (H1038)*.
- Among them are spectra of independent samples from 39 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-Carnitin (H1038)	1500003-0	1
HCK	L-Carnitin (H1038)	15000053-2	2
HCK	L-Carnitin (H1038)	15000054-0	4
Hepart AG, CH-8280 K...	L-Carnitin (H1038)	1184965901	1
Hepart AG, CH-8280 K...	L-Carnitin (H1038)	26010	1
Hepart AG, CH-8280 K...	L-Carnitin (H1038)	26020	2
Hepart AG/Unisan	L-Carnitin (H1038)	18000538/0	1
Hepart AG/Unisan	L-Carnitin (H1038)	18000539/0	1
Hepart AG/Unisan	L-Carnitin (H1038)	20001491/0	1
Hepart AG/Unisan	L-Carnitin (H1038)	20001492/0	1
Hepart AG	L-Carnitin (H1038)	1184026001	1
Hepart AG	L-Carnitin (H1038)	130605300	1
Hepart AG	L-Carnitin (H1038)	130605301	2
Hepart AG	L-Carnitin (H1038)	16000453/1	2
Hepart AG	L-Carnitin (H1038)	16000454/0	5
Hepart AG	L-Carnitin (H1038)	18000538/0	2
Hepart AG	L-Carnitin (H1038)	26001	1
Hepart AG	L-Carnitin (H1038)	26010	3
Hepart AG	L-Carnitin (H1038)	480g	1
Hepart/Unisan	L-Carnitin (H1038)	20001491/0	1
Hepart	L-Carnitin (H1038)	15000052	1
Hepart	L-Carnitin (H1038)	15000054/1	2
Hepart	L-Carnitin (H1038)	160000453	1
Hepart	L-Carnitin (H1038)	16000450-1	1
Hepart	L-Carnitin (H1038)	16000451/0	1
Hepart	L-Carnitin (H1038)	16000453	1
Hepart	L-Carnitin (H1038)	16000453/0	3
Hepart	L-Carnitin (H1038)	16000453-0	2
Hepart	L-Carnitin (H1038)	160004531	3
Hepart	L-Carnitin (H1038)	16000454	2
Hepart	L-Carnitin (H1038)	16000454/0	5
Hepart	L-Carnitin (H1038)	18000538/0	2
Hepart	L-Carnitin (H1038)	20001491	1
Hepart	L-Carnitin (H1038)	20001491/0	1
Hepart	L-Carnitin (H1038)	20001560/0	2
Hepart	L-Carnitin (H1038)	20001691/0	1
Unisan 2.10.2015	L-Carnitin (H1038)	15000052/0	2
Unisan	L-Carnitin (H1038)		2
Unisan	L-Carnitin (H1038)	1184026020	3
Unisan	L-Carnitin (H1038)	1184965901	1
Unisan	L-Carnitin (H1038)	130326002	1

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Supplier	Substance	Batch	Spectra
Unisan	L-Carnitin (H1038)	130605300	4
UNISAN	L-Carnitin (H1038)	130605300	3
Unisan	L-Carnitin (H1038)	130605300/3	1
Unisan	L-Carnitin (H1038)	130605301	1
Unisan	L-Carnitin (H1038)	130605302	2
UNISAN	L-Carnitin (H1038)	130605302	1
Unisan	L-Carnitin (H1038)	15000052	1
Unisan	L-Carnitin (H1038)	15000053	1
Unisan	L-Carnitin (H1038)	15000053/0	2
Unisan	L-Carnitin (H1038)	15000053/3	1
Unisan	L-Carnitin (H1038)	15000054	1
Unisan	L-Carnitin (H1038)	15000054/0	1
Unisan	L-Carnitin (H1038)	150000540	1
Unisan	L-Carnitin (H1038)	16000450	1
Unisan	L-Carnitin (H1038)	16000451	2
Unisan	L-Carnitin (H1038)	18000539/0	1
unisan	L-Carnitin (H1038)	26010	1
Unisan	L-Carnitin (H1038)	26010	2
Unisan	L-Carnitin (H1038)	965901	1
Unsan	L-Carnitin (H1038)	16000450	1

- 2869 spectra from 26 *Apo-Ident* customers from a total of 1416 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-Carnitin (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 *L-Carnitin (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	460	0	27 816
Type B	0	440	0	22 239
Type C	0	97	4	2869

The substance/substance group *L-Carnitin (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 % (> 99.9309 %)	100.0000 % (> 98.6957 %)
Type B	100.0000 % (> 99.8664 %)	100.0000 % (> 98.6364 %)
Type C	100.0000 % (> 98.8245 %)	96.0396 % (> 93.0693 %)

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

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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	23,74
80371	80371	0,00	39,20
80483	80483	0,00	33,06
80557	80557	0,00	33,48
80559	80559	0,00	34,60
80787	80787	0,00	35,29
81045	81045	0,00	33,25
81350	81350	0,00	34,93
81472	81472	0,00	32,36
81487	81487	0,00	24,01

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 2.8-2024-04

Validated substance/substance group **L-Carnosin (H1041)**
Substance class HCK
Report date 25/11/2024
Report number 80153-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Carnosin (H1041)

Special notes

When selecting the *L-Carnosin (H1041)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Carnosin (H1041)	2	1	9

Second-stage model

For differentiation of the substance/substance group *L-Carnosin (H1041)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Carnosin (H1041)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Glycin (H1021)	45,40	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-Carnosin (H1041)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Carnosin (H1041)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Carnosin (H1041)	074801	80393	40	from supplier
Hepart	L-Carnosin (H1041)	045901	80452	40	from supplier
Hepart	L-Carnosin (H1041)	074801	80655	60	from supplier

Validation samples

A total of 53 925 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 *L-Carnosin (H1041)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 28 136 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples

are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 L-Carnosin (H1041).
- 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	L-Carnosin (H1041)	18001109	81071	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 7 *Apo-Ident* customers from 9 batches from the substance/substance group L-Carnosin (H1041).
- 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
HCK	L-Carnosin (H1041)	1813979202	1
HCK	L-Carnosin (H1041)	74801/4	1
HCK	L-Carnosin (H1041)	74801-4	1
Hepart AG, CH-8280 K...	L-Carnosin (H1041)	1812045901	1
Hepart AG	L-Carnosin (H1041)	1812045901	1
Hepart AG	L-Carnosin (H1041)	1812979202	1
Hepart AG	L-Carnosin (H1041)	45901	1
Hepart	L-Carnosin (H1041)	18001109/0	1
Hepart	L-Carnosin (H1041)	74801-8	1
Purren Apotheke	L-Carnosin (H1041)	1813979202	1
Unisan/Hepart AG	L-Carnosin (H1041)	45901	1
UNISAN	L-Carnosin (H1041)	74801	1

- 2958 spectra from 26 *Apo-Ident* customers from a total of 1451 batches from a further 62 sub-

stances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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-*Carnosin* (*H1041*) can clearly be 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-*Carnosin* (*H1041*) and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 136
Type B	0	40	0	22 639
Type C	0	12	0	2958

The substance/substance group L-*Carnosin* (*H1041*) can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9314 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8521 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80393	80393	0,00	86,49
80452	80452	0,00	80,95
80655	80655	0,00	84,30

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 2.8-2024-04

Validated substance/substance group **Leaky Gut Komplex (H1802)**
Substance class HCK
Report date 25/11/2024
Report number 81039-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Leaky Gut Komplex (H1802)

Special notes

When selecting the *Leaky Gut Komplex (H1802)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Leaky Gut Komplex (H1802)	3	1	0

Second-stage model

For differentiation of the substance/substance group *Leaky Gut Komplex (H1802)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Leaky Gut Komplex (H1802)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Ginseng (H1018)	10,85	—
Coenzym Q10 (H1013)	16,51	—
Aroma Orange (H1405)	17,06	—
Haferkleie beta-Glucan (H1529)	17,91	—
Glutathion (H1020)	19,40	—
Vitamin E NAT (H1107)	23,47	—
Aminomix NAC (H1002)	25,81	—
PET Coenzym Q10 (H1505)	27,27	—
Antioxidantien NAT Komplex (H1004)	28,81	—
Ingwer Extrakt (H1437)	30,65	—
PET Gelenke (H1501)	31,51	—
L-Glutamin (H1043)	35,91	—
Óleo de zimbro (H1112)	38,63	—
Calcium L-(+) -Lactat Komplex (H1008)	38,94	—
Vitamin B1 (H1101)	39,23	—
Baobab (H1410)	40,05	—
Detox Komplex (H1111)	40,45	—
Lutein-Zeaxanthin-Astaxanthin (H1129)	41,03	—
Orthovimin Neutral Komplex (H1403)	42,15	—
Silicium (H1070)	43,51	—
Bor (H1005)	44,38	—
Garcinia Cambogia (H1017)	44,46	—
Isoflavone Extrakt (H1025)	47,19	—
Safran Griffel (H1434)	47,35	—
Artemisia annua Extrakt (H1118)	47,67	—
Vitamin K2 (75µg Mono) (H1108)	49,00	—
Lycopene (H1058)	49,10	—
Orthocolon Komplex (H1800)	49,11	—
L-Arginin (H1036)	49,96	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Leaky Gut Komplex (H1802)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 Komplex (H1802)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Leaky Gut Komplex (H1802)	18000638	81039	40	from supplier
Hepart	Leaky Gut Komplex (H1802)	20001259/0	81270	40	from supplier
Hepart	Leaky Gut Komplex (H1802)	22000099	81417	40	from supplier

Validation samples

A total of 53 925 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 *Leaky Gut Komplex (H1802)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 156 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 Komplex (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 Komplex (H1802)	18000639	81040	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B*

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

Type C Spectra of independent samples not included in the database structure. *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 Komplex (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 Komplex (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 Komplex (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	120	0	28 156
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Leaky Gut Komplex (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 % (> 99.9315 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81039	81039	0,00	28,81
81270	81270	0,00	18,48
81417	81417	0,00	18,41

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 2.8-2024-04

Validated substance/substance group **Leber Niere Komplex (H1801)**
Substance class HCK
Report date 25/11/2024
Report number 81036-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Leber Niere Komplex (H1801)

Special notes

When selecting the *Leber Niere Komplex (H1801)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Leber Niere Komplex (H1801)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Leber Niere Komplex (H1801)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Leber Niere Komplex (H1801)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	30,74	—
Taurin (H1084)	74,20	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Leber Niere Komplex (H1801)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Leber Niere Komplex (H1801)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Leber Niere Komplex (H1801)	18000635	81036	40	from supplier

Validation samples

A total of 53 925 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 *Leber Niere Komplex (H1801)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with

the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Leber Niere Komplex (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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Leber Niere Komplex (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Leber Niere Komplex (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 *Leber Niere Komplex (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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Leber Niere Komplex (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 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81036	81036	0,00	30,74

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 2.8-2024-04

Validated substance/substance group **L-Glutamin (H1043)**
Substance class HCK
Report date 25/11/2024
Report number 80089-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Glutamin (H1043)

Special notes

When selecting the *L-Glutamin (H1043)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Glutamin (H1043)	7	8	25

Second-stage model

For differentiation of the substance/substance group *L-Glutamin (H1043)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Glutamin (H1043)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Leaky Gut Komplex (H1802)	36,21	—
PET Haut und Haare (H1504)	38,45	—
Aminomix NAC (H1002)	40,64	—
Antibiose forte Komplex (H1115)	41,54	—
Coenzym Q10 (H1013)	41,87	—
PET Gelenke (H1501)	43,30	—
Vitamin E NAT (H1107)	43,78	—
Kürbiskernprotein (H1509)	51,68	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-Glutamin (H1043)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Glutamin (H1043)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Glutamin (H1043)	061501	80336	40	from supplier
Hepart	L-Glutamin (H1043)	15000017	80551	60	from supplier
Hepart	L-Glutamin (H1043)	15000018	80552	60	from supplier
Hepart	L-Glutamin (H1043)	16000940	80802	40	from supplier
Hepart	L-Glutamin (H1043)	20001001	81263	40	from supplier
Hepart	L-Glutamin (H1043)	20001021	81264	40	from supplier
Hepart	L-Glutamin (H1043)	22000156-157-158	81410	40	from supplier

Validation samples

A total of 53 925 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 *L-Glutamin (H1043)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 27 956 spectra from a total of 565 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 330 spectra of 8 reference samples from the substance/substance group *L-Glutamin (H1043)*.
- 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	L-Glutamin (H1043)	16000941	80803	40
Hepart	L-Glutamin (H1043)	16000942	80804	40
Hepart	L-Glutamin (H1043)	17000902	80930	40
Hepart	L-Glutamin (H1043)	17000901	80931	40
Hepart	L-Glutamin (H1043)	19000531	81190	40
Hepart	L-Glutamin (H1043)	19000650/0	81191	40
Hepart	L-Glutamin (H1043)	21000248	81351	40
Hepart	L-Glutamin (H1043)	21001702	81363	50

- 22 349 spectra from a total of 488 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 61 spectra from 16 *Apo-Ident* customers from 30 batches from the substance/substance group *L-Glutamin (H1043)*.
- Among them are spectra of independent samples from 25 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-Glutamin (H1043)	15000017/1	1
HCK	L-Glutamin (H1043)	16000941	2
Hepart / Unisan	L-Glutamin (H1043)	16000942	1
Hepart ag/Unisan	L-Glutamin (H1043)	20001001	1
Hepart AG	L-Glutamin (H1043)	15000017/1	1
Hepart AG	L-Glutamin (H1043)	160009420	1
Hepart AG	L-Glutamin (H1043)	17000901/0	2
Hepart, 27.03.19	L-Glutamin (H1043)	17000901/0	1
Hepart	L-Glutamin (H1043)	15000018-2	1
Hepart	L-Glutamin (H1043)	16000940/1	1
Hepart	L-Glutamin (H1043)	16000942/0	3
Hepart	L-Glutamin (H1043)	16000942-0	2
Hepart	L-Glutamin (H1043)	16001349/0	1
Hepart	L-Glutamin (H1043)	17000901	1
Hepart	L-Glutamin (H1043)	17000901/1	1
Hepart	L-Glutamin (H1043)	19000531	1
Hepart	L-Glutamin (H1043)	19000531/0	2
Hepart	L-Glutamin (H1043)	20001001	1
Hepart	L-Glutamin (H1043)	20001001/0	1
Hepart	L-Glutamin (H1043)	200010011	1
Unisan Gmbh, 78465 K...	L-Glutamin (H1043)	26904	1
Unisan/Hepart AG	L-Glutamin (H1043)	26901	1
Unisan	L-Glutamin (H1043)		1
Unisan	L-Glutamin (H1043)	15000017	1
Unisan	L-Glutamin (H1043)	15000017/0	1
UNISAN	L-Glutamin (H1043)	15000017/0	1
Unisan	L-Glutamin (H1043)	15000018	1
Unisan	L-Glutamin (H1043)	15000018/0	1
Unisan	L-Glutamin (H1043)	16000940	1
Unisan	L-Glutamin (H1043)	16000940/0	3
Unisan	L-Glutamin (H1043)	16000941	1
Unisan	L-Glutamin (H1043)	16000942	3
Unisan	L-Glutamin (H1043)	1814026901	5
Unisan	L-Glutamin (H1043)	26903	2
Unisan	L-Glutamin (H1043)	26904	1
Unisan	L-Glutamin (H1043)	61501	8
UNISAN	L-Glutamin (H1043)	61501	2
Unisan	L-Glutamin (H1043)	61501/4	1

- 2909 spectra from 26 *Apo-Ident* customers from a total of 1432 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-Glutamin (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 *L-Glutamin (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	320	0	27 956
Type B	0	330	0	22 349
Type C	0	57	4	2909

The substance/substance group *L-Glutamin (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 % (> 99.9310 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.8666 %)	100.0000 % (> 98.1818 %)
Type C	100.0000 % (> 98.8270 %)	93.4426 % (> 88.5246 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80336	80336	0,00	36,21
80551	80551	0,00	40,26
80552	80552	0,00	38,45
80802	80802	0,00	44,70
81263	81263	0,00	46,25
81264	81264	0,00	44,13
81410	81410	0,00	45,29

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 2.8-2024-04

Validated substance/substance group **L-Isoleucin (H1045)**
Substance class HCK
Report date 25/11/2024
Report number 80134-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Isoleucin (H1045)

Special notes

When selecting the *L-Isoleucin (H1045)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Isoleucin (H1045)	5	2	12

Second-stage model

For differentiation of the substance/substance group *L-Isoleucin (H1045)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Isoleucin (H1045)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
L-Leucin (H1046)	18,89	—
L-Valin (H1056)	21,43	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-Isoleucin (H1045)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Isoleucin (H1045)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Isoleucin (H1045)	066301	80368	40	from supplier
Hepart	L-Isoleucin (H1045)	14001772	80498	60	from supplier
Hepart	L-Isoleucin (H1045)	15001641	80678	60	from supplier
Hepart	L-Isoleucin (H1045)	15001640	80679	60	from supplier
Hepart	L-Isoleucin (H1045)	23000368	81485	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 5 reference samples from the substance/substance group *L-Isoleucin (H1045)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 28 016 spectra from a total of 567 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the

substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *L-Isoleucin (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	L-Isoleucin (H1045)	17000900	80909	40
Hepart	L-Isoleucin (H1045)	18001412	81111	40

- 22599 spectra from a total of 494 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 24 spectra from 9 *Apo-Ident* customers from 14 batches from the substance/substance group *L-Isoleucin (H1045)*.
- 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
Fritz Schiele	L-Isoleucin (H1045)	1805027701	1
HCK	L-Isoleucin (H1045)	14001772/3	1
HCK	L-Isoleucin (H1045)	15001641	2
Hepart AG, CH-8280 K...	L-Isoleucin (H1045)	1804968701	1
Hepart AG, CH-8280 K...	L-Isoleucin (H1045)	66301	1
Hepart AG	L-Isoleucin (H1045)	15001640/2	1
Hepart AG	L-Isoleucin (H1045)	15001641	1
Hepart AG	L-Isoleucin (H1045)	1805027701	2
Hepart AG	L-Isoleucin (H1045)	66301	1
Hepart	L-Isoleucin (H1045)	150001640-2	1
Hepart	L-Isoleucin (H1045)	15001640-2	2
Hepart	L-Isoleucin (H1045)	15001641-0	2

