

Validation documentation
TCM - Granulated herbal extracts (PhytoComm)

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 *TCM - Granulated herbal extracts (PhytoComm)*.

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 *TCM - Granulated herbal extracts (PhytoComm)*. Validation documentation is created for each published version of the reference database for all substance classes incorporated.

The reference database is incorporated in the software module *IdentModule*. During identification testing with *Apo-Ident*, spectra which are used for evaluation purposes are presented to it by the *QuickStep* software. In the same manner, the *IdentModule* is presented all validation spectra successively during the validation runs for evaluation purposes. The *IdentModule* responds respectively (without taking the initial assumption into account) with the identified substance or rejects it as unknown. The correctness of this response is checked for each possible initial assumption and counted.

The results are summarised for each substance and reproduced in this document. The core statement of this validation report is that the following criteria must be fulfilled for each database entry, so that *Apo-Ident* offers verification of identity by means of NIR for the relevant substance/substance group:

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

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

Validation concept

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

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

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

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

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

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

Model creation procedure and validation runs

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

1. Collecting the reference spectra (calibration sample)

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

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

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

2. Generating the chemometric models (calibration)

- a) Determination of the transformation matrix from the reference spectra using variance maximisation [8, 9]. (All reference spectra are always included, even if only a few spectra are added for an update.) All reference spectra receive the same data pre-treatment, which is also later applied to all measurement spectra in the field (in the pharmacies).
- b) Checking that the number of principal components used is still sufficient.
- c) Calculating the limits for each substance from the spread of the reference spectra. The calculation regulation is identical for each substance in a substance class.
- d) Überprüfen der Abstände zwischen den Grenzen der trennbaren Substanzen: Die Distanzmatrix enthält die *Mahalanobis-Abstände* von jeder Substanz zu jeder anderen. Die Werte hin und zurück sind jeweils unterschiedlich, weil die Streuung der Ausgangssubstanz eingeht. Ist eine Distanz kleiner als der Mindestabstand, so gelten die Substanzen als nicht sicher trennbar. Der Mindestabstand ist auf 9 festgelegt. Der Entwickler des Modells darf einen größeren Mindestabstand festlegen (ein Wert für das gesamte *chemometrische Modell*), um die Trennschärfe zu erhöhen.
- e) Überprüfung des Modells anhand der Referenzspektren. Es sind keine *falsch-positiven* Ergebnisse erlaubt.

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

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

3. Set of validation spectra (validation samples)

The following is provided for validation:

- 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.)
- 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.)
- 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 *TCM - Granulated herbal extracts (PhytoComm)* in the respective validation reports; otherwise in attachments *A*, *B* and *C*.

Furthermore remains valid: validation spectra may only be removed if a error in the spectrum can be proven. Here, the spectra are not deleted, but instead placed on a *blacklist* incorporating the reason, date and initials in the commentary.

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

4. Validation runs and approval

- Validation spectra are transferred holistically to the *IdentModule* for evaluation in the same way as the spectroscopy software *QuickStep* transfers measured spectra.
- Following the provision of each spectrum, the *IdentModule* responds as to whether it has recognised a substance and which substance was recognised.
- The correctness of this response is checked for each possible initial assumption (each measurable substance with the substance class) and counted according to *true negative*, *false negative*, *true positive* and *false positive*. These figures are provided for each substance and additionally in the section *Summary*, separated according to types *A*, *B* and *C*.

- d) No *false positive* results whatsoever are permissible.
- e) If the criterion is also met for all substance classes, the *IdentModule* is approved.

Particularities of individual substance classes

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

The substance class **APIs & excipients, liquid/semi-solid (other)** (often described as cosmetics) incorporates substances for which no specification of the requirements of the pharmaceutical quality is determined, neither in a Pharmacopoeia monograph, a DAC/NRF monograph nor via a manufacturer's specification. Consequently, neither the identity nor contents can be tested independently. No certificates whatsoever exist for the reference samples. So here, merely the matching of the sample with former samples of this product is established and confusion with the other substances is ruled-out. (If the manufacturer of such a substance prepares a specification, determines testing methods and provides manufacturer's certificates in accordance with *ApBetrO* [Pharmacies Rules and Regulations] §§ 6, 11, *HiperScan GmbH* can assign the substance to the substance class *APIs & excipients, liquid/semi-solid (with analysis certificate)* again in the future).

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

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

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

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

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

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

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

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

Significance of testing with *Apo-Ident*

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

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

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

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

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

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

Conclusion

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

Explanation of terminology

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

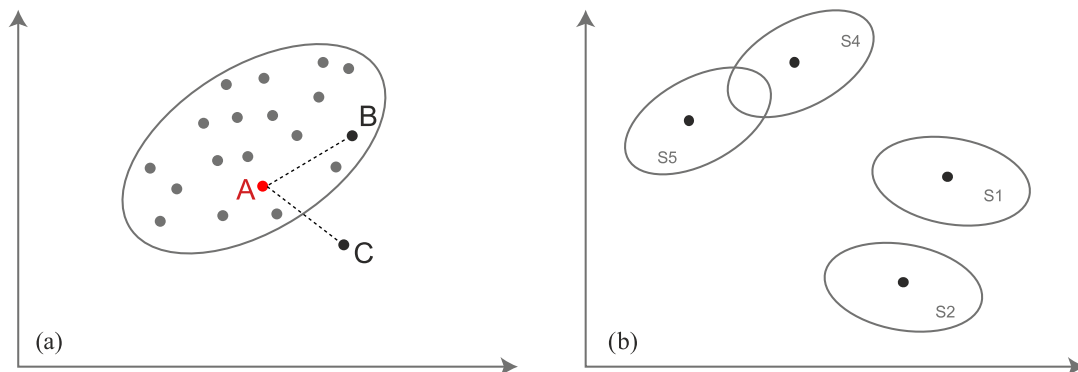


Figure 1: (a) The *Mahalanobis distance* from *A* to *B* is less than from *A* to *C*. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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

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

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

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

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

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

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

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

Summary

A total of 30 254 spectra from 760 different batches for a total of 233 substances were used to validate the substance class *TCM - Granulated herbal extracts (PhytoComm)*.

Validation samples

The validation samples can be categorised as follows:

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

Substance class	Substances	Batches	Spectra
TCM - Granulated herbal extracts (PhytoComm)	159	244	19 480

From category *A* a total of 19 480 spectra from 244 batches for a total of 159 substances were taken into account for validation.

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

Substance class	Substances	Batches	Spectra
TCM - Granulated herbal extracts (PhytoComm)	159	244	9917

From category *B* a total of 9917 spectra from 244 batches for a total of 159 substances were taken into account for validation.

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

Substance class	Substances	Batches	Spectra
TCM - Granulated herbal extracts (PhytoComm)	216	519	857

From category *C* a total of 857 spectra from 519 batches for a total of 216 substances were taken into account for validation.

Validation results

The validation runs checked whether the substances/substance groups in the substance class *TCM - Granulated herbal extracts (PhytoComm)* can be distinguished from 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 *TCM - Granulated herbal extracts (PhytoComm)* 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	59	19 330	150	3 077 781
Type B	126	9739	178	1 566 760
Type C	139	67	596	135 461

Some substances/substance groups in the substance class *TCM - Granulated herbal extracts (PhytoComm)* can only be distinguished from other substances with limitations. (*False positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Typ A	99.998 00 % (> 99.997 89 %)	99.326 52 % (> 99.308 25 %)
Typ B	99.991 40 % (> 99.991 17 %)	98.224 58 % (> 98.188 98 %)
Typ C	99.891 95 % (> 99.888 27 %)	7.670 11 % (> 6.946 58 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 2.3-2020-05

Validated substance/substance group **(Bai) Dou Kou**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002257-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

(Bai) Dou Kou; Amomi cardamomi fructus

Special notes

When selecting the *(Bai) Dou Kou* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
(Bai) Dou Kou	1	0	2

Second-stage model

For differentiation of the substance/substance group *(Bai) Dou Kou* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	(Bai) Dou Kou	G016H0508921	62761	40	from supplier
PhytoComm	(Bai) Dou Kou	G016H0508921	62762	40	from supplier

Validation samples

A total of 30 254 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 *(Bai) Dou Kou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *(Bai) Dou Kou*.
- 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
PhytoComm	(Bai) Dou Kou	G016H0508921	62761 [†]	20
PhytoComm	(Bai) Dou Kou	G016H0508921	62762 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

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

Supplier	Substance	Batch	Spectra
Phytocomm	(Bai) Dou Kou	G016H0508521	1
Phytocomm	(Bai) Dou Kou	G016H0508521	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	2	855

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group (*Bai Dou Kou*) in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ji Li	14.54	—
Sha Ren	14.62	—
Jiang Huang	14.70	—
Gui Zhi	18.57	—
He Huan Pi	19.41	—
E Zhu	21.04	—
Sha Shen (Bei)	22.79	—
Mang Xiao	24.35	—
Yu Jin	24.69	—
Chen Pi	26.71	—
Fu Zi	27.37	—
Wu Yao	28.53	—
Xian He Cao	30.22	—
Ba Ji Tian	30.43	—
Cang Er Zi	30.78	—
Shan Yao	31.38	—
Zhu Ling	31.59	—
Yan Hu Suo	32.81	—
Mu Dan Pi	32.87	—
Niu Bang Zi	34.88	—
Sheng Jiang	36.25	—
Zi Su Zi	36.27	—
Xiang Fu	37.03	—
Huang Lian	37.32	—
He Shou Wu	37.46	—
Chuan Lian Zi	37.61	—
Zhi Ke	39.57	—
Du Huo	39.67	—
Xi Xian Cao	40.52	—
(Huai) Niu Xi	41.67	—
Bai Bian Dou	41.68	—
Bai Xian Pi	41.89	—
Xin Yi	41.96	—
Di Gu Pi	41.97	—
Yuan Zhi	42.19	—
Sang Zhi	42.76	—
Dang Gui	42.82	—
Hu Zhang	42.86	—
Sang Ji Shend	43.13	—
Wang Bu Liu Xing	43.14	—
Sang Bai Pi	43.18	—
Qiang Huo	43.41	—
(Shi) Chang Pu	43.55	—
Hong Jing Tian	43.61	—
Fang Feng	43.61	—
Lai Fu Zi	43.74	—
San Qi	44.68	—
Du Zhong	45.31	—
Qing Pi	46.71	—
Gu Sui Bu	47.36	—
Fu Ling	47.66	—
Mao Dong Qing	48.47	—

continued on the next page

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Substanz	Distance in main model	Distance in second-stage model
Tian Hua Fen	48.64	—
Yin Chen Hao	49.22	—
Dan Dou Chi	49.32	—
Tu Fu Ling	49.45	—
Mai Ya	49.62	—
Bu Gu Zhi	49.82	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62761	62761	0.00	14.54
62762	62762	0.00	14.68

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 2.3-2020-05

Validated substance/substance group (Huai) Niu Xi
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002255-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

(Huai) Niu Xi; Achyranthis bidentatae radix

Special notes

When selecting the (Huai) Niu Xi substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
(Huai) Niu Xi	1	0	4

Second-stage model

For differentiation of the substance/substance group (Huai) Niu Xi the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	(Huai) Niu Xi	G003H1905921	62759	40	from supplier
PhytoComm	(Huai) Niu Xi	G003H1905921	62760	40	from supplier

Validation samples

A total of 30 254 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 (*Huai*) *Niu Xi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group (*Huai*) *Niu Xi*.
- 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
PhytoComm	(Huai) Niu Xi	G003H1905921	62759 [†]	20
PhytoComm	(Huai) Niu Xi	G003H1905921	62760 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

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

Supplier	Substance	Batch	Spectra
Phytocomm	(Huai) Niu Xi	G003H1905222	1
Phytocomm	(Huai) Niu Xi	g003h1905222	1
Phytocomm	(Huai) Niu Xi	G003H1905321	3
Phytocomm	(Huai) Niu Xi	G003H1905422	1
PhytoComm	(Huai) Niu Xi	G003H1905222	1
PhytoComm	(Huai) Niu Xi	G003H1905222	1
PhytoComm	(Huai) Niu Xi	G003H1905422	1

- 848 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	6	0	9	842

The substance/substance group (*Huai*) *Niu Xi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.3488 % (> 98.7614 %)	n/a (n/a)