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Supplier	Substance	Batch	Spectra
Hepart	L-Isoleucin (H1045)	17000900	1
Hepart	L-Isoleucin (H1045)	17000900/0	2
Unisan	L-Isoleucin (H1045)	15001640	1
Unisan	L-Isoleucin (H1045)	1805968701	1
Unisan	L-Isoleucin (H1045)	27701	1
Unisan	L-Isoleucin (H1045)	66301	2

- 2946 spectra from 26 *Apo-Ident* customers from a total of 1446 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-Isoleucin (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 *L-Isoleucin (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	260	0	28 016
Type B	0	80	0	22 599
Type C	0	18	6	2946

The substance/substance group *L-Isoleucin (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 % (> 99.9311 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.8684 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8364 %)	75.0000 % (> 62.5000 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80368	80368	0,00	32,37
80498	80498	0,00	32,50
80678	80678	0,00	32,74
80679	80679	0,00	28,92
81485	81485	0,00	43,61

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 2.8-2024-04

Validated substance/substance group **L-Leucin (H1046)**
Substance class HCK
Report date 25/11/2024
Report number 80150-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Leucin (H1046)

Special notes

When selecting the *L-Leucin (H1046)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Leucin (H1046)	4	3	9

Second-stage model

For differentiation of the substance/substance group L-*Leucin* (H1046) the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group L-*Leucin* (H1046) in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
L-Isoleucin (H1045)	38,25	–
L-Valin (H1056)	45,73	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group L-*Leucin* (H1046) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-*Leucin* (H1046):

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Leucin (H1046)	965101	80333	60	from supplier
Hepart	L-Leucin (H1046)	074301	80410	40	from supplier
Hepart	L-Leucin (H1046)	21001145	81362	50	from supplier
Hepart	L-Leucin (H1046)	22001194	81428	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 190 spectra of 4 reference samples from the substance/substance group L-*Leucin* (H1046). These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 28 086 spectra from a total of 568 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the

substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 L-Leucin (H1046).
- 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	L-Leucin (H1046)	15000283	80570	60
Hepart	L-Leucin (H1046)	18001305	81074	40
Hepart	L-Leucin (H1046)	20001576	81286	40

- 22 539 spectra from a total of 493 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 10 batches from the substance/substance group L-Leucin (H1046).
- 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
HCK	L-Leucin (H1046)	74301/3	1
HCK	L-Leucin (H1046)	965101	1
Hepart AG	L-Leucin (H1046)	15000283/1	1
Hepart AG	L-Leucin (H1046)	18001305/0	2
Hepart AG	L-Leucin (H1046)	1809994101	1
Hepart	L-Leucin (H1046)	15000283	1
Hepart	L-Leucin (H1046)	18001305	1
Purren Apotheke	L-Leucin (H1046)	1809965101	1
Unisan GmbH, 78465 K...	L-Leucin (H1046)	52601	2
Unisan/Hepart AG	L-Leucin (H1046)	52601	1
Unisan	L-Leucin (H1046)	15000283	1

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Supplier	Substance	Batch	Spectra
Unisan	L-Leucin (H1046)	15000283/0	1
Unisan	L-Leucin (H1046)	15000283/1	1
Unisan	L-Leucin (H1046)	1809965101	1
Unisan	L-Leucin (H1046)	52601	1

- 2953 spectra from 26 *Apo-Ident* customers from a total of 1450 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-Leucin (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 *L-Leucin (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	190	0	28 086
Type B	0	140	0	22 539
Type C	0	14	3	2953

The substance/substance group *L-Leucin (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 % (> 99.9312 %)	100.0000 % (> 96.8421 %)
Type B	100.0000 % (> 99.8674 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 98.8429 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80333	80333	0,00	44,05
80410	80410	0,00	50,90
81362	81362	0,00	49,88
81428	81428	0,00	57,37

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 2.8-2024-04

Validated substance/substance group **L-Lysin (H1047)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80151-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Lysin (H1047)

Special notes

When selecting the *L-Lysin (H1047)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Lysin (H1047)	8	4	24

Second-stage model

For differentiation of the substance/substance group *L-Lysin (H1047)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Lysin (H1047)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	47,42	—
L-Carnosin (H1041)	47,77	—
Glycin (H1021)	52,37	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-Lysin (H1047)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Lysin (H1047)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Lysin (H1047)	065401	80343	40	from supplier
Hepart	L-Lysin (H1047)	028801	80360	40	from supplier
Hepart	L-Lysin (H1047)	065401	80453	40	from supplier
Hepart	L-Lysin (H1047)	028801	80458	40	from supplier
Hepart	L-Lysin (H1047)	14000944	80468	40	from supplier
Hepart	L-Lysin (H1047)	15000372	80562	60	from supplier
Hepart	L-Lysin (H1047)	16001395/0	80847	40	from supplier
Hepart	L-Lysin (H1047)	18001389	81131	40	from supplier
Hepart	L-Lysin (H1047)	21001735	81376	50	not required
Hepart	L-Lysin (H1047)	22000055	81413	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 430 spectra of 10 reference samples from the substance/substance group L-Lysin (H1047). These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 27 846 spectra from a total of 564 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 160 spectra of 4 reference samples from the substance/substance group L-Lysin (H1047).
- Among them are spectra of independent samples from 4 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	L-Lysin (H1047)	16001503/0	80848	40
Hepart	L-Lysin (H1047)	19001154	81208	40
Hepart	L-Lysin (H1047)	20000950	81268	40
Hepart	L-Lysin (H1047)	23000775	81491	40

- 22 519 spectra from a total of 492 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 47 spectra from 14 *Apo-Ident* customers from 28 batches from the substance/substance group L-Lysin (H1047).
- Among them are spectra of independent samples from 24 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Flaigg Ag CH-4147 Ae...	L-Lysin (H1047)	18001389	1
Flaigg Ag CH-4147 Ae...	L-Lysin (H1047)	18001389/2	1
HCK	L-Lysin (H1047)	14000944/1	1
HCK	L-Lysin (H1047)	15000372	1

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Supplier	Substance	Batch	Spectra
HCK	L-Lysin (H1047)	15000372/0	2
Hepart AG, CH-8280 K...	L-Lysin (H1047)	1800955002	1
Hepart ag/Unisan	L-Lysin (H1047)	19001154	2
Hepart AG	L-Lysin (H1047)	15000372/2	1
Hepart AG	L-Lysin (H1047)	16001395/1	3
Hepart AG	L-Lysin (H1047)	16001503/0	2
Hepart AG	L-Lysin (H1047)	16001503/1	1
Hepart AG	L-Lysin (H1047)	65401	1
Hepart	L-Lysin (H1047)		1
Hepart	L-Lysin (H1047)	15000372-1	2
Hepart	L-Lysin (H1047)	16001395	4
Hepart	L-Lysin (H1047)	16001395/1	1
Hepart	L-Lysin (H1047)	16001503	2
Hepart	L-Lysin (H1047)	16001503/0	2
Hepart	L-Lysin (H1047)	18001389/0	1
Hepart	L-Lysin (H1047)	19001154	1
Hepart	L-Lysin (H1047)	19001154/0	4
Hepart	L-Lysin (H1047)	19001154/1	1
Hepart	L-Lysin (H1047)	1900154/1	1
Hepart	L-Lysin (H1047)	20000950	1
Hepart	L-Lysin (H1047)	20000950/0	1
Hepart	L-Lysin (H1047)	20000950/2	1
Hepart	L-Lysin (H1047)	21001735/0	1
Unisan/Hepart AG	L-Lysin (H1047)	65401	1
Unisan	L-Lysin (H1047)	14000944	1
Unisan	L-Lysin (H1047)	15000372/0	1
Unisan	L-Lysin (H1047)	1800017302	1
Unisan	L-Lysin (H1047)	1801028801	1
Unisan	L-Lysin (H1047)	65401/4	1

- 2923 spectra from 26 *Apo-Ident* customers from a total of 1432 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-Lysin (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 *L-Lysin (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	430	0	27 846
Type B	0	160	0	22 519
Type C	0	45	2	2923

The substance/substance group *L-Lysin (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 % (> 99.9309 %)	100.0000 % (> 98.6047 %)
Type B	100.0000 % (> 99.8672 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 98.8288 %)	95.7447 % (> 89.3617 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80343	80343	0,00	49,32
80360	80360	0,00	60,01
80453	80453	0,00	51,22
80458	80458	0,00	50,17
80468	80468	0,00	61,28
80562	80562	0,00	58,69
80847	80847	0,00	70,19
81131	81131	0,00	65,33
81376	81376	0,00	47,42
81413	81413	0,00	68,91

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 2.8-2024-04

Validated substance/substance group **L-Ornithin (H1048)**
Substance class HCK
Report date 25/11/2024
Report number 80175-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Ornithin (H1048)

Special notes

When selecting the L-Ornithin (H1048) substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Ornithin (H1048)	6	2	12

Second-stage model

For differentiation of the substance/substance group L-*Ornithin* (H1048) the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group L-*Ornithin* (H1048) in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
L-Lysin (H1047)	25,98	—
L-Tyrosin (H1054)	47,03	—
Antibiose forte Komplex (H1115)	63,88	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group L-*Ornithin* (H1048) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-*Ornithin* (H1048):

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Ornithin (H1048)	15000004	80629	60	from supplier
Hepart	L-Ornithin (H1048)	15001364	80667	60	from supplier
Hepart	L-Ornithin (H1048)	15001364(F1)	80669	60	from supplier
Hepart	L-Ornithin (H1048)	16000935	80811	40	from supplier
Hepart	L-Ornithin (H1048)	20002205	81321	40	from supplier
Hepart	L-Ornithin (H1048)	21001080	81366	50	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 310 spectra of 6 reference samples from the substance/substance group L-*Ornithin* (H1048). These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.

- 27966 spectra from a total of 566 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 L-Ornithin (H1048).
- 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	L-Ornithin (H1048)	15001364 (F2)	80668	60
Hepart	L-Ornithin (H1048)	23001728	81505	40

- 22579 spectra from a total of 494 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 13 batches from the substance/substance group L-Ornithin (H1048).
- 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
HCK	L-Ornithin (H1048)	15000004-3	1
Hepart / Unisan	L-Ornithin (H1048)	15000004	2
Hepart AG	L-Ornithin (H1048)	16000935/1	1
Hepart	L-Ornithin (H1048)	16000935/0	2
Hepart	L-Ornithin (H1048)	16000935/1	1
Hepart	L-Ornithin (H1048)	16000935/2	1
Hepart	L-Ornithin (H1048)	16000935/3	2
Hepart	L-Ornithin (H1048)	16000935/4	1
Hepart	L-Ornithin (H1048)	16000935-0	2
Hepart	L-Ornithin (H1048)	16000935-2	2

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Supplier	Substance	Batch	Spectra
Purren Apotheke	L-Ornithin (H1048)	1817979301	1
Unisan	L-Ornithin (H1048)	16000935/0	1
Unisan	L-Ornithin (H1048)	1816979301	1
Unisan	L-Ornithin (H1048)	27001	2
Unisan	L-Ornithin (H1048)	979301	2

- 2948 spectra from 26 *Apo-Ident* customers from a total of 1447 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-Ornithin (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 *L-Ornithin (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	310	0	27 966
Type B	0	100	0	22 579
Type C	0	16	6	2948

The substance/substance group *L-Ornithin (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 % (> 98.0645 %)
Type B	100.0000 % (> 99.8679 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.8379 %)	72.7273 % (> 59.0909 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80629	80629	0,00	77,81
80667	80667	0,00	75,35
80669	80669	0,00	79,84
80811	80811	0,00	66,61
81321	81321	0,00	72,48
81366	81366	0,00	63,88

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 2.8-2024-04

Validated substance/substance group **L-Phenylalanin (H1049)**
Substance class HCK
Report date 25/11/2024
Report number 80090-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Phenylalanin (H1049)

Special notes

When selecting the *L-Phenylalanin (H1049)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Phenylalanin (H1049)	4	1	10

Second-stage model

For differentiation of the substance/substance group *L-Phenylalanin (H1049)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Phenylalanin (H1049)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
L-Tryptophan (H1053)	25,52	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-Phenylalanin (H1049)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Phenylalanin (H1049)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Phenylalanin (H1049)	074401	80400	40	from supplier
Hepart	L-Phenylalanin (H1049)	16001096	80852	40	from supplier
Hepart	L-Phenylalanin (H1049)	19000779	81167	40	from supplier
Hepart	L-Phenylalanin (H1049)	21001354	81359	50	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 170 spectra of 4 reference samples from the substance/substance group *L-Phenylalanin (H1049)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 28 106 spectra from a total of 568 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A*

section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *L-Phenylalanin (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	L-Phenylalanin (H1049)	17000876	80916	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 27 spectra from 9 *Apo-Ident* customers from 12 batches from the substance/substance group *L-Phenylalanin (H1049)*.
- Among them are spectra of independent samples from 10 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-Phenylalanin (H1049)	74401/1	2
HCK	L-Phenylalanin (H1049)	74401/2	1
Hepart AG	L-Phenylalanin (H1049)	17000876/0	1
Hepart AG	L-Phenylalanin (H1049)	17000876/1	1
Hepart AG	L-Phenylalanin (H1049)	74401/1	1
Hepart	L-Phenylalanin (H1049)	16001096	1
Hepart	L-Phenylalanin (H1049)	16001096-1	1
Hepart	L-Phenylalanin (H1049)	17000876	1
Hepart	L-Phenylalanin (H1049)	17000876/1	3
Hepart	L-Phenylalanin (H1049)	170008760	3
Hepart	L-Phenylalanin (H1049)	19000779	1
Unisan/Hepart AG	L-Phenylalanin (H1049)	1828025009	1
Unisan	L-Phenylalanin (H1049)	16001096	2
Unisan	L-Phenylalanin (H1049)	25009	7
Unisan	L-Phenylalanin (H1049)	74401/0	1

- 2943 spectra from 26 *Apo-Ident* customers from a total of 1448 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-Phenylalanin (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 *L-Phenylalanin (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	170	0	28 106
Type B	0	40	0	22 639
Type C	0	18	9	2943

The substance/substance group *L-Phenylalanin (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 % (> 96.4706 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8347 %)	66.6667 % (> 55.5556 %)

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

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

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

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	41,41
80852	80852	0,00	41,04
81167	81167	0,00	41,00
81359	81359	0,00	47,95

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 2.8-2024-04

Validated substance/substance group **L-Threonin (H1052)**
Substance class HCK
Report date 25/11/2024
Report number 80107-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Threonin (H1052)

Special notes

When selecting the *L-Threonin (H1052)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Threonin (H1052)	1	2	15

Second-stage model

For differentiation of the substance/substance group *L-Threonin (H1052)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Threonin (H1052)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Glycin (H1021)	48,69	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-Threonin (H1052)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Threonin (H1052)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Threonin (H1052)	14001718	80496	60	from supplier
Hepart	L-Threonin (H1052)	14001718	81018	40	from supplier

Validation samples

A total of 53 925 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 *L-Threonin (H1052)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 176 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with

the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *L-Threonin (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	L-Threonin (H1052)	17000875	80920	40
Hepart	L-Threonin (H1052)	18001023	81077	40

- 22 599 spectra from a total of 494 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 25 spectra from 11 *Apo-Ident* customers from 16 batches from the substance/substance group *L-Threonin (H1052)*.
- 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
HCK	L-Threonin (H1052)	14001718/2	1
HCK	L-Threonin (H1052)	14001718/9	1
HCK	L-Threonin (H1052)	14001718-4	2
HCK	L-Threonin (H1052)	14001718-5	2
Hedinger	L-Threonin (H1052)	25708	3
Hepart AG	L-Threonin (H1052)	1700875/5	1
Hepart/Unisan	L-Threonin (H1052)	14001718/3	1
Hepart/Unisan	L-Threonin (H1052)	14001718/9	1
Hepart	L-Threonin (H1052)	14001718-6	1
Hepart	L-Threonin (H1052)	14001718-7	1
Hepart	L-Threonin (H1052)	14001718-9	1
Hepart	L-Threonin (H1052)	17000875	1
Hepart	L-Threonin (H1052)	17000875/1	1
Purren Apotheke	L-Threonin (H1052)	1833014901	1
Unisan	L-Threonin (H1052)	14001718	2

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Supplier	Substance	Batch	Spectra
Unisan	L-Threonin (H1052)	14001718/1	1
Unisan	L-Threonin (H1052)	14001718/7	1
unisan	L-Threonin (H1052)	25708	1
Unisan	L-Threonin (H1052)	25708	1
UNISAN	L-Threonin (H1052)	25708	1

- 2945 spectra from 26 *Apo-Ident* customers from a total of 1444 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-Threonin (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 *L-Threonin (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	28 176
Type B	0	80	0	22 599
Type C	0	19	6	2945

The substance/substance group *L-Threonin (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 % (> 99.9316 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8684 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8358 %)	76.0000 % (> 64.0000 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80496	80496	0,00	55,76
81018	81018	0,00	59,12

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 2.8-2024-04

Validated substance/substance group **L-Tryptophan (H1053)**
Substance class HCK
Report date 25/11/2024
Report number 80127-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Tryptophan (H1053)

Special notes

When selecting the *L-Tryptophan (H1053)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Tryptophan (H1053)	6	2	30

Second-stage model

For differentiation of the substance/substance group *L-Tryptophan (H1053)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Tryptophan (H1053)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
L-Phenylalanin (H1049)	31,19	—
Antibiose forte Komplex (H1115)	63,26	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-Tryptophan (H1053)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Tryptophan (H1053)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Tryptophan (H1053)	074501	80401	40	from supplier
Hepart	L-Tryptophan (H1053)	15000441	80581	60	from supplier
Hepart	L-Tryptophan (H1053)	16001394	80845	40	from supplier
Hepart	L-Tryptophan (H1053)	16001404	80846	40	from supplier
Hepart	L-Tryptophan (H1053)	20001589	81284	40	from supplier
Hepart	L-Tryptophan (H1053)	21001643	81379	50	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 270 spectra of 6 reference samples from the substance/substance group *L-Tryptophan (H1053)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.