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

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group (*Huai*) *Niu Xi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yuan Zhi	10.74	—
Gua Lou	13.63	—
Huang Qi	13.95	—
Bai Mao Gen	14.56	—
Jie Geng	15.42	—
Sang Zhi	16.74	—
Qing Pi	18.89	—
Di Gu Pi	20.45	—
Chi Shao (Yao)	24.10	—
Bai Zhu	24.33	—
(Shi) Chang Pu	24.40	—
Ku Shen	25.00	—
Xiang Fu	26.22	—
Tian Hua Fen	26.35	—
Niu Bang Zi	26.77	—
Du Huo	27.93	—
Fang Feng	29.32	—
Xie Bai	29.43	—
Shan Yao	30.35	—
Ju Hua	30.35	—
Lai Fu Zi	31.11	—
Ji Li	31.23	—
Dang Gui	31.52	—
Mu Dan Pi	32.00	—
Gui Zhi	32.39	—
Sheng Jiang	32.72	—
Zhi Ke	33.37	—
Mang Xiao	33.84	—
Qin Jiao	35.16	—
Zi Su Zi	35.20	—
E Zhu	36.63	—
Cang Er Zi	37.07	—
San Qi	37.47	—
Ba Ji Tian	37.70	—
Jin Yin Hua	39.22	—
Pu Gong Ying	39.32	—
Gan Cao	39.35	—
Wu Yao	39.36	—
Dong Gua Zi	39.53	—
Chen Pi	39.58	—
Sha Shen (Bei)	39.70	—
Lian Zi	40.05	—
Jiang Huang	40.84	—
Shan Yu Rou	40.98	—
Wu Wei Zi	41.69	—
Bai Bian Dou	41.69	—
Yan Hu Suo	41.74	—
Fu Zi	42.19	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Xian Pi	42.87	—
Zhe Bei Mu	43.93	—
Yi Mu Cao	44.99	—
(Bai) Dou Kou	45.09	—
Chai Hu	45.71	—
Chuan Lian Zi	46.33	—
Qiang Huo	46.79	—
Long Dan (Cao)	46.97	—
Sha Ren	47.25	—
Lian Qiao	47.98	—
Chuan Xiong	47.99	—
Tu Fu Ling	48.02	—
Xian He Cao	48.75	—
Bai Shao Yao	48.85	—
Mai Men Dong	48.90	—
Huang Bo	49.32	—
Ban Zhi Lian	49.52	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62760	62760	0.00	12.43
62759	62759	0.00	10.74

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 2.3-2020-05

Validated substance/substance group (Ku) Xing Ren
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50290-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

(Ku) Xing Ren; Armeniacae amarum semen

Special notes

When selecting the (Ku) Xing Ren substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
(Ku) Xing Ren	3	0	5

Second-stage model

For differentiation of the substance/substance group (Ku) Xing Ren the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	(Ku) Xing Ren	G029H0708821	62393	40	from supplier
PhytoComm	(Ku) Xing Ren	G029H0708821	62394	40	from supplier
PhytoComm	(Ku) Xing Ren	G029H0708823	62509	40	from supplier
PhytoComm	(Ku) Xing Ren	G029H0708823	62510	40	from supplier
PhytoComm	(Ku) Xing Ren	G029H0708921	62767	40	from supplier
PhytoComm	(Ku) Xing Ren	G029H0708921	62768	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *(Ku) Xing Ren*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *(Ku) Xing Ren*.
- 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
PhytoComm	(Ku) Xing Ren	G029H0708821	62393 [†]	20
PhytoComm	(Ku) Xing Ren	G029H0708821	62394 [†]	20
PhytoComm	(Ku) Xing Ren	G029H0708823	62509 [†]	20
PhytoComm	(Ku) Xing Ren	G029H0708823	62510 [†]	20
PhytoComm	(Ku) Xing Ren	G029H0708921	62767 [†]	20
PhytoComm	(Ku) Xing Ren	G029H0708921	62768 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 10 spectra from 7 *Apo-Ident* customers from 6 batches from the substance/substance group *(Ku) Xing Ren*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
phytocomm	(Ku) Xing Ren	g029h0708322	2
Phytocomm	(Ku) Xing Ren	G029H0708125	2
Phytocomm	(Ku) Xing Ren	g029h0708122	1
PhytoComm	(Ku) Xing Ren	G029H708125	1
PhytoComm	(Ku) Xing Ren	G029H0708125	1
PhytoComm	(Ku) Xing Ren	G029H0708322	2
PhytoComm	(Ku) Xing Ren	G029H0708622	1

- 847 spectra from 13 *Apo-Ident* customers from a total of 513 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	240	0	19 240
Type B	0	120	0	9797
Type C	0	0	10	847

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9281 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8250 %)	n/a (n/a)

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group (*Ku*) *Xing Ren* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hua Shi	59.61	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62767	62767	0.00	59.61
62510	62510	0.00	61.23
62393	62393	0.00	61.93
62768	62768	0.00	59.66
62394	62394	0.00	61.97
62509	62509	0.00	61.22

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 2.3-2020-05

Validated substance/substance group (Sheng) Di Huang
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60005-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

(Sheng) Di Huang; Rehmanniae radix

Special notes

When selecting the (Sheng) Di Huang substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
(Sheng) Di Huang	2	0	5

Second-stage model

For differentiation of the substance/substance group (Sheng) Di Huang the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	(Sheng) Di Huang	G211H0532822	62311	40	from supplier
PhytoComm	(Sheng) Di Huang	G211H0532822	62312	40	from supplier
PhytoComm	(Sheng) Di Huang	G211H0532921	62749	40	from supplier
PhytoComm	(Sheng) Di Huang	G211H0532921	62750	40	from supplier

Validation samples

A total of 30 254 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 *(Sheng) Di Huang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *(Sheng) Di Huang*.
- 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
PhytoComm	(Sheng) Di Huang	G211H0532822	62311 [†]	20
PhytoComm	(Sheng) Di Huang	G211H0532822	62312 [†]	20
PhytoComm	(Sheng) Di Huang	G211H0532921	62749 [†]	20
PhytoComm	(Sheng) Di Huang	G211H0532921	62750 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 8 spectra from 5 *Apo-Ident* customers from 5 batches from the substance/substance group (*Sheng*) *Di Huang*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	(Sheng) Di Huang	g211h0532121	1
Phytocomm	(Sheng) Di Huang	g211h053221	1
Phytocomm	(Sheng) Di Huang	G211H0532521	4
PhytoComm	(Sheng) Di Huang	G211H0532621	1
	(Sheng) Di Huang	g211h0532323	1