- 28 006 spectra from a total of 566 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *L-Tryptophan (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	L-Tryptophan (H1053)	15000443	80582	60
Hepart	L-Tryptophan (H1053)	19001101	81219	40

- 22 579 spectra from a total of 494 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 64 spectra from 16 *Apo-Ident* customers from 33 batches from the substance/substance group *L-Tryptophan (H1053)*.
- Among them are spectra of independent samples from 30 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	L-Tryptophan (H1053)	15000441/4	1
Caelo	L-Tryptophan (H1053)	15000443/0	1
Fagron	L-Tryptophan (H1053)	1824027901	2
HCK	L-Tryptophan (H1053)	15000441	2
HCK	L-Tryptophan (H1053)	15000441/2	1
HCK	L-Tryptophan (H1053)	15000441-2	1
HCK	L-Tryptophan (H1053)	15000443	2
HCK	L-Tryptophan (H1053)	15000443-0	2
HCK	L-Tryptophan (H1053)	15000443-1	2
HCK	L-Tryptophan (H1053)	16001404	1

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Supplier	Substance	Batch	Spectra
Hepart AG, CH-8280 K...	L-Tryptophan (H1053)	27901	1
Hepart ag/Unisan	L-Tryptophan (H1053)	19001101/0	1
Hepart AG	L-Tryptophan (H1053)	160001404/3	1
Hepart AG	L-Tryptophan (H1053)	16001394/2	1
Hepart AG	L-Tryptophan (H1053)	16001404/3	3
Hepart AG	L-Tryptophan (H1053)	27901	4
Hepart AG	L-Tryptophan (H1053)	27902	1
Hepart	L-Tryptophan (H1053)	15000443-2	3
Hepart	L-Tryptophan (H1053)	15000443-3	1
Hepart	L-Tryptophan (H1053)	15000443-4	1
Hepart	L-Tryptophan (H1053)	16001394/0	3
Hepart	L-Tryptophan (H1053)	16001394/2	1
Hepart	L-Tryptophan (H1053)	16001404-0	5
Hepart	L-Tryptophan (H1053)	16001404-1	1
Hepart	L-Tryptophan (H1053)	19001101	1
Hepart	L-Tryptophan (H1053)	19001101/0	1
Hepart	L-Tryptophan (H1053)	20001589/0	1
Hepart	L-Tryptophan (H1053)	9001101/01	1
Purren Apotheke	L-Tryptophan (H1053)	1825950001	1
Purren Apotheke	L-Tryptophan (H1053)	978501	1
Unisan/Hepart AG	L-Tryptophan (H1053)	27901	1
unisan	L-Tryptophan (H1053)		1
Unisan	L-Tryptophan (H1053)	150000441	1
Unisan	L-Tryptophan (H1053)	15000441/4	1
Unisan	L-Tryptophan (H1053)	15000443	2
Unisan	L-Tryptophan (H1053)	15000443/0	1
Unisan	L-Tryptophan (H1053)	1824950001	2
Unisan	L-Tryptophan (H1053)	27901	1
Unisan	L-Tryptophan (H1053)	27902	2
Unisan	L-Tryptophan (H1053)	74501	2
Unisan	L-Tryptophan (H1053)	74501/4	1
Unisan	L-Tryptophan (H1053)	950001	1

- 2906 spectra from 26 *Apo-Ident* customers from a total of 1428 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-Tryptophan (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 *L-Tryptophan (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	270	0	28 006
Type B	0	100	0	22 579
Type C	0	47	17	2906

The substance/substance group *L-Tryptophan (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 % (> 97.7778 %)
Type B	100.0000 % (> 99.8679 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.8267 %)	73.4375 % (> 68.7500 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80401	80401	0,00	33,46
80581	80581	0,00	45,36
80845	80845	0,00	63,26
80846	80846	0,00	57,90
81284	81284	0,00	50,11
81379	81379	0,00	66,56

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 2.8-2024-04

Validated substance/substance group **L-Tyrosin (H1054)**
Substance class HCK
Report date 25/11/2024
Report number 80121-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Tyrosin (H1054)

Special notes

When selecting the *L-Tyrosin (H1054)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Tyrosin (H1054)	3	2	11

Second-stage model

For differentiation of the substance/substance group *L-Tyrosin (H1054)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *L-Tyrosin (H1054)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Glycin (H1021)	63,97	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-Tyrosin (H1054)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Tyrosin (H1054)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Tyrosin (H1054)	074601	80386	100	from supplier
Hepart	L-Tyrosin (H1054)	15001380	80704	60	from supplier
Hepart	L-Tyrosin (H1054)	18000412	81050	40	from supplier

Validation samples

A total of 53 925 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 *L-Tyrosin (H1054)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 076 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples

are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *L-Tyrosin (H1054)*.
- 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	L-Tyrosin (H1054)	20000220	81267	40
Hepart	L-Tyrosin (H1054)	23001739	81506	40

- 22 599 spectra from a total of 494 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 25 spectra from 9 *Apo-Ident* customers from 11 batches from the substance/substance group *L-Tyrosin (H1054)*.
- 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	L-Tyrosin (H1054)	1380	1
Hepart AG	L-Tyrosin (H1054)	15001380/0	2
Hepart AG	L-Tyrosin (H1054)	29502	1
Hepart AG	L-Tyrosin (H1054)	74601	1
Hepart	L-Tyrosin (H1054)	15001380-1	5
Hepart	L-Tyrosin (H1054)	15001380-4	2
Hepart	L-Tyrosin (H1054)	18000412/0	2
Hepart	L-Tyrosin (H1054)	20000220	1
Unisan	L-Tyrosin (H1054)	29501	3
Unisan	L-Tyrosin (H1054)	29502	4
UNISAN	L-Tyrosin (H1054)	74601	1
Unisan	L-Tyrosin (H1054)	74601/3	1
Unisan	L-Tyrosin (H1054)	979102	1

- 2945 spectra from 26 *Apo-Ident* customers from a total of 1449 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-Tyrosin (*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 L-Tyrosin (*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	28 076
Type B	0	80	0	22 599
Type C	0	17	8	2945

The substance/substance group L-Tyrosin (*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 % (> 99.9312 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.8684 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8358 %)	68.0000 % (> 56.0000 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80386	80386	0,00	91,60
80704	80704	0,00	95,93
81050	81050	0,00	92,29

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 2.8-2024-04

Validated substance/substance group **Lupinenprotein BCAA Komplex (H1510)**
Substance class **HCK**
Report date 25/11/2024
Report number 10006135-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lupinenprotein BCAA Komplex (H1510)

Special notes

When selecting the *Lupinenprotein BCAA Komplex (H1510)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Lupinenprotein BCAA Komplex (H1510)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Lupinenprotein BCAA Komplex (H1510)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Lupinenprotein BCAA Komplex (H1510)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Coenzym Q10 (H1013)	21,47	—
Aminomix NAC (H1002)	22,54	—
Amino V Komplex (H1400)	22,67	—
Antibiose forte Komplex (H1115)	27,16	—
L-Glutamin (H1043)	42,39	—
Erbsenprotein BCAA Komplex (H1507)	50,06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lupinenprotein BCAA Komplex (H1510)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lupinenprotein BCAA Komplex (H1510)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Lupinenprotein BCAA Kompl...	23000731	81484	40	from supplier

Validation samples

A total of 53 925 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 *Lupinenprotein BCAA Komplex (H1510)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the

substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Lupinenprotein BCAA Komplex (H1510)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Lupinenprotein BCAA Komplex (H1510)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Lupinenprotein BCAA Komplex (H1510)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lupinenprotein BCAA Komplex (H1510)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Lupinenprotein BCAA Komplex (H1510)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81484	81484	0,00	24,03

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 2.8-2024-04

Validated substance/substance group **L-Valin (H1056)**
Substance class HCK
Report date 25/11/2024
Report number 80145-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-Valin (H1056)

Special notes

When selecting the L-Valin (H1056) substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
L-Valin (H1056)	4	1	9

Second-stage model

For differentiation of the substance/substance group L-Valin (H1056) the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group L-Valin (H1056) in the substance class HCK. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
L-Leucin (H1046)	55,57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group L-Valin (H1056) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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-Valin (H1056):

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	L-Valin (H1056)	14001947	80520	60	from supplier
Hepart	L-Valin (H1056)	16001380/0	80844	40	from supplier
Hepart	L-Valin (H1056)	21002275	81401	50	from supplier
Hepart	L-Valin (H1056)	23000774	81494	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 190 spectra of 4 reference samples from the substance/substance group L-Valin (H1056). These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 28 086 spectra from a total of 568 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples

are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 L-Valin (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	L-Valin (H1056)	15001436	80670	60

- 22619 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 11 batches from the substance/substance group L-Valin (H1056).
- 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
HCK	L-Valin (H1056)	15001436-1	1
HCK	L-Valin (H1056)	7016659	1
Hepart AG	L-Valin (H1056)		1
Hepart AG	L-Valin (H1056)	15001436	1
Hepart AG	L-Valin (H1056)	16001380/0	1
Hepart AG	L-Valin (H1056)	16001380/2	1
Hepart AG	L-Valin (H1056)	1807025012	1
Purren Apotheke	L-Valin (H1056)	1807936701	1
Unisan	L-Valin (H1056)	15001436	2
Unisan	L-Valin (H1056)	15001436/1	1
Unisan	L-Valin (H1056)	1807961101	2
Unisan	L-Valin (H1056)	25012	2

- 2955 spectra from 26 *Apo-Ident* customers from a total of 1449 batches from a further 62 sub-

stances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance 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-*Valin (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 L-*Valin (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	190	0	28 086
Type B	0	55	5	22 619
Type C	0	14	1	2955

The substance/substance group L-*Valin (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 % (> 99.9312 %)	100.0000 % (> 96.8421 %)
Type B	100.0000 % (> 99.8693 %)	91.6667 % (> 86.6667 %)
Type C	100.0000 % (> 98.8458 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80520	80520	0,00	74,11
80844	80844	0,00	64,54
81401	81401	0,00	60,14
81494	81494	0,00	64,76

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 2.8-2024-04

Validated substance/substance group **Magen Komplex (H1120)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80666-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Magen Komplex (H1120)

Special notes

When selecting the *Magen Komplex (H1120)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Magen Komplex (H1120)	2	1	0

Second-stage model

For differentiation of the substance/substance group *Magen Komplex (H1120)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Magen Komplex (H1120)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
PET Immunsystem (H1502)	25,13	—
PET Basis (H1503)	30,45	—
Antibiose forte Komplex (H1115)	36,32	—
Grüner Kaffee Extrakt (H1433)	42,69	—
L-Carnitin (H1038)	43,64	—
Coenzym Q10 (H1013)	43,85	—
Antioxidantien NAT Komplex (H1004)	44,11	—
a-Liponsäure (H1000)	45,36	—
Hanfprotein (H1406)	50,76	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Magen Komplex (H1120)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Magen Komplex (H1120)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Magen Komplex (H1120)	15001350	80666	60	from supplier
Hepart	Magen Komplex (H1120)	16001138	80888	40	from supplier

Validation samples

A total of 53 925 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 *Magen Komplex (H1120)*.

These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.

- 28 176 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Magen Komplex (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	Magen Komplex (H1120)	16001139	80889	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Magen Komplex (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Magen Komplex (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 *Magen Komplex (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	28 176
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Magen Komplex (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 % (> 99.9316 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80666	80666	0,00	25,13
80888	80888	0,00	36,32

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 2.8-2024-04

Validated substance/substance group **Magnésio (H1060) / Complexo de oligoelementos JK (H1080)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80061-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Magnésio (H1060) / Complexo de oligoelementos JK (H1080); Magnesium (H1060); Spurenelemente JK Komplex (H1080)

Special notes

When selecting the *Magnésio (H1060) / Complexo de oligoelementos JK (H1080)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Magnésio (H1060) / Complexo de oligoelementos JK (H1080)	12	39	85

Second-stage model

For differentiation of the substance/substance group *Magnésio (H1060) / Complexo de oligoelementos JK (H1080)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Magnésio (H1060) / Complexo de oligoelementos JK (H1080)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Spurenelemente BAG (H1078)	29,77	—
Garcinia Cambogia (H1017)	39,62	—
Coenzym Q10 (H1013)	54,06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Magnésio (H1060) / Complexo de oligoelementos JK (H1080)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Magnésio (H1060) / Complexo de oligoelementos JK (H1080)*:

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
Hepart	Magnesium (H1060)	21000494-495-493	81327	40	from supplier
Hepart	Spurenelemente JK Komplex...	072701	80387	40	from supplier
Hepart	Spurenelemente JK Komplex...	072901	80388	40	from supplier
Hepart	Spurenelemente JK Komplex...	072801	80389	40	from supplier
Hepart	Spurenelemente JK Komplex...	072901	80701	60	from supplier
Hepart	Spurenelemente JK Komplex...	15000526	80766	60	from supplier
Hepart	Spurenelemente JK Komplex...	18000455	81029	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 620 spectra of 13 reference samples from the substance/substance group *Magnésio (H1060) / Complexo de oligoelementos JK (H1080)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 12 different batches.
- 27 656 spectra from a total of 560 batches from further 129 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 1810 spectra of 39 reference samples from the substance/substance group *Magnésio (H1060) / Complexo de oligoelementos JK (H1080)*.
- Among them are spectra of independent samples from 39 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

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Supplier	Substance	Batch	Sample ID	Spectra
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
Hepart	Magnesium (H1060)	210020-27-28-29-30	81397	50
Hepart	Spurenelemente JK Komplex...	15000525	80673	60
Hepart	Spurenelemente JK Komplex...	17000870	80932	40
Hepart	Spurenelemente JK Komplex...	17000871	80933	40
Hepart	Spurenelemente JK Komplex...	17000869	80934	40
Hepart	Spurenelemente JK Komplex...	18000456	81030	40
Hepart	Spurenelemente JK Komplex...	18000457	81031	40
Hepart	Spurenelemente JK Komplex...	18000484	81032	40
Hepart	Spurenelemente JK Komplex...	21000245-376	81352	40

- 20 869 spectra from a total of 457 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 193 spectra from 21 *Apo-Ident* customers from 88 batches from the substance/substance group *Magnésio (H1060) / Complexo de oligoelementos JK (H1080)*.
- Among them are spectra of independent samples from 85 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	Spurenelemente JK Komplex...	15000526/0	1
HCK	Magnesium (H1060)	14001893/0	2
HCK	Spurenelemente JK Komplex...	15000526-1	1
HCK	Spurenelemente JK Komplex...	15000527-0	1
HCK	Magnesium (H1060)	16000272	1
Hepart / Unisan	Magnesium (H1060)	19001560	1
Hepart AG, CH-8280 K...	Magnesium (H1060)	1134043601	1
Hepart AG, CH-8280 K...	Magnesium (H1060)	1134973501	2
Hepart AG, CH-8280 K...	Magnesium (H1060)	43602	1
Hepart AG/Unisan	Spurenelemente JK Komplex...	18000484/0	1
Hepart AG/Unisan	Spurenelemente JK Komplex...	18000484/1	1
Hepart AG/Unisan	Magnesium (H1060)	18000951/0	1
Hepart AG/Unisan	Magnesium (H1060)	19001558/0	1
Hepart AG/Unisan	Magnesium (H1060)	19001561/0	2
Hepart AG	Spurenelemente JK Komplex...	1026011701	2
Hepart AG	Magnesium (H1060)	1134973501	5
Hepart AG	Spurenelemente JK Komplex...	11701	8
Hepart AG	Magnesium (H1060)	14001894/0	1
Hepart AG	Magnesium (H1060)	14001895/2	1
Hepart AG	Spurenelemente JK Komplex...	15000525	1
Hepart AG	Spurenelemente JK Komplex...	15000528/0	2
Hepart AG	Magnesium (H1060)	16000269	1

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Supplier	Substance	Batch	Spectra
Hepart AG	Magnesium (H1060)	16000272/0	2
Hepart AG	Magnesium (H1060)	16001703/0	1
Hepart AG	Magnesium (H1060)	16001704/0	2
Hepart AG	Magnesium (H1060)	16001705	1
Hepart AG	Magnesium (H1060)	16001705/0	2
Hepart AG	Spurenelemente JK Komplex...	17000869	1
Hepart AG	Spurenelemente JK Komplex...	17000869/0	1
Hepart AG	Spurenelemente JK Komplex...	17000870/0	3
Hepart AG	Spurenelemente JK Komplex...	18000456/0	1
Hepart AG	Magnesium (H1060)	18000950/0	1
Hepart AG	Magnesium (H1060)	18000952/0	1
Hepart AG	Magnesium (H1060)	43501	1
Hepart AG	Magnesium (H1060)	43601	2
Hepart AG	Magnesium (H1060)	43602	4
Hepart AG	Magnesium (H1060)	43701	1
Hepart AG	Magnesium (H1060)	69901	3
Hepart AG	Spurenelemente JK Komplex...	72701	1
Hepart/Unisan	Magnesium (H1060)	16000267/0	1
Hepart	Magnesium (H1060)	14001893	1
Hepart	Magnesium (H1060)	14001893/0	1
Hepart	Spurenelemente JK Komplex...	15000525	1
Hepart	Spurenelemente JK Komplex...	15000527-1	1
Hepart	Spurenelemente JK Komplex...	15000529/0	1
Hepart	Magnesium (H1060)	16000265-0	2
Hepart	Magnesium (H1060)	16000269	1
Hepart	Magnesium (H1060)	16000269/0	1
Hepart	Magnesium (H1060)	16000272	1
Hepart	Magnesium (H1060)	16000272/0	2
Hepart	Magnesium (H1060)	16001702/0	1
Hepart	Magnesium (H1060)	16001704	1
Hepart	Magnesium (H1060)	16001704/0	1
Hepart	Magnesium (H1060)	16001706/0	3
Hepart	Spurenelemente JK Komplex...	17000869	1
Hepart	Spurenelemente JK Komplex...	17000869/0	2
Hepart	Spurenelemente JK Komplex...	17000870-0	1
Hepart	Spurenelemente JK Komplex...	17000871/0	1
Hepart	Spurenelemente JK Komplex...	17000896/0	1
Hepart	Magnesium (H1060)	18000420/0	1
Hepart	Spurenelemente JK Komplex...	18000455/0	1
Hepart	Spurenelemente JK Komplex...	18000456/0	2
Hepart	Spurenelemente JK Komplex...	18000457	1
Hepart	Spurenelemente JK Komplex...	18000457/0	2
Hepart	Spurenelemente JK Komplex...	18000484/0	2
Hepart	Spurenelemente JK Komplex...	18000484/1	1
Hepart	Magnesium (H1060)	18000949/0	1
Hepart	Magnesium (H1060)	18000950/0	1
Hepart	Magnesium (H1060)	18000951/0	3
Hepart	Magnesium (H1060)	18000952/0	1
Hepart	Magnesium (H1060)	18000953	1
Hepart	Magnesium (H1060)	18000953/0	1
Hepart	Magnesium (H1060)	1900	1
Hepart	Magnesium (H1060)	19001153/0	4
Hepart	Magnesium (H1060)	19001558	1
Hepart	Magnesium (H1060)	19001558/0	2
Hepart	Magnesium (H1060)	19001559/0	2
Hepart	Magnesium (H1060)	19001561/0	2
Hepart	Spurenelemente JK Komplex...	21000245/0	2
Hepart	Spurenelemente JK Komplex...	21000376	1
Hepart	Spurenelemente JK Komplex...	21000376/0	1
Hepart	Magnesium (H1060)	21000493/0	1

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Supplier	Substance	Batch	Spectra
Hepart	Magnesium (H1060)	21000494	1
Hepart	Magnesium (H1060)	21000494/0	3
Hepart	Magnesium (H1060)	21000495	1
Hepart	Magnesium (H1060)	21002028	1
Hepart	Magnesium (H1060)	21002028/0	1
Hepart	Magnesium (H1060)	21002029/0	2
Hepart	Spurenelemente JK Komplex...	22000100/0	1
Unisan Gmbh, 78465 K...	Spurenelemente JK Komplex...	1026011701	1
Unisan Gmbh, 78465 K...	Magnesium (H1060)	43702	1
Unisan/Hepart AG	Spurenelemente JK Komplex...	11701	3
Unisan/Hepart AG	Magnesium (H1060)	43601	1
Unisan/Hepart AG	Magnesium (H1060)	973501	1
Unisan	Spurenelemente JK Komplex...	1026011701	1
Unisan	Spurenelemente JK Komplex...	1026956901	1
Unisan	Spurenelemente JK Komplex...	1028956901	1
Unisan	Magnesium (H1060)	1134973501	2
Unisan	Spurenelemente JK Komplex...	11701	3
Unisan	Magnesium (H1060)	14001893	1
unisan	Magnesium (H1060)	14001895	2
Unisan	Magnesium (H1060)	14001895	4
Unisan	Spurenelemente JK Komplex...	15000525/0	1
Unisan	Spurenelemente JK Komplex...	15000526	1
Unisan	Magnesium (H1060)	16000265	1
Unisan	Magnesium (H1060)	16000265/0	1
Unisan	Magnesium (H1060)	16000265/1	3
Unisan	Magnesium (H1060)	16000272	1
Unisan	Spurenelemente JK Komplex...	17000870	2
Unisan	Magnesium (H1060)	43501	2
Unisan	Magnesium (H1060)	43601	1
Unisan	Magnesium (H1060)	43701	3
unisan	Magnesium (H1060)	43702	1
Unisan	Magnesium (H1060)	69601	1
Unisan	Magnesium (H1060)	69701	3
UNISAN	Magnesium (H1060)	69701	3
Unisan	Magnesium (H1060)	69801	4
Unisan	Magnesium (H1060)	69801/2	1
Unisan	Spurenelemente JK Komplex...	72701	1
UNISAN	Spurenelemente JK Komplex...	72701	1
Unisan	Spurenelemente JK Komplex...	72901	1
Unisan	Magnesium (H1060)	973501	2
Unisan	Magnesium (H1060)	H106021	1

- 2777 spectra from 26 *Apo-Ident* customers from a total of 1372 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 *Magnésio (H1060) / Complexo de oligoelementos 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 *Magnésio (H1060) / Complexo de oligoelementos 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	620	0	27 656
Type B	0	1807	3	20 869
Type C	0	171	22	2777

The substance/substance group *Magnésio (H1060) / Complexo de oligoelementos 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 % (> 99.0323 %)
Type B	100.0000 % (> 99.8661 %)	99.8343 % (> 99.6685 %)
Type C	100.0000 % (> 98.8228 %)	88.6010 % (> 87.0466 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80378	80378	0,00	82,19
80387	80387	0,00	36,79
80388	80388	0,00	36,25
80389	80389	0,00	37,53
80515	80515	0,00	79,81
80701	80701	0,00	40,32
80766	80766	0,00	51,37
80767	80767	0,00	60,66
80770	80770	0,00	55,02
80856	80856	0,00	61,97
81029	81029	0,00	29,77
81058	81058	0,00	64,32
81327	81327	0,00	45,22

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 2.8-2024-04

Validated substance/substance group **Methylsulfonylmethan MSM (H1062)**
Substance class **HCK**
Report date 25/11/2024
Report number 80102-2024-11-25
Executing company HiperScan GmbH
 Weißeritzstraße 3
 01067 Dresden
 Germany

Relevant substance names

Methylsulfonylmethan MSM (H1062)

Special notes

When selecting the *Methylsulfonylmethan MSM (H1062)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Methylsulfonylmethan MSM (H1062)	8	1	14

Second-stage model

For differentiation of the substance/substance group *Methylsulfonylmethan MSM (H1062)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Methylsulfonylmethan MSM (H1062)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	48,97	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methylsulfonylmethan MSM (H1062)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Methylsulfonylmethan MSM ...	056201	80332	60	from supplier
Hepart	Methylsulfonylmethan MSM ...	14000921	80467	40	from supplier
Hepart	Methylsulfonylmethan MSM ...	15001371	80703	120	from supplier
Hepart	Methylsulfonylmethan MSM ...	17001247	80957	40	from supplier
Hepart	Methylsulfonylmethan MSM ...	18001387	81117	40	from supplier
Hepart	Methylsulfonylmethan MSM ...	20000221	81262	40	from supplier
Hepart	Methylsulfonylmethan MSM ...	21000404	81333	40	from supplier
Hepart	Methylsulfonylmethan MSM ...	21001430	81386	50	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 430 spectra of 8 reference samples from the substance/substance group *Methylsulfonylmethan MSM (H1062)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.

- 27 846 spectra from a total of 564 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Methylsulfonylmethan 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	Methylsulfonylmethan MSM ...	16000449/0	80782	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 25 spectra from 8 *Apo-Ident* customers from 19 batches from the substance/substance group *Methylsulfonylmethan MSM (H1062)*.
- 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	Methylsulfonylmethan MSM ...	1400921/1	1
Hepart AG	Methylsulfonylmethan MSM ...	15001371	1
Hepart	Methylsulfonylmethan MSM ...	16000449/4	2
Hepart	Methylsulfonylmethan MSM ...	16000449-3	1
Hepart	Methylsulfonylmethan MSM ...	17001247	1
Hepart	Methylsulfonylmethan MSM ...	18001387	1
Hepart	Methylsulfonylmethan MSM ...	18001387/0	1
Hepart	Methylsulfonylmethan MSM ...	18001387/1	3
Hepart	Methylsulfonylmethan MSM ...	20000221	1
Hepart	Methylsulfonylmethan MSM ...	20000221/0	1

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Supplier	Substance	Batch	Spectra
Hepart	Methylsulfonylmethan MSM ...	210000404/0	1
Hepart	Methylsulfonylmethan MSM ...	21000404	1
Hepart	Methylsulfonylmethan MSM ...	21000404/1	1
Unisan/Hepart AG	Methylsulfonylmethan MSM ...	1819025013	1
Unisan	Methylsulfonylmethan MSM ...	15001371	1
Unisan	Methylsulfonylmethan MSM ...	16000449/1	1
Unisan	Methylsulfonylmethan MSM ...	25013	2
Unisan	Methylsulfonylmethan MSM ...	26101	1
Unisan	Methylsulfonylmethan MSM ...	56201	2
Unisan	Methylsulfonylmethan MSM ...	979401	1

- 2945 spectra from 26 *Apo-Ident* customers from a total of 1441 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 *Methylsulfonylmethan 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 *Methylsulfonylmethan 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	430	0	27 846
Type B	0	40	0	22 639
Type C	0	21	4	2945

The substance/substance group *Methylsulfonylmethan 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 % (> 99.9309 %)	100.0000 % (> 98.6047 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8358 %)	84.0000 % (> 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.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the [Mahalanobis distance](#) to the reference sample is specified as well 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	68,81
80467	80467	0,00	78,15
80703	80703	0,00	72,82
80957	80957	0,00	57,81
81117	81117	0,00	57,80
81262	81262	0,00	58,58
81333	81333	0,00	48,97
81386	81386	0,00	58,23

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 2.8-2024-04

Validated substance/substance group **Moringa (H1131)**
Substance class HCK
Report date 25/11/2024
Report number 10006003-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Moringa (H1131)

Special notes

When selecting the *Moringa (H1131)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Moringa (H1131)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Moringa (H1131)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Moringa (H1131)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
PET Basis (H1503)	21,82	—
Kakao (H1521)	26,91	—
Ginkgo Extrakt (H1024)	34,23	—
PET Immunsystem (H1502)	37,65	—
PET Well-Aging (H1500)	40,62	—
Kupfer (H1032)	46,11	—
Eisen (H1015)	55,29	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Moringa (H1131)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Moringa (H1131)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Moringa (H1131)	22001058	81434	40	from supplier
Hepart	Moringa (H1131)	23002138	81514	40	from supplier

Validation samples

A total of 53 925 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 *Moringa (H1131)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.

- 28 196 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Moringa (H1131)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Moringa (H1131)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Moringa (H1131)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Moringa (H1131)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 196
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Moringa (H1131)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9319 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81434	81434	0,00	21,82
81514	81514	0,00	34,14

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 2.8-2024-04

Validated substance/substance group **Niacin (Inositol Hexanicotinat) (H1022)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80087-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Niacin (Inositol Hexanicotinat) (H1022)

Special notes

When selecting the *Niacin (Inositol Hexanicotinat) (H1022)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Niacin (Inositol Hexanicotinat) (H1022)	6	4	18

Second-stage model

For differentiation of the substance/substance group *Niacin (Inositol Hexanicotinat) (H1022)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Niacin (Inositol Hexanicotinat) (H1022)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	58,54	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Niacin (Inositol Hexanicotinat) (H1022)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Niacin (Inositol Hexanico...	046001	80320	60	from supplier
Hepart	Niacin (Inositol Hexanico...	14000920	80465	40	from supplier
Hepart	Niacin (Inositol Hexanico...	15000013	80554	60	from supplier
Hepart	Niacin (Inositol Hexanico...	18001390/0	81116	40	from supplier
Hepart	Niacin (Inositol Hexanico...	22002214	81459	40	from supplier
Hepart	Niacin (Inositol Hexanico...	21002810/1	81544	40	from supplier

Validation samples

A total of 53 925 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 *Niacin (Inositol Hexanicotinat) (H1022)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 27 996 spectra from a total of 566 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the

substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 160 spectra of 4 reference samples from the substance/substance group *Niacin (Inositol Hexanicotinat) (H1022)*.
- Among them are spectra of independent samples from 4 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	Niacin (Inositol Hexanico...	16000750	80814	40
Hepart	Niacin (Inositol Hexanico...	20000182	81231	40
Hepart	Niacin (Inositol Hexanico...	20001828	81314	40
Hepart	Niacin (Inositol Hexanico...	23000655/0	81545	40

- 22 519 spectra from a total of 492 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 25 spectra from 8 *Apo-Ident* customers from 20 batches from the substance/substance group *Niacin (Inositol Hexanicotinat) (H1022)*.
- Among them are spectra of independent samples from 18 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	Niacin (Inositol Hexanico...	1811046001	1
Flaigg Ag CH-4147 Ae...	Niacin (Inositol Hexanico...	16000750/13	1
Flaigg Ag CH-4147 Ae...	Niacin (Inositol Hexanico...	18001390/3	1
HCK	Niacin (Inositol Hexanico...	15000013/3	1
HCK	Niacin (Inositol Hexanico...	19000750/4	1
Hepart AG	Niacin (Inositol Hexanico...	15000013	1
Hepart AG	Niacin (Inositol Hexanico...	16000750/4	1
Hepart AG	Niacin (Inositol Hexanico...	1811979201	1
Hepart	Niacin (Inositol Hexanico...	16000750	1

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Supplier	Substance	Batch	Spectra
Hepart	Niacin (Inositol Hexanico...	16000750/12	1
Hepart	Niacin (Inositol Hexanico...	16000750/2	1
Hepart	Niacin (Inositol Hexanico...	18001390/3	1
Hepart	Niacin (Inositol Hexanico...	18001390/4	2
Hepart	Niacin (Inositol Hexanico...	20000182/0	1
Hepart	Niacin (Inositol Hexanico...	20001828/0	1
Hepart	Niacin (Inositol Hexanico...	20001828/1	1
Hepart	Niacin (Inositol Hexanico...	20001828/2	1
Hepart	Niacin (Inositol Hexanico...	20001828/3	1
Hepart	Niacin (Inositol Hexanico...	20001828/4	1
Purren Apotheke	Niacin (Inositol Hexanico...	1811979201	1
Unisan/Hepart AG	Niacin (Inositol Hexanico...	46001	1
Unisan	Niacin (Inositol Hexanico...	14000920	1
unisan	Niacin (Inositol Hexanico...	15000013	1
Unisan	Niacin (Inositol Hexanico...	46001	1

- 2945 spectra from 26 *Apo-Ident* customers from a total of 1440 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 *Niacin (Inositol Hexanicotinat) (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 *Niacin (Inositol Hexanicotinat) (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	280	0	27 996
Type B	0	160	0	22 519
Type C	0	25	0	2945

The substance/substance group *Niacin (Inositol Hexanicotinat) (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 % (> 97.8571 %)
Type B	100.0000 % (> 99.8672 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 98.8358 %)	100.0000 % (> 76.0000 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80320	80320	0,00	84,43
80465	80465	0,00	85,81
80554	80554	0,00	85,40
81116	81116	0,00	58,54
81459	81459	0,00	75,04
81544	81544	0,00	73,75

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 2.8-2024-04

Validated substance/substance group **Niacin (Nicotinamid) (H1133)**
Substance class **HCK**
Report date **25/11/2024**
Report number **10006004-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Niacin (Nicotinamid) (H1133)

Special notes

When selecting the *Niacin (Nicotinamid) (H1133)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Niacin (Nicotinamid) (H1133)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Niacin (Nicotinamid) (H1133)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Niacin (Nicotinamid) (H1133)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Curcumin und Piperin (H1014)	52,72	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Niacin (Nicotinamid) (H1133)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Niacin (Nicotinamid) (H1133)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Niacin (Nicotinamid) (H1133)	22000701	81436	40	from supplier
Hepart	Niacin (Nicotinamid) (H1133)	23002220	81527	40	from supplier

Validation samples

A total of 53 925 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 *Niacin (Nicotinamid) (H1133)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 28 196 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with

the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Niacin (Nicotinamid) (H1133)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Niacin (Nicotinamid) (H1133)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Niacin (Nicotinamid) (H1133)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Niacin (Nicotinamid) (H1133)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 196
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Niacin (Nicotinamid) (H1133)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9319 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81436	81436	0,00	61,86
81527	81527	0,00	58,23

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 2.8-2024-04

Validated substance/substance group **Oligoelementos BAG (H1078) / Zinco (H1110)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80503-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Oligoelementos BAG (H1078) / Zinco (H1110); Spurenelemente BAG (H1078); Zink (H1110)

Special notes

When selecting the *Oligoelementos BAG (H1078) / Zinco (H1110)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Oligoelementos BAG (H1078) / Zinco (H1110)	9	4	28

Second-stage model

For differentiation of the substance/substance group *Oligoelementos BAG (H1078) / Zinco (H1110)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Oligoelementos BAG (H1078) / Zinco (H1110)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Vitamin B12 (H1102)	15,14	—
Selen (H1067)	18,67	—
Magnesium (H1060)	18,71	—
Orthovimin Neutral Komplex (H1403)	22,52	—
Biotin (H1007)	22,67	—
Ginseng (H1018)	24,08	—
Chrom (H1012)	24,11	—
Vitamin D3 (H1105)	24,68	—
Selenhefe (H1068)	30,65	—
Safran Griffel (H1434)	30,93	—
Vitamin K2 (75µg Mono) (H1108)	31,23	—
Spurenelemente JK Komplex (H1080)	31,34	—
Lycopon (H1058)	34,06	—
Artischocke Extrakt (H1440)	34,50	—
Enzian Extrakt (H1438)	35,47	—
Chondroitinsulfat (H1065)	38,00	—
Eibisch Extrakt (H1439)	38,26	—
Bor (H1005)	38,63	—
Coenzym Q10 (H1013)	38,63	—
Ashwagandha (H1132)	41,59	—
Vitamin E NAT (H1107)	42,37	—
Guar-Granulat (H1023)	43,22	—
Folat (L-5-MTHF) (H1128)	49,90	—
Artemisia annua Extrakt (H1118)	49,96	—
Garcinia Cambogia (H1017)	49,96	—
Flohsamenschalen (H1527)	49,98	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Oligoelementos BAG (H1078) / Zinco (H1110)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Oligoelementos BAG (H1078) / Zinco (H1110)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Spurenelemente BAG (H1078)	16000795	80799	40	from supplier
Hepart	Spurenelemente BAG (H1078)	16000796	80800	40	from supplier
Hepart	Zink (H1110)	14001803	80503	60	from supplier
Hepart	Zink (H1110)	16000196	80761	60	from supplier
Hepart	Zink (H1110)	16000518	80789	40	from supplier
Hepart	Zink (H1110)	18001012	81068	40	from supplier
Hepart	Zink (H1110)	18000559	81069	40	from supplier
Hepart	Zink (H1110)	21001425	81358	50	from supplier
Hepart	Zink (H1110)	22000935	81431	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 410 spectra of 9 reference samples from the substance/substance group *Oligoelementos BAG (H1078)* / *Zinco (H1110)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 27 866 spectra from a total of 563 batches from further 129 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 180 spectra of 4 reference samples from the substance/substance group *Oligoelementos BAG (H1078)* / *Zinco (H1110)*.
- Among them are spectra of independent samples from 4 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	Spurenelemente BAG (H1078)	16000797	80801	40
Hepart	Zink (H1110)	14001753	80489	60
Hepart	Zink (H1110)	16000519	80790	40
Hepart	Zink (H1110)	20002833	81353	40