- 849 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group (*Sheng*) *Di Huang* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with (*Sheng*) *Di Huang* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	1	2	6	848

The substance/substance group (*Sheng*) *Di Huang* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.9690 % (> 99.3816 %)	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

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group (*Sheng*) *Di Huang* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yu Xing Cao	9.38	—
Wu Jia Pi	20.61	—
Pu Gong Ying	24.82	—
Shu Di (Huang)	25.64	—
Ai Ye	29.97	—
Sha Ren	30.78	—
Jing Jie	35.86	—
Dan Zhu Ye	39.81	—
Sang Bai Pi	40.88	—
Guang Huo Xiang	40.97	—
Jue Ming Zi	43.75	—
Hua Shi	45.54	—
Ge Gen	48.26	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62311	62311	0.00	9.38
62312	62312	0.00	9.57
62749	62749	0.00	11.63
62750	62750	0.00	11.92

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 2.3-2020-05

Validated substance/substance group (Shi) Chang Pu
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60426-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

(Shi) Chang Pu; Acori rhizoma

Special notes

When selecting the (Shi) Chang Pu substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
(Shi) Chang Pu	1	0	5

Second-stage model

For differentiation of the substance/substance group (Shi) Chang Pu the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	(Shi) Chang Pu	G006H0544821	62399	40	from supplier
PhytoComm	(Shi) Chang Pu	G006H0544821	62400	40	from supplier

Validation samples

A total of 30 254 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 *(Shi) Chang Pu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *(Shi) Chang Pu*.
- 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
PhytoComm	(Shi) Chang Pu	G006H0544821	62399 [†]	20
PhytoComm	(Shi) Chang Pu	G006H0544821	62400 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 5 spectra from 3 *Apo-Ident* customers from 5 batches from the substance/substance group *(Shi) Chang Pu*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Herbasinica	(Shi) Chang Pu	g006h0544321	1
Phytocomm	(Shi) Chang Pu	G006H0544322	1
Phytocomm	(Shi) Chang Pu	G006H0544122	1
Phytocomm	(Shi) Chang Pu	g006h0544023	1
Phytocomm	(Shi) Chang Pu	G006HS2700N1	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	1	1	4	851

The substance/substance group *(Shi) Chang Pu* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.5349 % (> 98.9480 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group (*Shi*) *Chang Pu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Xiang Fu	9.10	—
Du Huo	11.96	—
Qing Pi	16.15	—
Dang Gui	17.74	—
Bai Mao Gen	18.52	—
Wu Yao	19.20	—
Tian Hua Fen	19.27	—
Gua Lou	19.85	—
Sang Zhi	19.90	—
Mu Dan Pi	21.65	—
Di Gu Pi	22.21	—
Fang Feng	22.84	—
Ju Hua	22.91	—
(Huai) Niu Xi	22.95	—
Huang Qi	24.12	—
Shan Yao	25.73	—
Gui Zhi	26.06	—
Ji Li	26.71	—
Jiang Huang	26.79	—
Sha Ren	27.28	—
Chen Pi	27.58	—
Xie Bai	28.57	—
(Bai) Dou Kou	28.99	—
Xian He Cao	29.34	—
Yan Hu Suo	29.52	—
Fu Zi	29.98	—
Ku Shen	30.46	—
Jie Geng	30.61	—
Pu Gong Ying	31.68	—
Zhi Ke	31.71	—
Ba Ji Tian	31.82	—
E Zhu	32.22	—
Cang Er Zi	32.28	—
Niu Bang Zi	33.06	—
Chi Shao (Yao)	33.11	—
Mang Xiao	33.83	—
Yi Mu Cao	34.22	—
Zi Su Zi	34.49	—
Qiang Huo	34.59	—
Xin Yi	36.39	—
Gu Sui Bu	36.69	—
Huang Lian	36.78	—
Wu Wei Zi	37.12	—
He Huan Pi	37.27	—
Huang Bo	37.33	—
Sha Shen (Bei)	37.36	—
Yu Jin	37.39	—
Chuan Lian Zi	37.95	—
Wu Zhu Yu	38.93	—
Sheng Jiang	39.26	—
Qin Jiao	39.29	—
Sang Ye	39.56	—

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Substanz	Distance in main model	Distance in second-stage model
Mao Dong Qing	39.95	—
Bai Zhu	40.09	—
Xu Duan	40.61	—
Lai Fu Zi	41.22	—
Yuan Zhi	41.46	—
He Shou Wu	42.23	—
Nü Zhen Zi	43.06	—
Du Zhong	43.23	—
Jin Yin Hua	43.60	—
Tu Fu Ling	43.64	—
Hong Jing Tian	44.27	—
Sang Ji Shend	45.10	—
Ge Gen	45.60	—
Gan Cao	46.40	—
Zi Hua Di Ding	46.57	—
Sang Bai Pi	46.78	—
Bai Xian Pi	46.94	—
Lian Zi	47.00	—
Dan Dou Chi	47.36	—
Dong Gua Zi	48.08	—
Yin Chen Hao	48.23	—
Hu Zhang	48.29	—
Dan Shen	48.44	—
Xi Xian Cao	48.68	—
Ye Jiao Teng	49.44	—
San Qi	49.66	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62399	62399	0.00	10.03
62400	62400	0.00	9.10

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Ai Ye**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002258-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ai Ye; Artemisiae argyi folium

Special notes

When selecting the *Ai Ye* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ai Ye	1	0	3

Second-stage model

For differentiation of the substance/substance group *Ai Ye* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ai Ye	G033H0613821	62771	40	from supplier
PhytoComm	Ai Ye	G033H0613821	62772	40	from supplier

Validation samples

A total of 30 254 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 *Ai Ye*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ai Ye*.
- 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
PhytoComm	Ai Ye	G033H0613821	62771 [†]	20
PhytoComm	Ai Ye	G033H0613821	62772 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Ai Ye*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ai Ye	G033H0613022	1
Phytocomm	Ai Ye	G033H0613421	1
PhytoComm	Ai Ye	G033H0613021	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	3	854