- 22 499 spectra from a total of 492 batches from further 78 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

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

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

- 96 spectra from 20 *Apo-Ident* customers from 32 batches from the substance/substance group *Oligoelementos BAG (H1078) / Zink (H1110)*.
- 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	Zink (H1110)	14001753/1	1
HCK	Zink (H1110)	14001803/2	1
HCK	Zink (H1110)	14001803-3	1
HCK	Zink (H1110)	16000196/0	1
HCK	Zink (H1110)	16000196-1	1
Hepart ag /Unisan	Zink (H1110)	18001012	2
Hepart AG, CH-8280 K...	Zink (H1110)	1164991001	1
Hepart AG	Zink (H1110)	1164991001	3
Hepart AG	Zink (H1110)	14001803/2	1
Hepart AG	Zink (H1110)	16000518/1	1
Hepart AG	Zink (H1110)	16000519/0	9
Hepart AG	Zink (H1110)	18000559/1	1
Hepart AG	Zink (H1110)	41501	7
Hepart AG	Zink (H1110)	991001	3
Hepart/Unisan	Zink (H1110)	14001803/2	1
Hepart/Unisan	Zink (H1110)	18001012/0	1
Hepart	Zink (H1110)	14001803	1
Hepart	Zink (H1110)	16000196	3
Hepart	Zink (H1110)	16000518	2
Hepart	Zink (H1110)	16000518/1	3
Hepart	Zink (H1110)	16000518-1	1
Hepart	Zink (H1110)	16000519	1
Hepart	Zink (H1110)	16000519/0	2
Hepart	Zink (H1110)	16000519/1	1
Hepart	Zink (H1110)	18000559/0	3
Hepart	Zink (H1110)	18000559/1	2
Hepart	Zink (H1110)	18000559/2	2
Hepart	Zink (H1110)	18001012/0	2
Hepart	Zink (H1110)	18001012/1	1
Hepart	Zink (H1110)	18001012/2	3
Hepart	Zink (H1110)	1800559/0	1
Hepart	Zink (H1110)	20002833/0	2
Hepart	Zink (H1110)	21001425/0	1
Hepart	Zink (H1110)	21001425/1	1
Hepart	Zink (H1110)	xxxx	1
Unisan GmbH, 78465 K...	Zink (H1110)	991001	1
Unisan	Zink (H1110)	1164949701	1
Unisan	Zink (H1110)	1164991001	2
Unisan	Zink (H1110)	14001753	1
Unisan	Zink (H1110)	14001753/0	1
Unisan	Zink (H1110)	14001803	3
Unisan	Zink (H1110)	14001803/1	1
Unisan	Zink (H1110)	16000196	3
Unisan	Zink (H1110)	16000196/0	2
Unisan	Zink (H1110)	16000518	1
Unisan	Zink (H1110)	41501	5

continued on the next page

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Supplier	Substance	Batch	Spectra
Unisan	Zink (H1110)	991001	7

- 2874 spectra from 26 *Apo-Ident* customers from a total of 1428 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 *Oligoelementos BAG (H1078) / Zinco (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 *Oligoelementos BAG (H1078) / Zinco (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	410	0	27 866
Type B	0	176	4	22 499
Type C	0	93	3	2874

The substance/substance group *Oligoelementos BAG (H1078) / Zinco (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 % (> 99.9309 %)	100.0000 % (> 98.5366 %)
Type B	100.0000 % (> 99.8671 %)	97.7778 % (> 96.1111 %)
Type C	100.0000 % (> 98.8247 %)	96.8750 % (> 93.7500 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80503	80503	0,00	26,38
80761	80761	0,00	24,08
80789	80789	0,00	19,82

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80799	80799	0,00	22,52
80800	80800	0,00	22,92
81068	81068	0,00	21,89
81069	81069	0,00	23,99
81358	81358	0,00	20,49
81431	81431	0,00	22,46

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 2.8-2024-04

Validated substance/substance group **Orthovimin Neutral Komplex (H1403)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80744-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Orthovimin Neutral Komplex (H1403)

Special notes

When selecting the *Orthovimin Neutral Komplex (H1403)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Orthovimin Neutral Komplex (H1403)	4	2	0

Second-stage model

For differentiation of the substance/substance group *Orthovimin Neutral Komplex (H1403)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Orthovimin Neutral Komplex (H1403)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Zink (H1110)	16,66	—
Safran Griffel (H1434)	17,73	—
Konjak Glucomannan (H1530)	20,78	—
Garcinia Cambogia (H1017)	21,08	—
Bor (H1005)	24,46	—
Ginseng (H1018)	26,02	—
Vitamin B1 (H1101)	26,42	—
Silicium (H1070)	27,22	—
Lycopen (H1058)	27,41	—
Rhodiola (H1064)	28,00	—
Magnesium (H1060)	28,52	—
Artischocke Extrakt (H1440)	29,28	—
Óleo de zimbro (H1112)	29,55	—
Orthocolon Komplex (H1800)	29,58	—
Baobab (H1410)	29,83	—
Detox Komplex (H1111)	31,56	—
Eibisch Extrakt (H1439)	31,69	—
Coenzym Q10 (H1013)	31,84	—
L-Arginin (H1036)	35,97	—
Enzian Extrakt (H1438)	36,05	—
Vitamin K2 (75µg Mono) (H1108)	36,07	—
Chondroitinsulfat (H1065)	37,79	—
Selen (H1067)	37,80	—
Calcium L-(+) -Lactat Komplex (H1008)	38,18	—
Spurenelemente BAG (H1078)	39,45	—
Flohsamenschalen (H1527)	39,52	—
Vitamin B12 (H1102)	40,05	—
Vitamine BAG Komplex (H1091)	40,12	—
Glutathion (H1020)	40,52	—
Silymarin (H1071)	40,82	—
Selenhefe (H1068)	41,23	—
Ingwer Extrakt (H1437)	42,27	—
Grüner Kaffee Extrakt (H1433)	42,29	—
Safran Blüten (H1435)	44,54	—
Spurenelemente JK Komplex (H1080)	45,05	—
Vitamin D3 (H1105)	45,12	—
Ashwagandha (H1132)	45,24	—
Artemisia annua Extrakt (H1118)	45,70	—

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Substanz	Distance in main model	Distance in second-stage model
Betain Hydrochlorid (H1119)	46,25	—
Leaky Gut Komplex (H1802)	47,20	—
OPC Proanthocyanidine (Pine Bark) (...)	47,35	—
Aminomix NAC (H1002)	47,50	—
Guar-Granulat (H1023)	47,89	—
Kupfer (H1032)	47,90	—
Vitamin E NAT (H1107)	49,76	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Orthovimin Neutral Komplex (H1403)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 Komplex (H1403)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Orthovimin Neutral Komple...	15001850	80744	60	from supplier
Hepart	Orthovimin Neutral Komple...	17001152	81020	40	from supplier
Hepart	Orthovimin Neutral Komple...	18001065	81073	40	from supplier
Hepart	Orthovimin Neutral Komple...	19000033	81149	40	from supplier

Validation samples

A total of 53 925 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 Komplex (H1403)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 28 096 spectra from a total of 568 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 Komplex (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 Komple...	17001625	80983	40
Hepart	Orthovimin Neutral Komple...	19001312	81182	40

- 22 599 spectra from a total of 494 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 Komplex (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 Komplex (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 Komplex (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	28 096
Type B	0	80	0	22 599
Type C	0	0	0	2970

The substance/substance group *Orthovimin Neutral Komplex (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 % (> 99.9312 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.8684 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80744	80744	0,00	26,70
81020	81020	0,00	20,78
81073	81073	0,00	24,46
81149	81149	0,00	25,49

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 2.8-2024-04

Validated substance/substance group **PET Coenzym Q10 (H1505)**
Substance class HCK
Report date 25/11/2024
Report number 80561-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

PET Coenzym Q10 (H1505)

Special notes

When selecting the *PET Coenzym Q10 (H1505)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
PET Coenzym Q10 (H1505)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET Coenzym Q10 (H1505)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *PET Coenzym Q10 (H1505)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Vitamin E NAT (H1107)	12,53	—
Ginseng (H1018)	13,97	—
Coenzym Q10 (H1013)	23,50	—
Ingwer Extrakt (H1437)	24,72	—
Aroma Orange (H1405)	29,49	—
Chondroitinsulfat (H1065)	35,26	—
Bor (H1005)	38,90	—
Haferkleie beta-Glucan (H1529)	41,10	—
Vitamin K2 (75µg Mono) (H1108)	41,77	—
Aminomix NAC (H1002)	45,34	—
Garcinia Cambogia (H1017)	49,93	—
Glutathion (H1020)	50,73	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET Coenzym Q10 (H1505)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 Coenzym Q10 (H1505)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET Coenzym Q10 (H1505)	15000401	80561	60	from supplier
Hepart	PET Coenzym Q10 (H1505)	15000401	80635	60	from supplier

Validation samples

A total of 53 925 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 Coenzym Q10 (H1505)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 156 spectra from a total of 572 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 Coenzym Q10 (H1505)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 Coenzym Q10 (H1505)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 Coenzym Q10 (H1505)* can clearly be 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 Coenzym Q10 (H1505)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 156
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *PET Coenzyme Q10 (H1505)* can be clearly distinguished from all other substances. In order to make these figures comparable, 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 % (> 95.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80561	80561	0,00	23,62
80635	80635	0,00	21,21

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 2.8-2024-04

Validated substance/substance group **PET Gelenke (H1501)**
Substance class HCK
Report date 25/11/2024
Report number 80567-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

PET Gelenke (H1501)

Special notes

When selecting the *PET Gelenke (H1501)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
PET Gelenke (H1501)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET Gelenke (H1501)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *PET Gelenke (H1501)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
PET Basis (H1503)	18,04	—
Coenzym Q10 (H1013)	27,89	—
Rhodiola (H1064)	33,95	—
Aminomix NAC (H1002)	35,78	—
Antioxidantien NAT Komplex (H1004)	36,14	—
Calcium L-(+) -Lactat Komplex (H1008)	40,87	—
Aroma Orange (H1405)	40,88	—
Glutathion (H1020)	41,33	—
PET Well-Aging (H1500)	43,97	—
L-Glutamin (H1043)	47,72	—
Antibiose forte Komplex (H1115)	48,99	—
Vitamin B1 (H1101)	49,10	—
Garcinia Cambogia (H1017)	49,15	—
L-Arginin (H1036)	50,40	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET Gelenke (H1501)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 Gelenke (H1501)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET Gelenke (H1501)	15000404	80567	60	from supplier
Hepart	PET Gelenke (H1501)	15000404	80630	60	from supplier

Validation samples

A total of 53 925 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 Gelenke (H1501)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 156 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 Gelenke (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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 Gelenke (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 Gelenke (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 Gelenke (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	28 156
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *PET Gelenke (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 % (> 99.9315 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80567	80567	0,00	18,04
80630	80630	0,00	20,39

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 2.8-2024-04

Validated substance/substance group **PET Haut und Haare (H1504)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80565-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

PET Haut und Haare (H1504)

Special notes

When selecting the *PET Haut und Haare (H1504)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
PET Haut und Haare (H1504)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET Haut und Haare (H1504)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *PET Haut und Haare (H1504)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	50,38	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET Haut und Haare (H1504)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 Haut und Haare (H1504)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET Haut und Haare (H1504)	15000403	80565	60	from supplier
Hepart	PET Haut und Haare (H1504)	15000403	80633	60	from supplier

Validation samples

A total of 53 925 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 Haut und Haare (H1504)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 156 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with

the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 Haut und Haare (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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 Haut und Haare (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 Haut und Haare (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 Haut und Haare (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	28 156
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *PET Haut und Haare (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 % (> 99.9315 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80565	80565	0,00	51,34
80633	80633	0,00	50,38

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 2.8-2024-04

Validated substance/substance group **PET Immunsystem (H1502)**
Substance class HCK
Report date 25/11/2024
Report number 80564-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

PET Immunsystem (H1502)

Special notes

When selecting the *PET Immunsystem (H1502)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
PET Immunsystem (H1502)	1	0	0

Second-stage model

For differentiation of the substance/substance group *PET Immunsystem (H1502)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *PET Immunsystem (H1502)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
PET Basis (H1503)	24,65	—
Ginkgo Extrakt (H1024)	29,90	—
PET Well-Aging (H1500)	35,21	—
Chiasamenprotein (H1506)	41,16	—
Magen Komplex (H1120)	44,10	—
Kakao (H1521)	44,45	—
Antibiose forte Komplex (H1115)	44,96	—
Vitamin C (H1104)	55,74	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *PET Immunsystem (H1502)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 Immunsystem (H1502)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	PET Immunsystem (H1502)	15000405	80564	60	from supplier
Hepart	PET Immunsystem (H1502)	15000405	80634	60	from supplier

Validation samples

A total of 53 925 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 Immunsystem (H1502)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.

- 28 156 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 Immunsystem (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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 Immunsystem (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 Immunsystem (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 Immunsystem (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	28 156
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *PET Immunsystem (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 % (> 99.9315 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80564	80564	0,00	26,47
80634	80634	0,00	24,65

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 2.8-2024-04

Validated substance/substance group **PET Well-Aging (H1500)**
Substance class **HCK**
Report date 25/11/2024
Report number 80563-2024-11-25
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

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	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

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *PET Well-Aging (H1500)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
PET Basis (H1503)	14,41	—
Vitamin B1 (H1101)	28,06	—
Rhodiola (H1064)	29,06	—
PET Gelenke (H1501)	29,10	—
Aroma Orange (H1405)	33,68	—
Ginkgo Extrakt (H1024)	35,13	—
PET Immunsystem (H1502)	36,11	—
L-Carnitin (H1038)	40,45	—
Grüner Kaffee Extrakt (H1433)	41,09	—
L-Arginin (H1036)	45,32	—
Antibiose forte Komplex (H1115)	46,88	—
Calcium L-(+) -Lactat Komplex (H1008)	48,09	—
Antioxidantien NAT Komplex (H1004)	52,37	—

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.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 (H1500)	15000401	80563	60	from supplier
Hepart	PET Well-Aging (H1500)	15000406	80631	60	from supplier

Validation samples

A total of 53 925 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.
- 28 156 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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	28 156
Type B	0	0	0	22 679
Type C	0	0	0	2970

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 % (> 99.9315 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80563	80563	0,00	15,75
80631	80631	0,00	14,41

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 2.8-2024-04

Validated substance/substance group **Potássio (H1030)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80043-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Potássio (H1030)

Special notes

When selecting the *Potássio (H1030)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Potássio (H1030)	8	15	34

Second-stage model

For differentiation of the substance/substance group *Potássio (H1030)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Potássio (H1030)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Eisen (H1015)	41,68	—
Calcium L-(+) -Lactat Komplex (H1008)	48,12	—
Vitamin C (H1104)	54,26	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Potássio (H1030)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Potássio (H1030)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Potássio (H1030)	039302	80372	40	from supplier
Hepart	Potássio (H1030)	15000597	80571	60	from supplier
Hepart	Potássio (H1030)	15000598(B1)	80574	60	from supplier
Hepart	Potássio (H1030)	15000599	80576	60	from supplier
Hepart	Potássio (H1030)	15000600	80578	60	from supplier
Hepart	Potássio (H1030)	16001645	80868	40	from supplier
Hepart	Potássio (H1030)	19000026	81154	40	from supplier
Hepart	Potássio (H1030)	21002001	81396	50	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 410 spectra of 8 reference samples from the substance/substance group *Potássio (H1030)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.

- 27 866 spectra from a total of 564 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 700 spectra of 15 reference samples from the substance/substance group *Potássio (H1030)*.
- 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	Potássio (H1030)	130328001	80347	40
Hepart	Potássio (H1030)	069201	80376	30
Hepart	Potássio (H1030)	15000597(B1)	80572	60
Hepart	Potássio (H1030)	15000598	80573	60
Hepart	Potássio (H1030)	15000598(F2)	80575	60
Hepart	Potássio (H1030)	15000599(F2)	80577	60
Hepart	Potássio (H1030)	15000600(B1)	80579	60
Hepart	Potássio (H1030)	16001646	80869	40
Hepart	Potássio (H1030)	16001647	80870	40
Hepart	Potássio (H1030)	19000027	81155	40
Hepart	Potássio (H1030)	19000028	81156	40
Hepart	Potássio (H1030)	20001174	81283	40
Hepart	Potássio (H1030)	20001173	81287	40
Hepart	Potássio (H1030)	2100-1999-2000	81398	50
Hepart	Potássio (H1030)	23000438-439	81477	40

- 21 979 spectra from a total of 481 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 88 spectra from 18 *Apo-Ident* customers from 37 batches from the substance/substance group *Potássio (H1030)*.
- 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
Fagron	Potássio (H1030)	39301	1
HCK	Potássio (H1030)	15000597-1	1
HCK	Potássio (H1030)	15000599	1
Hepart / Unisan	Potássio (H1030)	160016460	1
Hepart AG	Potássio (H1030)	1124028903	1
Hepart AG	Potássio (H1030)	1124944201	1
Hepart AG	Potássio (H1030)	15000597/0	1
Hepart AG	Potássio (H1030)	16001645/0	4
Hepart AG	Potássio (H1030)	16001646/0	6
Hepart AG	Potássio (H1030)	16001647/0	1
Hepart AG	Potássio (H1030)	39301	1
Hepart AG	Potássio (H1030)	39302	1
Hepart	Potássio (H1030)	15000598	1
Hepart	Potássio (H1030)	15000598-3	1
Hepart	Potássio (H1030)	15000599/1	1
Hepart	Potássio (H1030)	16001645	1
Hepart	Potássio (H1030)	16001645/0	2
Hepart	Potássio (H1030)	16001646	1
Hepart	Potássio (H1030)	16001647	1
Hepart	Potássio (H1030)	16001647/0	2
Hepart	Potássio (H1030)	19000026/0	3
Hepart	Potássio (H1030)	19000027	1
Hepart	Potássio (H1030)	19000027/0	7
Hepart	Potássio (H1030)	19000028	1
Hepart	Potássio (H1030)	19000028/0	6
Hepart	Potássio (H1030)	20001173	1
Hepart	Potássio (H1030)	20001173/0	2
Hepart	Potássio (H1030)	20001174/0	1
Hepart	Potássio (H1030)	21001999/0	1
Unisan/Hepart AG	Potássio (H1030)	39302	1
Unisan	Potássio (H1030)	1124944201	1
Unisan	Potássio (H1030)	130328001	3
Unisan	Potássio (H1030)	15000597/0	1
Unisan	Potássio (H1030)	15000597/1	1
Unisan	Potássio (H1030)	15000598	1
Unisan	Potássio (H1030)	15000599	1
Unisan	Potássio (H1030)	15000599/0	1
Unisan	Potássio (H1030)	15000600	2
Unisan	Potássio (H1030)	288903	1
Unisan	Potássio (H1030)	28903	1
Unisan	Potássio (H1030)	39301	8
Unisan	Potássio (H1030)	39302	1
Unisan	Potássio (H1030)	69201	3
UNISAN	Potássio (H1030)	69201	1
Unisan	Potássio (H1030)	69301	3
Unisan	Potássio (H1030)	69401	1
Unisan	Potássio (H1030)	69401/0	1
Unisan	Potássio (H1030)	944201	3

- 2882 spectra from 26 *Apo-Ident* customers from a total of 1423 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 *Potássio (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 *Potássio (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	410	0	27 866
Type B	0	700	0	21 979
Type C	0	85	3	2882

The substance/substance group *Potássio (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 % (> 99.9309 %)	100.0000 % (> 98.5366 %)
Type B	100.0000 % (> 99.8662 %)	100.0000 % (> 99.1429 %)
Type C	100.0000 % (> 98.8251 %)	96.5909 % (> 93.1818 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80372	80372	0,00	38,78
80571	80571	0,00	47,13
80574	80574	0,00	48,09
80576	80576	0,00	48,98
80578	80578	0,00	48,26
80868	80868	0,00	49,15
81154	81154	0,00	43,49
81396	81396	0,00	48,93

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 2.8-2024-04

Validated substance/substance group **Prolin (L-) NF (H1050)**
Substance class HCK
Report date 25/11/2024
Report number 80905-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Prolin (L-) NF (H1050)

Special notes

When selecting the *Prolin (L-) NF (H1050)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Prolin (L-) NF (H1050)	3	0	1

Second-stage model

For differentiation of the substance/substance group *Prolin (L-) NF (H1050)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Prolin (L-) NF (H1050)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	23,37	—
L-Carnitin (H1038)	53,15	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prolin (L-) NF (H1050)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prolin (L-) NF (H1050)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Prolin (L-) NF (H1050)	16000951	80905	40	from supplier
Hepart	Prolin (L-) NF (H1050)	17000952	80935	40	from supplier
Hepart	Prolin (L-) NF (H1050)	18000403	81023	40	from supplier
Hepart	Prolin (L-) NF (H1050)	16000951	81146	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Prolin (L-) NF (H1050)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 116 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the

substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Prolin (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	Prolin (L-) NF (H1050)	16000951	80936	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 3 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Prolin (L-) NF (H1050)*.
- Among them are spectra of independent samples from 1 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	Prolin (L-) NF (H1050)	17000952	2
Hepart	Prolin (L-) NF (H1050)	17000952/0	1

- 2967 spectra from 26 *Apo-Ident* customers from a total of 1458 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 *Prolin (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 *Prolin (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	160	0	28 116
Type B	0	36	4	22 639
Type C	0	3	0	2967

The substance/substance group *Prolin (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 % (> 96.2500 %)
Type B	100.0000 % (> 99.8709 %)	90.0000 % (> 82.5000 %)
Type C	100.0000 % (> 98.9458 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80905	80905	0,00	26,67
80935	80935	0,00	25,81
81023	81023	0,00	28,41
81146	81146	0,00	23,37

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 2.8-2024-04

Validated substance/substance group **Quercetin Dihydrat (H1130)**
Substance class HCK
Report date 25/11/2024
Report number 10006007-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Quercetin Dihydrat (H1130)

Special notes

When selecting the *Quercetin Dihydrat (H1130)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Quercetin Dihydrat (H1130)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Quercetin Dihydrat (H1130)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Quercetin Dihydrat (H1130)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Eisen (H1015)	32,67	—
Calcium L-(+) -Lactat Komplex (H1008)	49,49	—
Griffonia (H1035)	51,14	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Quercetin Dihydrat (H1130)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Quercetin Dihydrat (H1130)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Quercetin Dihydrat (H1130)	22000700	81442	40	from supplier
Hepart	Quercetin Dihydrat (H1130)	24000012	81530	40	from supplier

Validation samples

A total of 53 925 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 *Quercetin Dihydrat (H1130)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 28 196 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A*

section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Quercetin Dihydrat (H1130)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Quercetin Dihydrat (H1130)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Quercetin Dihydrat (H1130)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Quercetin Dihydrat (H1130)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 196
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Quercetin Dihydrat (H1130)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9319 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81442	81442	0,00	69,61
81530	81530	0,00	51,41

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 2.8-2024-04

Validated substance/substance group **Resveratrol (H1063)**
Substance class HCK
Report date 25/11/2024
Report number 10006137-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Resveratrol (H1063)

Special notes

When selecting the *Resveratrol (H1063)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Resveratrol (H1063)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Resveratrol (H1063)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Resveratrol (H1063)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Eisen (H1015)	65,51	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Resveratrol (H1063)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Resveratrol (H1063)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Resveratrol (H1063)	23001206	81492	35	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 35 spectra of 1 reference samples from the substance/substance group *Resveratrol (H1063)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 241 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Resveratrol (H1063)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Resveratrol (H1063)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Resveratrol (H1063)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Resveratrol (H1063)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	35	0	28 241
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Resveratrol (H1063)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9333 %)	100.0000 % (> 82.8571 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81492	81492	0,00	87,89

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 2.8-2024-04

Validated substance/substance group **s-Adenosyl-L-methionin (H1441)**
Substance class HCK
Report date 25/11/2024
Report number 10006407-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

s-Adenosyl-L-methionin (H1441)

Special notes

When selecting the *s-Adenosyl-L-methionin (H1441)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
s-Adenosyl-L-methionin (H1441)	1	0	0

Second-stage model

For differentiation of the substance/substance group *S-Adenosyl-L-methionin (H1441)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *S-Adenosyl-L-methionin (H1441)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	52,09	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *S-Adenosyl-L-methionin (H1441)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *S-Adenosyl-L-methionin (H1441)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	s-Adenosyl-L-methionin (H1441)	24000214/0	81537	40	from supplier

Validation samples

A total of 53 925 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 *S-Adenosyl-L-methionin (H1441)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with

the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *s-Adenosyl-L-methionin (H1441)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *s-Adenosyl-L-methionin (H1441)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *s-Adenosyl-L-methionin (H1441)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *s-Adenosyl-L-methionin (H1441)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *s-Adenosyl-L-methionin (H1441)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81537	81537	0,00	52,09

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 2.8-2024-04

Validated substance/substance group **Silymarin (H1071)**
Substance class HCK
Report date 25/11/2024
Report number 80068-2024-11-25
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

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Silymarin (H1071)	3	3	18

Second-stage model

For differentiation of the substance/substance group *Silymarin (H1071)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Silymarin (H1071)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Calcium L-(+)-Lactat Komplex (H1008)	20,54	—
Ginkgo Extrakt (H1024)	21,74	—
L-Carnitin (H1038)	21,88	—
OPC Proanthocyanidine (Pine Bark) (...)	22,36	—
Coenzym Q10 (H1013)	25,27	—
Betain Hydrochlorid (H1119)	26,02	—
Antioxidantien NAT Komplex (H1004)	30,28	—
Orthocolon Komplex (H1800)	34,87	—
Rhodiola (H1064)	35,19	—
L-Arginin (H1036)	36,78	—
Aminomix NAC (H1002)	38,45	—
Garcinia Cambogia (H1017)	41,47	—
Aroma Orange (H1405)	41,95	—
Vitamin B1 (H1101)	42,35	—
Griffonia (H1035)	42,72	—
Sonnenblumenkernprotein (H1511)	46,82	—
Glutathion (H1020)	46,99	—
Vitamin B6 (Pyridoxal-5-phosphat) (...)	47,18	—
Sanddorn (H1523)	48,06	—
Antibiose forte Komplex (H1115)	48,76	—
Isoflavone Extrakt (H1025)	49,75	—
PET Gelenke (H1501)	50,23	—

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.

Calibration samples

Only spectra which have been recorded by *HiperScan 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
Hepart	Silymarin (H1071)	21001429	81360	50	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 150 spectra of 3 reference samples from the substance/substance group *Silymarin (H1071)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 126 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Silymarin (H1071)*.
- 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	Silymarin (H1071)	067701	80375	40
Hepart	Silymarin (H1071)	16001084/0	81159	40
Hepart	Silymarin (H1071)	20002154	81322	40

- 22 559 spectra from a total of 493 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 34 spectra from 12 *Apo-Ident* customers from 19 batches from the substance/substance group *Silymarin (H1071)*.
- Among them are spectra of independent samples from 18 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Flaigg Ag CH-4147 Ae...	Silymarin (H1071)	16001084/2	1
HCK	Silymarin (H1071)	15001046/0	1
HCK	Silymarin (H1071)	67701/7	1
Hepart AG, CH-8280 K...	Silymarin (H1071)	1241046101	1
Hepart AG, CH-8280 K...	Silymarin (H1071)	1241950401	1
Hepart AG, CH-8280 K...	Silymarin (H1071)	29901	2
Hepart AG	Silymarin (H1071)	1244029901	1
hepart ag	Silymarin (H1071)	1244950401	1
Hepart AG	Silymarin (H1071)	67701	1
Hepart	Silymarin (H1071)	15001046	1
Hepart	Silymarin (H1071)	16001084/1	1
Hepart	Silymarin (H1071)	16001084/2	2
Hepart	Silymarin (H1071)	16001084/3	1
Hepart	Silymarin (H1071)	20001783/0	1
Hepart	Silymarin (H1071)	20002154/0	2
Hepart	Silymarin (H1071)	20002154/1	2
Hepart	Silymarin (H1071)	60010841	1
Unisan/Hepart AG	Silymarin (H1071)	29901	1
Unisan	Silymarin (H1071)	15001046	2
Unisan	Silymarin (H1071)	15001046/1	1
Unisan	Silymarin (H1071)	29901	3
Unisan	Silymarin (H1071)	46101	1
Unisan	Silymarin (H1071)	67701	2
UNISAN	Silymarin (H1071)	67701	1
Unisan	Silymarin (H1071)	67701/7	1
Unisan	Silymarin (H1071)	950401	1

- 2936 spectra from 26 *Apo-Ident* customers from a total of 1441 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	150	0	28 126
Type B	0	88	32	22 559
Type C	0	20	14	2936

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 % (> 99.9313 %)	100.0000 % (> 96.0000 %)
Type B	100.0000 % (> 99.8676 %)	73.3333 % (> 70.8333 %)
Type C	100.0000 % (> 98.8318 %)	58.8235 % (> 50.0000 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80671	80671	0,00	26,02
80861	80861	0,00	23,65
81360	81360	0,00	22,30

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 2.8-2024-04

Validated substance/substance group **Sonnenblumenkernprotein (H1511)**
Substance class **HCK**
Report date **25/11/2024**
Report number **10006063-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sonnenblumenkernprotein (H1511)

Special notes

When selecting the *Sonnenblumenkernprotein (H1511)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Sonnenblumenkernprotein (H1511)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Sonnenblumenkernprotein (H1511)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Sonnenblumenkernprotein (H1511)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Coenzym Q10 (H1013)	23,58	—
L-Carnitin (H1038)	24,45	—
Calcium L-(+) -Lactat Komplex (H1008)	26,87	—
Silymarin (H1071)	32,61	—
Vitamin B1 (H1101)	32,69	—
Ginkgo Extrakt (H1024)	33,06	—
Aminomix NAC (H1002)	34,35	—
Aroma Orange (H1405)	34,77	—
L-Arginin (H1036)	35,79	—
Leaky Gut Komplex (H1802)	36,33	—
Orthocolon Komplex (H1800)	37,02	—
Isoflavone Extrakt (H1025)	37,86	—
Kürbiskernprotein (H1509)	38,01	—
Antioxidantien NAT Komplex (H1004)	38,20	—
Betain Hydrochlorid (H1119)	40,92	—
Glutathion (H1020)	42,08	—
Antibiose forte Komplex (H1115)	43,74	—
Haferkleie beta-Glucan (H1529)	44,53	—
OPC Proanthocyanidine (Pine Bark) (...)	45,33	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sonnenblumenkernprotein (H1511)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sonnenblumenkernprotein (H1511)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Sonnenblumenkernprotein (...)	22002178	81453	40	from supplier

Validation samples

A total of 53 925 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 *Sonnenblumenkernprotein (H1511)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Sonnenblumenkernprotein (H1511)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Sonnenblumenkernprotein (H1511)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Sonnenblumenkernprotein (H1511)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sonnenblumenkernprotein (H1511)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Sonnenblumenkernprotein (H1511)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81453	81453	0,00	29,40

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 2.8-2024-04

Validated substance/substance group **Spurenelemente BAG Komplex (H1079)**
Substance class **HCK**
Report date 25/11/2024
Report number 10006318-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Spurenelemente BAG Komplex (H1079)

Special notes

When selecting the *Spurenelemente BAG Komplex (H1079)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Spurenelemente BAG Komplex (H1079)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Spurenelemente BAG Komplex (H1079)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Spurenelemente BAG Komplex (H1079)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Magnesium (H1060)	16,02	—
Garcinia Cambogia (H1017)	21,47	—
Spurenelemente JK Komplex (H1080)	32,33	—
Kupfer (H1032)	33,65	—
Spurenelemente SE Komplex (H1082)	34,47	—
Potássio (H1030)	49,82	—
Eisen (H1015)	50,94	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Spurenelemente BAG Komplex (H1079)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Spurenelemente BAG Komplex (H1079)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Spurenelemente BAG Komple...	23002044	81511	40	from supplier

Validation samples

A total of 53 925 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 *Spurenelemente BAG Komplex (H1079)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.

- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Spurenelemente BAG Komplex (H1079)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Spurenelemente BAG Komplex (H1079)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Spurenelemente BAG Komplex (H1079)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Spurenelemente BAG Komplex (H1079)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Spurenelemente BAG Komplex (H1079)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81511	81511	0,00	20,89

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 2.8-2024-04

Validated substance/substance group **Spurenelemente SE Komplex (H1082)**
Substance class **HCK**
Report date 25/11/2024
Report number 10005866-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Spurenelemente SE Komplex (H1082)

Special notes

When selecting the *Spurenelemente SE Komplex (H1082)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Spurenelemente SE Komplex (H1082)	14	15	13

Second-stage model

For differentiation of the substance/substance group *Spurenelemente SE Komplex (H1082)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Spurenelemente SE Komplex (H1082)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Kupfer (H1032)	21,19	—
Magnesium (H1060)	25,46	—
Garcinia Cambogia (H1017)	29,98	—
Eisen (H1015)	35,41	—
Chaga (H1011)	36,57	—
Argentum (H1116)	40,46	—
Walnussblatt Extrakt (H1114)	49,19	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Spurenelemente SE Komplex (H1082)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Spurenelemente SE Komplex (H1082)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Spurenelemente SE Komplex...	14000722	80459	40	from supplier
Hepart	Spurenelemente SE Komplex...	14000721	80461	40	from supplier
Hepart	Spurenelemente SE Komplex...	14000721	80464	40	from supplier
Hepart	Spurenelemente SE Komplex...	15000555	80588	60	from supplier
Hepart	Spurenelemente SE Komplex...	15000555(F2)	80590	60	from supplier
Hepart	Spurenelemente SE Komplex...	15000556(B1)	80592	60	from supplier
Hepart	Spurenelemente SE Komplex...	15000557	80594	60	from supplier
Hepart	Spurenelemente SE Komplex...	15000557(B1)	80595	60	from supplier
Hepart	Spurenelemente SE Komplex...	15000558(B1)	80598	60	from supplier
Hepart	Spurenelemente SE Komplex...	15000553	80600	60	from supplier
Hepart	Spurenelemente SE Komplex...	15000553(F2)	80602	60	from supplier
Hepart	Spurenelemente SE Komplex...	17000888	80961	40	from supplier
Hepart	Spurenelemente SE Komplex...	17000887	80962	40	from supplier
Hepart	Spurenelemente SE Komplex...	19001260	81187	40	from supplier
Hepart	Spurenelemente SE Komplex...	21000339	81407	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 760 spectra of 15 reference samples from the substance/substance group *Spurenelemente SE Komplex (H1082)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 14 different batches.
- 27 516 spectra from a total of 558 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 860 spectra of 18 reference samples from the substance/substance group *Spurenelemente SE Komplex (H1082)*.
- 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	Spurenelemente SE Komplex...	14000720	80460	40
Hepart	Spurenelemente SE Komplex...	15000555 (B1)	80589	60
Hepart	Spurenelemente SE Komplex...	15000556	80591	60
Hepart	Spurenelemente SE Komplex...	15000556 (F2)	80593	60
Hepart	Spurenelemente SE Komplex...	15000557 (F2)	80596	60
Hepart	Spurenelemente SE Komplex...	15000558	80597	60
Hepart	Spurenelemente SE Komplex...	15000558 (F2)	80599	60
Hepart	Spurenelemente SE Komplex...	15000553 (B1)	80601	60
Hepart	Spurenelemente SE Komplex...	17000886	80960	40
Hepart	Spurenelemente SE Komplex...	19001256	81186	40
Hepart	Spurenelemente SE Komplex...	20000407	81260	40
Hepart	Spurenelemente SE Komplex...	20001880	81277	40
Hepart	Spurenelemente SE Komplex...	20002693	81296	40
Hepart	Spurenelemente SE Komplex...	21000339-338-261	81339	40
Hepart	Spurenelemente SE Komplex...	23001536	81504	40
Hepart	Spurenelemente SE Komplex...	14000722	80462	40
Hepart	Spurenelemente SE Komplex...	14000720	80463	40
Hepart	Spurenelemente SE Komplex...	15000558	80979	40