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8280 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ai Ye* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Jue Ming Zi	15.64	—
Shu Di (Huang)	19.50	—
Guang Huo Xiang	19.60	—
Yu Xing Cao	24.55	—
Pu Gong Ying	28.39	—
(Sheng) Di Huang	34.47	—
Hua Shi	44.55	—
Wu Mei	45.57	—
Xuan Shen	45.61	—
Jin Qian Cao	47.37	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62771	62771	0.00	15.64
62772	62772	0.00	16.04

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Ba Ji Tian**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60138-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ba Ji Tian; Morindae officinalis radix

Special notes

When selecting the *Ba Ji Tian* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ba Ji Tian	1	0	0

Second-stage model

For differentiation of the substance/substance group *Ba Ji Tian* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ba Ji Tian	G165H0445821	62407	40	from supplier
PhytoComm	Ba Ji Tian	G165H0445821	62408	40	from supplier

Validation samples

A total of 30 254 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 *Ba Ji Tian*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ba Ji Tian*.
- 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
PhytoComm	Ba Ji Tian	G165H0445821	62407 [†]	20
PhytoComm	Ba Ji Tian	G165H0445821	62408 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Ba Ji Tian*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ba Ji Tian* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

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

Substance	Distance in main model	Distance in second-stage model
Ji Li	13.86	—
Dang Gui	13.93	—
Sang Zhi	14.26	—
(Huai) Niu Xi	15.01	—
Jie Geng	16.97	—
Bai Mao Gen	17.44	—
Di Gu Pi	18.07	—
Chuan Lian Zi	18.62	—
Fang Feng	18.86	—
Xie Bai	20.23	—
Chen Pi	21.03	—
Du Huo	21.23	—
E Zhu	21.32	—
Long Dan (Cao)	21.40	—
Mu Dan Pi	23.05	—
Sheng Jiang	23.98	—
Huang Qi	24.04	—
Lai Fu Zi	24.23	—
San Qi	25.17	—
Gui Zhi	25.63	—
Mang Xiao	26.71	—
Tian Hua Fen	26.90	—
Bai Zhu	27.43	—
Zi Su Zi	29.41	—
Ju Hua	30.17	—
Jiang Huang	30.34	—
Sha Shen (Bei)	30.36	—
Qing Pi	30.86	—
Yan Hu Suo	30.94	—
Yuan Zhi	31.16	—
(Shi) Chang Pu	31.61	—
Mai Men Dong	31.63	—
Shan Yao	32.24	—
He Huan Pi	32.27	—
Bai Bian Dou	32.40	—
Xiang Fu	32.49	—
Mai Ya	33.28	—
Xian He Cao	34.09	—
Qin Jiao	34.66	—
Wu Yao	34.97	—
Da Zao	35.93	—
Gua Lou	37.26	—
Niu Bang Zi	37.48	—
Sha Ren	38.15	—
Cang Er Zi	38.46	—
(Bai) Dou Kou	38.86	—
Lian Zi	41.72	—
Zhu Ling	42.07	—
Wang Bu Liu Xing	42.60	—
Zhi Ke	43.35	—
Chi Shao (Yao)	43.39	—
Ku Shen	44.11	—
Yu Jin	44.15	—
Rou Gui	44.85	—
Bai Xian Pi	45.06	—
Fu Ling	45.31	—
Bai He	45.42	—
Jin Yin Hua	45.44	—
Qiang Huo	46.43	—

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Substanz	Distance in main model	Distance in second-stage model
Dong Gua Zi	46.73	—
Bai Shao Yao	47.51	—
Wu Wei Zi	48.27	—
Sang Ji Shend	48.40	—
Huang Lian	48.68	—
Gu Sui Bu	48.68	—
Ban Zhi Lian	49.48	—
Du Zhong	49.55	—
Tu Fu Ling	50.04	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62408	62408	0.00	13.86
62407	62407	0.00	13.93

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 2.3-2020-05

Validated substance/substance group **Bai Bian Dou**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60204-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bai Bian Dou; Dolichoris lablab semen

Special notes

When selecting the *Bai Bian Dou* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bai Bian Dou	1	0	1

Second-stage model

For differentiation of the substance/substance group *Bai Bian Dou* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bai Bian Dou	G093H0510821	62527	40	from supplier
PhytoComm	Bai Bian Dou	G093H0510821	62528	40	from supplier

Validation samples

A total of 30 254 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 *Bai Bian Dou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Bai Bian Dou*.
- 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
PhytoComm	Bai Bian Dou	G093H0510821	62527 [†]	20
PhytoComm	Bai Bian Dou	G093H0510821	62528 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Bai Bian Dou*.
- 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
Phytocomm	Bai Bian Dou	g093h0510221	1
Phytocomm	Bai Bian Dou	G093H0510221	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	2	855

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai Bian Dou* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zi Su Zi	15.38	—
Cang Er Zi	15.81	—
San Qi	21.23	—
Xie Bai	21.57	—
Lai Fu Zi	27.47	—
Mang Xiao	27.78	—
E Zhu	28.75	—
Ji Li	29.38	—
Shan Yao	29.50	—
Jiang Huang	31.21	—
Wang Bu Liu Xing	32.27	—
Dong Gua Zi	32.54	—
Niu Bang Zi	32.62	—
Di Gu Pi	33.07	—
Sang Zhi	33.30	—
Sheng Jiang	33.64	—
Chen Pi	34.76	—
Gui Zhi	34.88	—
Jie Geng	36.29	—
Ba Ji Tian	36.47	—
Long Dan (Cao)	38.23	—
Chuan Lian Zi	38.25	—
Yan Hu Suo	38.95	—
Tian Hua Fen	39.75	—
Sha Shen (Bei)	40.62	—
Fang Feng	41.98	—
(Huai) Niu Xi	42.14	—
Sha Ren	42.27	—
Bai Zhu	42.97	—
Mai Men Dong	43.00	—
Bai Xian Pi	43.16	—
Du Huo	44.11	—
Ku Shen	44.55	—
Xiang Fu	44.69	—
Huang Qi	44.73	—
Gua Lou	45.43	—
Qing Pi	45.53	—
(Bai) Dou Kou	45.92	—
Fu Ling	46.44	—
Qiang Huo	46.52	—
Dang Gui	47.05	—
Mu Dan Pi	47.85	—
He Huan Pi	48.04	—
(Shi) Chang Pu	49.17	—
Yuan Zhi	49.24	—
Wu Wei Zi	49.37	—
Lian Zi	49.75	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62527	62527	0.00	15.38
62528	62528	0.00	15.81