- 21 819 spectra from a total of 480 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 24 spectra from 9 *Apo-Ident* customers from 14 batches from the substance/substance group *Spurenelemente SE Komplex (H1082)*.
- 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 AG/Unisan	Spurenelemente SE Komplex...	19001256/0	1
Hepart AG/Unisan	Spurenelemente SE Komplex...	20001880/0	1
Hepart AG	Spurenelemente SE Komplex...	17000886/0	1
Hepart AG	Spurenelemente SE Komplex...	17000887/0	2
Hepart AG	Spurenelemente SE Komplex...	19001256/0	1
Hepart AG	Spurenelemente SE Komplex...	31301	2
Hepart/Unisan	Spurenelemente SE Komplex...	20001880/0	1
Hepart	Spurenelemente SE Komplex...	15000555/0	1
Hepart	Spurenelemente SE Komplex...	17000886/0	1
Hepart	Spurenelemente SE Komplex...	17000886/1	3
Hepart	Spurenelemente SE Komplex...	17000887/0	2
Hepart	Spurenelemente SE Komplex...	17000888/0	1
Hepart	Spurenelemente SE Komplex...	19001256	2
Hepart	Spurenelemente SE Komplex...	19001260/0	1
Hepart	Spurenelemente SE Komplex...	20000407	1
Hepart	Spurenelemente SE Komplex...	20001880	1
Unisan	Spurenelemente SE Komplex...	15000555	1
Unisan	Spurenelemente SE Komplex...	15000556/0	1

- 2946 spectra from 26 *Apo-Ident* customers from a total of 1446 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 *Spurenelemente SE Komplex (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 *Spurenelemente SE Komplex (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	760	0	27 516
Type B	0	860	0	21 819
Type C	0	22	2	2946

The substance/substance group *Spurenelemente SE Komplex (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 % (> 99.2105 %)
Type B	100.0000 % (> 99.8662 %)	100.0000 % (> 99.3023 %)
Type C	100.0000 % (> 98.8364 %)	91.6667 % (> 79.1667 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80459	80459	0,00	31,54
80461	80461	0,00	32,15
80464	80464	0,00	33,06
80588	80588	0,00	49,86
80590	80590	0,00	48,85
80592	80592	0,00	43,99
80594	80594	0,00	45,57
80595	80595	0,00	44,41
80598	80598	0,00	52,72
80600	80600	0,00	45,34
80602	80602	0,00	44,81
80961	80961	0,00	48,03
80962	80962	0,00	46,76
81187	81187	0,00	25,56
81407	81407	0,00	51,44

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 2.8-2024-04

Validated substance/substance group **Taurin (H1084)**
Substance class HCK
Report date 25/11/2024
Report number 80071-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Taurin (H1084)

Special notes

When selecting the *Taurin (H1084)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Taurin (H1084)	6	5	15

Second-stage model

For differentiation of the substance/substance group *Taurin (H1084)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Taurin (H1084)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antibiose forte Komplex (H1115)	57,30	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Taurin (H1084)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Taurin (H1084)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Taurin (H1084)	14001767	80497	60	from supplier
Hepart	Taurin (H1084)	16000946	80809	40	from supplier
Hepart	Taurin (H1084)	16000946	80887	40	from supplier
Hepart	Taurin (H1084)	18000419	81063	40	from supplier
Hepart	Taurin (H1084)	21001444	81355	50	from supplier
Hepart	Taurin (H1084)	20001267	81382	50	from supplier
Hepart	Taurin (H1084)	22000694	81425	40	from supplier

Validation samples

A total of 53 925 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 *Taurin (H1084)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 27 956 spectra from a total of 566 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the

substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 200 spectra of 5 reference samples from the substance/substance group *Taurin (H1084)*.
- Among them are spectra of independent samples from 5 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	Taurin (H1084)	16000947	80810	40
Hepart	Taurin (H1084)	19000847	81160	40
Hepart	Taurin (H1084)	20001002	81288	40
Hepart	Taurin (H1084)	22002118	81454	40
Hepart	Taurin (H1084)	23001634	81498	40

- 22 479 spectra from a total of 491 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 47 spectra from 18 *Apo-Ident* customers from 18 batches from the substance/substance group *Taurin (H1084)*.
- 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
HCK	Taurin (H1084)	14001767-6	1
Hepart AG, CH-8280 K...	Taurin (H1084)	25710	3
Hepart ag/Unisan	Taurin (H1084)	19000847	1
Hepart AG	Taurin (H1084)	14001767/3	4
Hepart AG	Taurin (H1084)	16000947/0	1
Hepart AG	Taurin (H1084)	16000947/2	3
Hepart AG	Taurin (H1084)	2656905/0	2
Hepart AG	Taurin (H1084)	28001	2
Hepart/Unisan	Taurin (H1084)	14001767/3	1

continued on the next page

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Supplier	Substance	Batch	Spectra
Hepart	Taurin (H1084)	16000946	1
Hepart	Taurin (H1084)	16000946/1	2
Hepart	Taurin (H1084)	160009460/2	1
Hepart	Taurin (H1084)	16000947	5
Hepart	Taurin (H1084)	16000947/0	1
Hepart	Taurin (H1084)	160009470	1
Hepart	Taurin (H1084)	20001002	1
Hepart	Taurin (H1084)	21001444	1
Unisan/Hepart AG	Taurin (H1084)	28001	1
Unisan	Taurin (H1084)	1294960201	2
unisan	Taurin (H1084)	14001767	2
Unisan	Taurin (H1084)	14001767/0	1
Unisan	Taurin (H1084)	16000946	1
Unisan	Taurin (H1084)	16000946/1	1
Unisan	Taurin (H1084)	28001	8

- 2923 spectra from 26 *Apo-Ident* customers from a total of 1442 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 *Taurin (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 *Taurin (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	320	0	27 956
Type B	0	200	0	22 479
Type C	0	46	1	2923

The substance/substance group *Taurin (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 % (> 99.9310 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.8669 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 98.8288 %)	97.8723 % (> 91.4894 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80497	80497	0,00	59,85
80809	80809	0,00	62,32
80887	80887	0,00	61,86
81063	81063	0,00	60,77
81355	81355	0,00	61,43
81382	81382	0,00	62,75
81425	81425	0,00	57,30

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 2.8-2024-04

Validated substance/substance group **Vitamin B6 (Pyridoxal-5-phosphat) (H1136)**
Substance class **HCK**
Report date 25/11/2024
Report number 10006320-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Vitamin B6 (Pyridoxal-5-phosphat) (H1136)

Special notes

When selecting the *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Vitamin B6 (Pyridoxal-5-phosphat) (H1136)	2	0	0

Second-stage model

For differentiation of the substance/substance group *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Vitamin C (H1104)	29,34	—
Aroma Orange (H1405)	33,57	—
Garcinia Cambogia (H1017)	35,02	—
Calcium L-(+) -Lactat Komplex (H1008)	38,61	—
Antioxidantien NAT Komplex (H1004)	38,75	—
Ginkgo Extrakt (H1024)	43,86	—
Potássio (H1030)	45,53	—
Antibiose forte Komplex (H1115)	47,89	—
Pathogene Komplex (H1803)	48,17	—
PET Basis (H1503)	48,40	—
Walnussblatt Extrakt (H1114)	50,16	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan 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 (Pyridoxal-5-phosphat) (H1136)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin B6 (Pyridoxal-5-p...	22000703	81523	30	from supplier
Hepart	Vitamin B6 (Pyridoxal-5-p...	23002378	81524	30	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 60 spectra of 2 reference samples from the substance/substance group *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 28 216 spectra from a total of 570 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)*.
- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)* can clearly be 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 (Pyridoxal-5-phosphat) (H1136)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 216
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Vitamin B6 (Pyridoxal-5-phosphat) (H1136)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9322 %)	100.0000 % (> 90.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81523	81523	0,00	42,00
81524	81524	0,00	37,68

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 2.8-2024-04

Validated substance/substance group **Vitamin C (H1104)**
Substance class HCK
Report date 25/11/2024
Report number 80009-2024-11-25
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

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Vitamin C (H1104)	14	21	37

Second-stage model

For differentiation of the substance/substance group *Vitamin C (H1104)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Vitamin C (H1104)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Antioxidantien NAT Komplex (H1004)	31,19	—
Aroma Orange (H1405)	33,01	—
Ginkgo Extrakt (H1024)	34,78	—
Calcium L-(+) -Lactat Komplex (H1008)	37,95	—
Vitamin B6 (Pyridoxal-5-phosphat) (...)	39,90	—
PET Basis (H1503)	40,20	—
Grüner Kaffee Extrakt (H1433)	43,32	—
Potássio (H1030)	43,33	—
Antibiose forte Komplex (H1115)	43,72	—
L-Arginin (H1036)	49,36	—
PET Immunsystem (H1502)	52,36	—

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.

Calibration samples

Only spectra which have been recorded by *HiperScan 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

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
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 53 925 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.
- 27 518 spectra from a total of 558 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 970 spectra of 21 reference samples 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. 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

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Supplier	Substance	Batch	Sample ID	Spectra
Hepart	Vitamin C (H1104)	19001006	81198	40
Hepart	Vitamin C (H1104)	19000134	81199	40
Hepart	Vitamin C (H1104)	20001591	81269	40
Hepart	Vitamin C (H1104)	20001556	81274	40
Hepart	Vitamin C (H1104)	20002432	81320	40
Hepart	Vitamin C (H1104)	2100112-6-9	81361	50

- 21 709 spectra from a total of 475 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 94 spectra from 20 *Apo-Ident* customers from 42 batches from the substance/substance group *Vitamin C (H1104)*.
- Among them are spectra of independent samples from 37 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
Falcento	Vitamin C (H1104)	44602	1
HCK	Vitamin C (H1104)	14001794/0	1
HCK	Vitamin C (H1104)	14001797/0	2
HCK	Vitamin C (H1104)	16000197-0	2
HCK	Vitamin C (H1104)	16000198-0	2
HCK	Vitamin C (H1104)	16000203/0	2
Hepart / Unisan	Vitamin C (H1104)	170009170	1
Hepart AG, CH-8280 K...	Vitamin C (H1104)	1084025019	1
Hepart AG	Vitamin C (H1104)	1084025020	3
Hepart AG	Vitamin C (H1104)	1085025020	1
Hepart AG	Vitamin C (H1104)	16000197/0	1
Hepart AG	Vitamin C (H1104)	16000198	1
Hepart AG	Vitamin C (H1104)	16000231/0	1
Hepart AG	Vitamin C (H1104)	17000915/0	2
Hepart AG	Vitamin C (H1104)	17000917/0	1
Hepart AG	Vitamin C (H1104)	17000920/0	1
Hepart AG	Vitamin C (H1104)	19001004/0	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/Unisan	Vitamin C (H1104)	19001006/0	1
Hepart	Vitamin C (H1104)	14001794	1
Hepart	Vitamin C (H1104)	16000199-0	1
Hepart	Vitamin C (H1104)	16000201-0	2
Hepart	Vitamin C (H1104)	16000203/0	2
Hepart	Vitamin C (H1104)	16000230-0	1
Hepart	Vitamin C (H1104)	16000231/0	1
Hepart	Vitamin C (H1104)	170009150	1
Hepart	Vitamin C (H1104)	17000919/0	2

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Supplier	Substance	Batch	Spectra
Hepart	Vitamin C (H1104)	17000920/0	1
Hepart	Vitamin C (H1104)	19001004	1
Hepart	Vitamin C (H1104)	19001004/0	3
Hepart	Vitamin C (H1104)	19001005/0	4
Hepart	Vitamin C (H1104)	19001006/0	3
Hepart	Vitamin C (H1104)	20001556/0	1
Hepart	Vitamin C (H1104)	21001126	2
Hepart	Vitamin C (H1104)	21001126/0	2
Unisan Gmbh, 78465 K...	Vitamin C (H1104)	25020	1
Unisan/Hepart AG	Vitamin C (H1104)	44501	1
Unisan/Hepart AG	Vitamin C (H1104)	44602	2
Unisan	Vitamin C (H1104)	1084025020	1
Unisan	Vitamin C (H1104)	1085025020	3
Unisan	Vitamin C (H1104)	14001780/0	1
Unisan	Vitamin C (H1104)	14001788	1
unisan	Vitamin C (H1104)	14001794	1
Unisan	Vitamin C (H1104)	14001797	1
Unisan	Vitamin C (H1104)	16000198	1
Unisan	Vitamin C (H1104)	16000200	1
Unisan	Vitamin C (H1104)	16000203	1
Unisan	Vitamin C (H1104)	16000203/0	1
Unisan	Vitamin C (H1104)	16000231	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)	74001	1

- 2876 spectra from 26 *Apo-Ident* customers from a total of 1418 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	27 518
Type B	0	970	0	21 709
Type C	0	89	5	2876

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 % (> 99.9308 %)	100.0000 % (> 99.2084 %)
Type B	100.0000 % (> 99.8662 %)	100.0000 % (> 99.3814 %)
Type C	100.0000 % (> 98.8248 %)	94.6809 % (> 91.4894 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80363	80363	0,00	50,74
80394	80394	0,00	34,67
80395	80395	0,00	32,97
80396	80396	0,00	43,75
80397	80397	0,00	31,19
80418	80418	0,00	44,45
80438	80438	0,00	50,58
80499	80499	0,00	31,26
80500	80500	0,00	33,65
80501	80501	0,00	36,81
80502	80502	0,00	45,91
80751	80751	0,00	47,16
80753	80753	0,00	50,74
80756	80756	0,00	48,17
80760	80760	0,00	46,90

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 2.8-2024-04

Validated substance/substance group **Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80010-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129); Lutein-Zeaxanthin-Astaxanthin (H1129); Vitamin E NAT (H1107)

Special notes

When selecting the *Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129)	13	22	38

Second-stage model

For differentiation of the substance/substance group *Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Coenzym Q10 (H1013)	18,10	—
Glutathion (H1020)	23,09	—
Ginseng (H1018)	24,06	—
Aroma Orange (H1405)	24,90	—
Haferkleie beta-Glucan (H1529)	25,11	—
Ingwer Extrakt (H1437)	26,84	—
PET Coenzym Q10 (H1505)	27,20	—
Aminomix NAC (H1002)	35,02	—
Kokos (H1522)	36,41	—
Leaky Gut Komplex (H1802)	42,52	—
Chondroitinsulfat (H1065)	43,49	—
L-Glutamin (H1043)	45,44	—
Vitamin K2 (75µg Mono) (H1108)	46,12	—
Bor (H1005)	46,78	—
Calcium L-(+) -Lactat Komplex (H1008)	50,91	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Lutein-Zeaxanthin-Astaxan...	22000706	81438	40	from supplier
Hepart	Lutein-Zeaxanthin-Astaxan...	23002235	81517	40	from supplier
Hepart	Vitamin E NAT (H1107)	071601	80421	40	from supplier
Hepart	Vitamin E NAT (H1107)	071701	80426	35	from supplier
Hepart	Vitamin E NAT (H1107)	14001815	80512	60	from supplier
Hepart	Vitamin E NAT (H1107)	14001821	80513	60	from supplier

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamin E NAT (H1107)	14001822	80514	60	from supplier
Hepart	Vitamin E NAT (H1107)	15001558	80688	60	from supplier
Hepart	Vitamin E NAT (H1107)	15001559(F2)	80690	60	from supplier
Hepart	Vitamin E NAT (H1107)	15001561	80693	60	from supplier
Hepart	Vitamin E NAT (H1107)	15001560(B1)	80694	60	from supplier
Hepart	Vitamin E NAT (H1107)	15001557	80697	60	from supplier
Hepart	Vitamin E NAT (H1107)	16001246	80826	40	from supplier

Validation samples

A total of 53 925 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 675 spectra of 13 reference samples from the substance/substance group *Vitamina E NAT (H1107)* / *Luteína-Zeaxantina-Astaxantina (H1129)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 13 different batches.
- 27 601 spectra from a total of 559 batches from further 129 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 1200 spectra of 25 reference samples from the substance/substance group *Vitamina E NAT (H1107)* / *Luteína-Zeaxantina-Astaxantina (H1129)*.
- 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 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

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Supplier	Substance	Batch	Sample ID	Spectra
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)	22000723	81429	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

- 21 479 spectra from a total of 474 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 74 spectra from 19 *Apo-Ident* customers from 42 batches from the substance/substance group *Vitamina E NAT (H1107) / Luteína-Zeaxantina-Astaxantina (H1129)*.
- Among them are spectra of independent samples from 38 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
	Vitamin E NAT (H1107)	25022	1
HCK	Vitamin E NAT (H1107)	14001822/0	1
HCK	Vitamin E NAT (H1107)	15001557-0	1
Hepart AG, CH-8280 K...	Vitamin E NAT (H1107)	1094017701	1
Hepart AG, CH-8280 K...	Vitamin E NAT (H1107)	65001	1
Hepart ag/ Unsisan	Vitamin E NAT (H1107)	19001883/0	1
Hepart AG	Vitamin E NAT (H1107)	1094025022	1
Hepart AG	Vitamin E NAT (H1107)	15001557	1
Hepart AG	Vitamin E NAT (H1107)	15001557/0	2
Hepart AG	Vitamin E NAT (H1107)	16001246/0	1
Hepart AG	Vitamin E NAT (H1107)	17000890/0	4
Hepart AG	Vitamin E NAT (H1107)	17000891/0	1
Hepart AG	Vitamin E NAT (H1107)	25022	2
Hepart AG	Vitamin E NAT (H1107)	65101	3
Hepart/Unisan	Vitamin E NAT (H1107)	19001496	1
Hepart	Vitamin E NAT (H1107)	14001821	1
Hepart	Vitamin E NAT (H1107)	16000588	1
Hepart	Vitamin E NAT (H1107)	16000588-0	1
Hepart	Vitamin E NAT (H1107)	16000590/0	1
Hepart	Vitamin E NAT (H1107)	16000591/0	1
Hepart	Vitamin E NAT (H1107)	160005910	1
Hepart	Vitamin E NAT (H1107)	16000591-0	1
Hepart	Vitamin E NAT (H1107)	16001246	1