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 2.3-2020-05

Validated substance/substance group **Bai He**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60093-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bai He; Lili bulb

Special notes

When selecting the *Bai He* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bai He	1	0	2

Second-stage model

For differentiation of the substance/substance group *Bai He* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bai He	G139H0607921	62739	40	from supplier
PhytoComm	Bai He	G139H0607921	62740	40	from supplier

Validation samples

A total of 30 254 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 *Bai He*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Bai He*.
- 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
PhytoComm	Bai He	G139H0607921	62739 [†]	20
PhytoComm	Bai He	G139H0607921	62740 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 5 spectra from 5 *Apo-Ident* customers from 3 batches from the substance/substance group *Bai He*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Bai He	g139h0607221	1
Phytocomm	Bai He	G139H0607421	2
PhytoComm	Bai He	G139H0607221	1
PhytoComm	Bai He	G139H0607421	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	39	1	9877
Type C	0	0	5	852

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai He* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chuan Lian Zi	9.35	—
Mai Men Dong	14.71	—
Mai Ya	15.00	—
Jie Geng	16.41	—
San Qi	17.16	—
Da Zao	17.53	—
Di Gu Pi	17.94	—
Sheng Jiang	19.24	—
Lai Fu Zi	21.46	—
Long Dan (Cao)	22.49	—
Dang Gui	23.28	—
Mang Xiao	23.84	—
Sang Zhi	24.38	—
Bai Zhu	26.42	—
Bai Bian Dou	26.60	—
Tian Hua Fen	27.31	—
E Zhu	27.88	—
Mu Dan Pi	30.04	—
Du Huo	30.10	—
Ba Ji Tian	31.33	—
Qin Jiao	34.07	—
Yan Hu Suo	34.35	—
Zhu Ling	36.23	—
Ban Zhi Lian	37.69	—
Huang Qi	38.73	—
Ji Li	39.17	—
Cang Er Zi	39.19	—
Rou Gui	39.21	—
Shan Yao	39.25	—
Yi Yi Ren	39.59	—
Zi Su Zi	39.83	—
Jiang Huang	39.94	—
Xie Bai	42.23	—
Qing Pi	42.42	—
(Huai) Niu Xi	42.76	—
Fu Ling	43.10	—
Gui Zhi	43.41	—
Fang Feng	44.36	—
Lian Zi	44.57	—
Tian Men Dong	45.89	—
Ma Huang Gen	45.90	—
Bai Xian Pi	48.05	—
Tu Fu Ling	48.35	—
(Shi) Chang Pu	48.76	—
Sha Shen (Bei)	49.10	—
Chen Pi	49.38	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62739	62739	0.00	9.40
62740	62740	0.00	9.35

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 2.3-2020-05

Validated substance/substance group **Bai Hua She She Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60039-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bai Hua She She Cao; Oldenlandiae diffusae herba

Special notes

When selecting the *Bai Hua She She Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bai Hua She She Cao	1	0	2

Second-stage model

For differentiation of the substance/substance group *Bai Hua She She Cao* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bai Hua She She ...	G173HS078RW1	62575	40	from supplier
PhytoComm	Bai Hua She She ...	G173HS078RW1	62576	40	from supplier

Validation samples

A total of 30 254 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 *Bai Hua She She Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Bai Hua She She Cao*.
- 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
PhytoComm	Bai Hua She She Cao	G173HS078RW1	62575 [†]	20
PhytoComm	Bai Hua She She Cao	G173HS078RW1	62576 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 7 spectra from 4 *Apo-Ident* customers from 2 batches from the substance/substance group *Bai Hua She She Cao*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Bai Hua She She Cao	G173H1153222	3
Phytocomm	Bai Hua She She Cao	G173H1153421	4

- 850 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	7	850

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8255 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai Hua She She Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Han Lian Cao	9.57	—
Xia Ku Cao	12.91	—
Hu Zhang	14.96	—
Zhi Shi	16.19	—
Sang Ye	16.95	—
Xi Xian Cao	17.43	—
Pu Gong Ying	21.41	—
Jiang Huang	22.97	—
Huang Lian	24.37	—
Xin Yi	25.02	—
Tu Fu Ling	25.50	—
Sha Ren	25.96	—
Shan Yao	28.30	—
Yi Mu Cao	29.11	—
He Huan Pi	29.83	—
Nü Zhen Zi	30.07	—
Rou Cong Rong	30.61	—
Fu Zi	30.66	—
Huang Bo	31.44	—
Gui Zhi	31.63	—
Qiang Huo	31.68	—
Gu Sui Bu	34.96	—
Sang Ji Shend	35.29	—
Dan Zhu Ye	35.70	—
Gou Teng	36.90	—
Du Zhong	45.19	—
Wu Yao	45.48	—
Qing Pi	45.52	—
Xu Duan	46.37	—
Ju Hua	47.66	—
Sang Bai Pi	47.88	—
Chen Pi	48.66	—
Wu Zhu Yu	49.26	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62576	62576	0.00	10.93
62575	62575	0.00	9.57

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Bai Mao Gen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60654-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bai Mao Gen; Imperatae cylindricae rhizoma

Special notes

When selecting the *Bai Mao Gen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bai Mao Gen	1	0	1

Second-stage model

For differentiation of the substance/substance group *Bai Mao Gen* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bai Mao Gen	G125H0512821	62537	40	from supplier
PhytoComm	Bai Mao Gen	G125H0512821	62538	40	from supplier

Validation samples

A total of 30 254 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 *Bai Mao Gen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Bai Mao Gen*.
- 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
PhytoComm	Bai Mao Gen	G125H0512821	62537 [†]	20
PhytoComm	Bai Mao Gen	G125H0512821	62538 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 2 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Bai Mao Gen*.
- 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
Phytocomm	Bai Mao Gen	G125H0512221	2

- 855 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	4	0	2	851

The substance/substance group *Bai Mao Gen* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.6554 % (> 99.0705 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai Mao Gen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Huang Qi	15.02	—
Sang Zhi	15.66	—
Dang Gui	16.12	—
Bai Zhu	17.09	—
(Huai) Niu Xi	17.21	—
Jie Geng	17.36	—
Ba Ji Tian	20.01	—
Du Huo	20.41	—
Fang Feng	20.68	—
Yuan Zhi	20.70	—
Mu Dan Pi	21.26	—
Tian Hua Fen	23.33	—
Di Gu Pi	24.47	—
Ju Hua	26.45	—
Ji Li	26.86	—
Gua Lou	27.19	—
Qing Pi	28.33	—
(Shi) Chang Pu	28.61	—
Chi Shao (Yao)	29.91	—
Xiang Fu	30.05	—
Chen Pi	30.99	—
Xie Bai	31.01	—
E Zhu	31.49	—
Mang Xiao	32.03	—
Qin Jiao	33.74	—
Lai Fu Zi	34.43	—
Mai Men Dong	35.11	—
Chuan Lian Zi	35.66	—
Zhi Ke	36.06	—
Shan Yao	36.43	—
Wu Yao	36.47	—
Gui Zhi	36.82	—
Sheng Jiang	37.76	—
Ku Shen	37.99	—
Long Dan (Cao)	38.16	—
San Qi	40.06	—
Sha Shen (Bei)	40.43	—
Zi Su Zi	40.46	—
Da Zao	43.58	—
He Huan Pi	43.74	—
Lian Zi	44.15	—
Jiang Huang	44.15	—
Jin Yin Hua	44.56	—
Xian He Cao	44.77	—
Long Yan Rou	45.12	—
Mai Ya	45.77	—
Niu Bang Zi	45.87	—
Yan Hu Suo	46.45	—
Gu Sui Bu	46.61	—
Cang Er Zi	46.65	—
Ban Zhi Lian	46.99	—
Sha Ren	47.35	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Xian Pi	47.42	—
Bai Shao Yao	47.93	—
Bai Bian Dou	48.40	—
Tu Fu Ling	49.04	—
Pu Gong Ying	49.38	—
Wu Wei Zi	49.51	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62538	62538	0.00	15.02
62537	62537	0.00	15.12

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 2.3-2020-05

Validated substance/substance group **Bai Shao Yao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60007-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bai Shao Yao; Paeoniae lactiflorae albus radix

Special notes

When selecting the *Bai Shao Yao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bai Shao Yao	3	0	5

Second-stage model

For differentiation of the substance/substance group *Bai Shao Yao* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bai Shao Yao	G179HS065RQ1	62275	40	from supplier
PhytoComm	Bai Shao Yao	G179HS065RT1	62435	40	from supplier
PhytoComm	Bai Shao Yao	G179HS065RT1	62436	40	from supplier
PhytoComm	Bai Shao Yao	G179HS065RW1	62601	40	from supplier
PhytoComm	Bai Shao Yao	G179HS065RW1	62602	40	from supplier

Validation samples

A total of 30 254 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 *Bai Shao Yao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 280 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 159 spectra of 6 reference samples from the substance/substance group *Bai Shao Yao*.
- 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
PhytoComm	Bai Shao Yao	G179HS065RQ1	62275 [†]	20
PhytoComm	Bai Shao Yao	G179HS065RQ1	62276	59
PhytoComm	Bai Shao Yao	G179HS065RT1	62435 [†]	20
PhytoComm	Bai Shao Yao	G179HS065RT1	62436 [†]	20
PhytoComm	Bai Shao Yao	G179HS065RW1	62601 [†]	20
PhytoComm	Bai Shao Yao	G179HS065RW1	62602 [†]	20

- 9758 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 11 spectra from 6 *Apo-Ident* customers from 6 batches from the substance/substance group *Bai Shao Yao*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Bai Shao Yao	G179H0502322	1
Phytocomm	Bai Shao Yao	G179H0502121	1
Phytocomm	Bai Shao Yao	g179h0502322	1
Phytocomm	Bai Shao Yao	g17h0502323	1
Phytocomm	Bai Shao Yao	G179H0502521	5
PhytoComm	Bai Shao Yao	1214401	1
PhytoComm	Bai Shao Yao	G179H0502322	1

- 846 spectra from 13 *Apo-Ident* customers from a total of 513 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Bai Shao Yao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Bai Shao Yao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 280
Type B	2	159	0	9756
Type C	1	0	11	845

The substance/substance group *Bai Shao Yao* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

[†]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*.

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.0000 %)
Type B	99.9895 % (> 99.9535 %)	100.0000 % (> 96.2264 %)
Type C	99.5349 % (> 98.9473 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai Shao Yao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tai Zi Shen	5.98	—
Ye Jiao Teng	7.24	—
Pi Pa Ye	7.96	—
Di Gu Pi	8.07	—
Gua Lou	8.21	—
He Huan Pi	8.23	—
Zhe Bei Mu	8.28	—
Yuan Zhi	9.55	—
Shen Qu	9.69	—
Ji Li	10.12	—
Zhu Ru	10.23	—
Ban Xia (Jiang)	10.27	—
Shan Yao	10.31	—
Fu Xiao Mai	10.92	—
Ci Wu Jia	11.00	—
Fo Shou	11.89	—
Bai Zi Ren	12.18	—
Tao Ren	12.46	—
Sheng Jiang	12.63	—
Tian Hua Fen	12.78	—
Rou Gui	12.81	—
Gui Zhi	13.25	—
Ji Xue Teng	14.01	—
Dang Shen	14.04	—
Chuan Xiong	14.18	—
Yi Yi Ren	14.51	—
Lian Qiao	14.69	—
Fu Ling	15.28	—
Gou Teng	15.74	—
Huo Ma Ren	15.87	—
Lian Zi	15.87	—
Chen Pi	16.64	—
Ling Zhi	18.24	—
San Qi	18.45	—
Dang Gui Wei	18.63	—
Ren Dong Teng	18.73	—