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Supplier	Substance	Batch	Spectra
Hepart	Vitamin E NAT (H1107)	17000890	1
Hepart	Vitamin E NAT (H1107)	17000891	1
Hepart	Vitamin E NAT (H1107)	17000891/0	2
Hepart	Vitamin E NAT (H1107)	17000892/0	1
Hepart	Vitamin E NAT (H1107)	18001024/0	3
Hepart	Vitamin E NAT (H1107)	18001026/0	1
Hepart	Vitamin E NAT (H1107)	19001496	1
Hepart	Vitamin E NAT (H1107)	19001496/0	2
Hepart	Vitamin E NAT (H1107)	19001883/0	1
Hepart	Vitamin E NAT (H1107)	19001884/0	2
Hepart	Vitamin E NAT (H1107)	210000619	1
Hepart	Vitamin E NAT (H1107)	21000619/0	1
Purren Apotheke	Vitamin E NAT (H1107)	945901	1
Unisan 02.04.2016	Vitamin E NAT (H1107)	15001558/0	1
Unisan 2.10.2015	Vitamin E NAT (H1107)	14001821/0	1
Unisan	Vitamin E NAT (H1107)	1094017701	1
Unisan	Vitamin E NAT (H1107)	1094025021	1
Unisan	Vitamin E NAT (H1107)	1095961301	1
Unisan	Vitamin E NAT (H1107)	14001821	1
Unisan	Vitamin E NAT (H1107)	14001821/0	1
Unisan	Vitamin E NAT (H1107)	15001557/0	1
Unisan	Vitamin E NAT (H1107)	15001558	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)	25022	2
Unisan	Vitamin E NAT (H1107)	65001	3
Unisan	Vitamin E NAT (H1107)	71501	4
UNISAN	Vitamin E NAT (H1107)	71701	1

- 2896 spectra from 26 *Apo-Ident* customers from a total of 1418 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 *Vitamina E NAT (H1107)* / *Luteína-Zeaxantina-Astaxantina (H1129)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamina E NAT (H1107)* / *Luteína-Zeaxantina-Astaxantina (H1129)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	675	0	27 601
Type B	0	1200	0	21 479
Type C	0	73	1	2896

The substance/substance group *Vitamina E NAT (H1107)* / *Luteína-Zeaxantina-Astaxantina (H1129)* can be clearly distinguished from all other substances. In order to make these figures comparable, 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 % (> 99.1111 %)
Type B	100.0000 % (> 99.8661 %)	100.0000 % (> 99.5000 %)
Type C	100.0000 % (> 98.8259 %)	98.6486 % (> 94.5946 %)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80421	80421	0,00	23,02
80426	80426	0,00	24,56
80512	80512	0,00	25,87
80513	80513	0,00	21,16
80514	80514	0,00	23,21
80688	80688	0,00	32,17
80690	80690	0,00	31,64
80693	80693	0,00	32,58
80694	80694	0,00	31,27
80697	80697	0,00	33,54
80826	80826	0,00	24,34
81438	81438	0,00	26,84
81517	81517	0,00	25,79

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 2.8-2024-04

Validated substance/substance group **Vitamine BAG Komplex (H1091)**
Substance class HCK
Report date 25/11/2024
Report number 10006323-2024-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Vitamine BAG Komplex (H1091)

Special notes

When selecting the *Vitamine BAG Komplex (H1091)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Vitamine BAG Komplex (H1091)	1	0	0

Second-stage model

For differentiation of the substance/substance group *Vitamine BAG Komplex (H1091)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Vitamine BAG Komplex (H1091)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Orthovimin Neutral Komplex (H1403)	14,59	—
Orthocolon Komplex (H1800)	17,82	—
Rhodiola (H1064)	22,45	—
L-Arginin (H1036)	23,48	—
Vitamin B1 (H1101)	24,49	—
Detox Komplex (H1111)	26,27	—
Safran Griffel (H1434)	30,90	—
Bor (H1005)	31,61	—
Artischocke Extrakt (H1440)	31,64	—
Baobab (H1410)	32,03	—
Óleo de zimbro (H1112)	32,13	—
Zink (H1110)	32,28	—
Leaky Gut Komplex (H1802)	35,24	—
Glutathion (H1020)	35,61	—
Eibisch Extrakt (H1439)	36,03	—
Coenzym Q10 (H1013)	36,10	—
Grüner Kaffee Extrakt (H1433)	36,50	—
Calcium L-(+) -Lactat Komplex (H1008)	36,78	—
Ginseng (H1018)	37,30	—
Silymarin (H1071)	38,89	—
Lycopen (H1058)	38,89	—
Silicium (H1070)	39,68	—
Garcinia Cambogia (H1017)	39,98	—
Konjak Glucomannan (H1530)	42,18	—
Magnesium (H1060)	42,21	—
Selenhefe (H1068)	43,42	—
Enzian Extrakt (H1438)	43,77	—
Granatapfel (H1409)	44,33	—
Aroma Orange (H1405)	45,81	—
OPC Proanthocyanidine (Pine Bark) (...)	46,48	—
Antioxidantien NAT Komplex (H1004)	48,24	—
Vitamin K2 (75µg Mono) (H1108)	50,55	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vitamine BAG Komplex (H1091)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Vitamine BAG Komplex (H1091)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Vitamine BAG Komplex (H1091)	23002040	81528	40	from supplier

Validation samples

A total of 53 925 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 *Vitamine BAG Komplex (H1091)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 28 236 spectra from a total of 571 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Vitamine BAG Komplex (H1091)*.
- 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.
- 22 679 spectra from a total of 496 batches from further 80 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Vitamine BAG Komplex (H1091)*.

- 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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Vitamine BAG Komplex (H1091)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vitamine BAG Komplex (H1091)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	28 236
Type B	0	0	0	22 679
Type C	0	0	0	2970

The substance/substance group *Vitamine BAG Komplex (H1091)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9330 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.8707 %)	n/a (n/a)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
81528	81528	0,00	13,95

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 2.8-2024-04

Validated substance/substance group **Walnussblatt Extrakt (H1114)**
Substance class **HCK**
Report date **25/11/2024**
Report number **80904-2024-11-25**
Executing company **HiperScan GmbH**
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Walnussblatt Extrakt (H1114)

Special notes

When selecting the *Walnussblatt Extrakt (H1114)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-8026-5 *European Pharmacopoeia 11th Edition, Basic Version 2022* [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/substance group	Type A	Type B	Type C
Walnussblatt Extrakt (H1114)	3	0	0

Second-stage model

For differentiation of the substance/substance group *Walnussblatt Extrakt (H1114)* the following second-stage model is used:

no second-stage model

Nearest chemometric neighbors (distance to the nearest foreign sample)

The following table lists the nearest chemometric neighbors of the substance/substance group *Walnussblatt Extrakt (H1114)* in the substance class *HCK*. For *Mahalanobis distances* M that do not meet the criterion $M \geq 9$, the differentiation is questioned. However, it is often possible that substances that the main model could not reliably separate from each other can be differentiated in a second-stage model.

A necessary condition for the output of a clear result is therefore: All substances in the second-stage model must have a distance $M \geq 9$ from each other. All remaining substances must reach $M \geq 9$ in the main model.

Where this is not achieved, an ambiguous result is shown as result which includes at least the two substances that are too close to each other as possible identities (substance group). Alternatively these substances can be excluded from the list of substances identifiable with Apo-Ident.

Substance	Distance in main model	Distance in second-stage model
Kupfer (H1032)	17,33	—
Chaga (H1011)	25,71	—
Spurenelemente SE Komplex (H1082)	26,10	—
Garcinia Cambogia (H1017)	28,55	—
Artemisia annua Extrakt (H1118)	31,76	—
Eisen (H1015)	33,22	—
Pathogene Komplex (H1803)	34,84	—
Antibiose mite Komplex (H1113)	39,56	—
Magnesium (H1060)	42,59	—
Argentum (H1116)	43,02	—
Potássio (H1030)	48,55	—
PET Basis (H1503)	52,04	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Walnussblatt Extrakt (H1114)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Walnussblatt Extrakt (H1114)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hepart	Walnussblatt Extrakt (H1114)	16001149	80904	40	from supplier
Hepart	Walnussblatt Extrakt (H1114)	15001009	80908	40	from supplier
Hepart	Walnussblatt Extrakt (H1114)	19000343/0	81162	40	from supplier

Validation samples

A total of 53 925 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 *Walnussblatt Extrakt (H1114)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 28 156 spectra from a total of 569 batches from further 130 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 *Walnussblatt Extrakt (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	Walnussblatt Extrakt (H1114)	16001149	80907	40

- 22 639 spectra from a total of 495 batches from further 79 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Walnussblatt Extrakt (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.
- 2970 spectra from 26 *Apo-Ident* customers from a total of 1460 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 *Walnussblatt Extrakt (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 *Walnussblatt Extrakt (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	28 156
Type B	0	40	0	22 639
Type C	0	0	0	2970

The substance/substance group *Walnussblatt Extrakt (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 % (> 99.9315 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.8709 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8776 %)	n/a (n/a)

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

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

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
80904	80904	0,00	25,71
80908	80908	0,00	34,84
81162	81162	0,00	30,76

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 10 batches. From these 440 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	L-Prolin (H1051)	066401	40	from supplier
Hepart	Melatonin (H1061)	069101	40	from supplier
Hepart	Melatonin (H1061)	069101	60	from supplier
Hepart	TopFlora multi forte Komplex (H1119)	15001135	60	from supplier
Hepart	Vitamine BAG (H1090)	20000156	40	from supplier
Hepart	Vitamine BAG (H1090)	19002541/0	40	from supplier
Hepart	Vitamine BAG (H1090)	19002481	40	from supplier
Hepart	Vitamine BAG (H1090)	20001365	40	from supplier
Hepart	Vitamine BAG (H1090)	20001935	40	from supplier
Hepart	Vitamine BAG (H1090)	21000740	40	from supplier

Appendix C: Additional validation samples (*Type C*)

Spectra for substances from the field which cannot be identified with this model also enter the validation. In this manner, it is verified that the model also rejects unknown substances. The spectra for these samples were recorded by *Apo-Ident* customers. They belong to *Type C*. The information provided by the customer regarding the manufacturer and batch number is taken over by *HiperScan GmbH* to a large extent unchecked.

The samples originate from 4 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.

0 A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Supplier	Substance	Batch	Spectra
Hepart AG	L-Prolin (H1051)	707801	2
Hepart AG	L-Prolin (H1051)	25707	2
Unisan	L-Prolin (H1051)	66401	3

V

Supplier	Substance	Batch	Spectra
Unisan	Vitamin K2-Ca-Mn Komplex (H...	69001	2

Appendix D: Requirements of validation

In order to ensure adherence to the safe scientific status, the individual methods for manufacturing and testing must be validated under certain circumstances (compare § 34 para. 1 no. 3, § 35 para. 1 no. 4 and para. 4 sentence 1 no. 2 b, para. 6 sentence 3 *ApoBetrO* [Pharmacies Rules and Regulations]). The *ApoBetrO* [Pharmacies Rules and Regulations] incorporates a legal definition in § 1 a para. 16 (quotation translated):

“Validation is the provision of documented proof which with a high degree of safety documents that, via a specific process or standard work process, a medicinal product is manufactured and tested, which is in accordance with previously determined quality features.”

Validation documentation can be used to prove that methods or devices which are not described in the Pharmacopoeia within the meaning of § 6 para. 1 sentence 3 *ApBetrO* [Pharmacies Rules and Regulations] achieve the same results as those in the Pharmacopoeia. On the other hand, with the requirements of the demanded validation it must be observed whether the respective testing method is already incorporated in the Pharmacopoeia.

NIR spectroscopy as a general testing method need not be validated in accordance with the express ruling in the *Ph. Eur. Section 1.1* [3], as it is already described in *Section 2.2.40* of the *Ph. Eur.* as an area of application for the identification of raw materials.

However, a special validation requirement exists for the reference database. This requirement is met with the existing document. Further requirements or rules as to how this proof must be furnished do not exist. It is required that the processes guarantee the same results as the methods and devices in the Pharmacopoeia [17].

Carrying out identity tests with *Apo-Ident* is therefore also possible if the NIR spectroscopy process is not required in the Pharmacopoeia monograph of the substance for identity testing. All NIR analyses with *Apo-Ident* prove several, often all molecule groups and are therefore comparable with a series of individual, targeted chemical proofs [4]. Therefore, the identity proof with *Apo-Ident* replaces the monograph test series (with two or more test combinations).

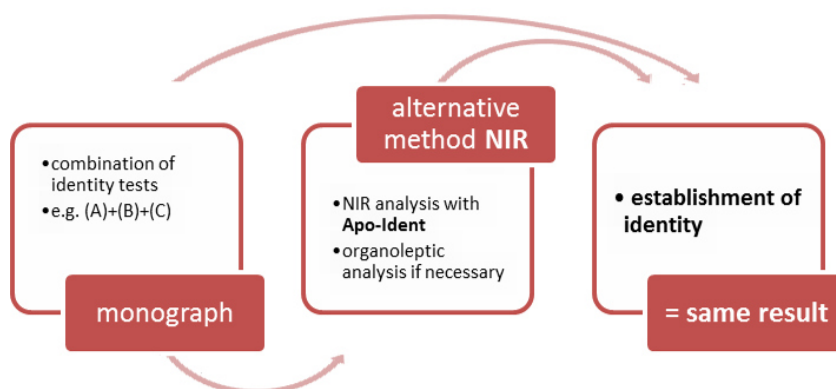


Figure 2: The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

With this validation documentation, proof is furnished that identical results are achieved with *Apo-Ident* and Pharmacopoeia methods, i.e. confirmation of the identity of the raw material [2].

Appendix E: Conformity of Apo-Ident with the European pharmacopeia

According to *Ph. Eur. Section 2.2.40*, NIR spectroscopy is basically suitable for: “Identification of agents, excipients, dosage forms, intermediate manufacturing products, chemical raw materials and packaging materials” ([3], quotation translated).

The fact that *Apo-Ident* meets the further criteria of the European Pharmacopoeia under the headings in *Section 2.2.40*

- Apparatus
- Measurement methods
- Sample preparation and presentation
- Testing the functionality of the instrument
- Identification and characterisation (qualitative analysis)
- Quantitative analysis
- Ongoing model evaluation
- Transfer of databases
- Data storage

can be proven based on the *HiperScan GmbH* documentation of “Meeting 2.2.40 *Ph. Eur.* by *Apo-Ident*” [4].

References

- [1] ABDA – BUNDESVEREINIGUNG DEUTSCHER APOTHEKERVERBÄNDE: Verordnung über den Betrieb von Apotheken (Apothekenbetriebsordnung – ApBetrO), 2012
- [2] REIMANN, B. ; REGIERUNGSPRÄSIDIUM DARMSTADT: Hinweise zur ordnungsgemäßen Prüfung von Arzneimitteln und Ausgangsstoffen (§§ 6 und 11 *ApBetrO*), 2007
- [3] *Europäisches Arzneibuch, Implementation 2022*. 11. Edition. Deutscher Apotheker Verlag (978-3-7692-8026-5)
- [4] HIPERSCAN GMBH: Erfüllung von 2.2.40 Ph. Eur. durch Apo-Ident, 2013
- [5] ARBEITSGEMEINSCHAFT DER PHARMAZIERÄTE DEUTSCHLANDS (APD): Resolution in Verbindung mit §§ 6 und 11 *ApBetrO* Verwendung eines Nah-Infrarot-Spektrometers (NIR) zur Identitätsprüfung, 16. 10. 2013, DAZ 48, November 2013
- [6] ARBEITSGEMEINSCHAFT DER PHARMAZIERÄTE DEUTSCHLANDS (APD): Resolution 2014, Arbeitsgemeinschaft der Pharmazieräte Deutschlands (APD), Oktober 2014
- [7] *DAC/NRF*. Govi-Verlag (978-3-7741-0044-2)
- [8] KESSLER, W.: *Multivariate Datenanalyse*. WILEY-VCH Verlag, 2007 (978-3-527-31262-7)
- [9] NÆS, T. ; ISAKSSON, T. ; FEARN, T. ; DAVIES, T.: *Multivariate Calibration and Classification*. NIR Publications, 2002 (978 0 9528666 2 6)
- [10] HANLEY, J. A. ; LIPPMAN-HAND, A.: If nothing goes wrong, is everything all right? In: *Journal of the American Medical Association* 249 (1983), S. 1743–1745
- [11] JOVANOVIĆ, B. D. ; LEVY, P. S.: A Look at the Rule of Three. In: *The American Statistician* 51 (1997), S. 137–139
- [12] BRONSTEIN, I. N. ; SEMENDJAJEW, K. A. ; MUSIOL, G. ; MÜHLIG, H.: *Taschenbuch der Mathematik*. 5. überarbeitete und erweiterte Auflage. Verlag Harri Deutsch, 2000 (3-8171-2015-2)
- [13] MAHALANOBIS, P.: On the generalized distance in statistics. In: *Proc. Nat. Inst. Sci. India (Calcutta)* 2 (1936), S. 49–55
- [14] YAMBOR, B. ; DRAPER, W. ; BEVERIDGE, R.: Analyzing PCA-based face recognition algorithms: Eigenvector selection and distance measures. In: *Second Workshop Empirical Evaluation in Computer Vision* (2000)
- [15] HIPERSCAN GMBH: Identifikationsmethodik Apo-Ident, 2012
- [16] HIPERSCAN GMBH: Datenvorbehandlung des Identifikationssystems Apo-Ident, 2012
- [17] CYRAN ; RÖTTA: Apothekenbetriebsordnung, Kommentar § 6 Rn. 10, 2010

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