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Substanz	Distance in main model	Distance in second-stage model
Da Zao	19.04	—
Long Yan Rou	19.63	—
Shan Yu Rou	19.65	—
Tian Men Dong	19.65	—
Fu Zi	20.72	—
Jin Yin Hua	21.98	—
Bai Xian Pi	21.99	—
Yu Zhu	22.34	—
Dang Gui	22.79	—
Zhi Mu	23.35	—
Zhi Ke	24.26	—
Jiao Gu Lan	24.29	—
Yan Hu Suo	24.81	—
Cang Zhu	24.92	—
Tu Fu Ling	25.02	—
Fu Shen	25.42	—
Ma Huang Gen	25.49	—
Huang Qin	26.59	—
Yu Jin	27.10	—
Hou Po	27.22	—
Ma Huang	27.45	—
Wu Wei Zi	27.50	—
Dan Shen	30.65	—
Che Qian Zi	30.73	—
Yin Yang Huo	31.79	—
Gou Qi Zi	31.82	—
Mao Dong Qing	31.97	—
Dan Dou Chi	32.08	—
Suan Zao Ren	32.66	—
Bai Zhu	35.76	—
Mai Men Dong	36.39	—
Chai Hu	37.22	—
Mu Dan Pi	38.45	—
Hong Jing Tian	39.23	—
Gan Cao	39.47	—
Jie Geng	39.82	—
Qiang Huo	41.81	—
Sang Zhi	42.63	—
Mang Xiao	42.82	—
Chuang Mu Xiang	44.39	—
Qing Pi	44.96	—
Huang Lian	45.67	—
Chi Shao (Yao)	48.15	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62602	62602	0.00	10.12
62275	62275	0.00	5.98
62436	62436	0.00	7.96
62435	62435	0.00	8.50
62601	62601	0.00	10.02

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 2.3-2020-05

Validated substance/substance group **Bai Xian Pi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60208-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bai Xian Pi; Dictamni cortex

Special notes

When selecting the *Bai Xian Pi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bai Xian Pi	2	0	1

Second-stage model

For differentiation of the substance/substance group *Bai Xian Pi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bai Xian Pi	G090HS335RP1	62285	40	from supplier
PhytoComm	Bai Xian Pi	G090HS335RP1	62286	40	from supplier
PhytoComm	Bai Xian Pi	G090HS335RN1	62449	40	from supplier
PhytoComm	Bai Xian Pi	G090HS335RN1	62450	40	from supplier

Validation samples

A total of 30 254 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 *Bai Xian Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Bai Xian Pi*.
- 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
PhytoComm	Bai Xian Pi	G090HS335RP1	62285 [†]	20
PhytoComm	Bai Xian Pi	G090HS335RP1	62286 [†]	20
PhytoComm	Bai Xian Pi	G090HS335RN1	62449 [†]	20
PhytoComm	Bai Xian Pi	G090HS335RN1	62450 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

Type C Spectra of independent samples not included in the database structure. *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 *Bai Xian Pi*.
- 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
Phytocomm	Bai Xian Pi	G090H0515121	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	4	155	5	19 316
Type B	6	80	0	9831
Type C	1	0	1	855

The substance/substance group *Bai Xian Pi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9684 % (> 99.9499 %)	96.8750 % (> 95.0000 %)
Type B	99.9288 % (> 99.8929 %)	100.0000 % (> 92.5000 %)
Type C	99.9225 % (> 99.3408 %)	n/a (n/a)

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

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai Xian Pi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dan Dou Chi	3.44	—
Ye Jiao Teng	5.89	—
Tu Fu Ling	6.29	—
Ling Zhi	6.98	—
Mao Dong Qing	8.28	—
Yin Yang Huo	8.52	—
Yu Jin	9.36	—
Ren Dong Teng	9.75	—
Lian Zi	11.38	—
Hou Po	11.42	—
Yuan Zhi	12.88	—
Qiang Huo	13.29	—
Shen Qu	13.31	—
Che Qian Zi	14.19	—
Rou Gui	14.32	—
Ji Xue Teng	14.42	—
Chai Hu	14.85	—
He Huan Pi	17.69	—
Dan Shen	17.72	—
Gou Teng	17.72	—
Ma Huang Gen	19.22	—
Ji Li	19.47	—
Yan Hu Suo	19.87	—
Shan Yao	20.09	—
Du Zhong	20.16	—
Lian Qiao	20.83	—
Huo Ma Ren	20.96	—
Chen Pi	21.13	—
Jiao Gu Lan	21.33	—
Pi Pa Ye	21.36	—
Sheng Jiang	21.94	—
Jin Yin Hua	21.95	—
Chuan Xiong	22.21	—
Zhi Ke	22.74	—
Gui Zhi	23.44	—
Ma Huang	23.63	—
Bai Shao Yao	23.84	—
Mu Dan Pi	24.60	—
Qing Pi	25.03	—
Di Gu Pi	25.28	—
Fu Zi	25.70	—
Yi Yi Ren	25.82	—
Zi Hua Di Ding	26.16	—
Hong Jing Tian	26.47	—
Gua Lou	26.95	—
Tao Ren	27.17	—
Fu Ling	27.71	—
Huang Lian	28.08	—

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Substanz	Distance in main model	Distance in second-stage model
Tian Hua Fen	28.16	—
Zhe Bei Mu	28.70	—
Wu Wei Zi	29.81	—
Tai Zi Shen	29.84	—
Cang Zhu	30.80	—
Fo Shou	31.13	—
Long Yan Rou	31.67	—
Ci Wu Jia	32.15	—
Fu Shen	32.45	—
Ban Zhi Lian	32.57	—
Gou Qi Zi	33.27	—
Da Zao	34.76	—
Ban Xia (Jiang)	35.27	—
Tian Men Dong	35.90	—
Huang Bai	36.28	—
Bai Zi Ren	36.37	—
Fu Xiao Mai	36.40	—
Mang Xiao	37.72	—
Sang Zhi	38.07	—
Yu Zhu	38.50	—
Suan Zao Ren	39.40	—
Dang Shen	39.92	—
Zhu Ru	40.95	—
Jie Geng	41.86	—
San Qi	42.24	—
Dang Gui Wei	42.75	—
Chi Shao (Yao)	43.04	—
Huang Qin	43.10	—
Wang Bu Liu Xing	43.38	—
Chuan Lian Zi	43.95	—
Pu Gong Ying	43.97	—
Chuang Mu Xiang	45.41	—
Dang Gui	45.54	—
Zi Su Zi	46.60	—
Shan Yu Rou	46.69	—
Bai Zhu	46.70	—
Bai Bian Dou	46.87	—
Cang Er Zi	49.58	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62449	62449	0.00	4.61
62450	62450	0.00	4.37
62286	62286	0.00	3.53
62285	62285	0.00	3.44

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 2.3-2020-05

Validated substance/substance group **Bai Zhu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60015-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bai Zhu; Atractylodis macrocephalae rhizoma

Special notes

When selecting the *Bai Zhu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bai Zhu	3	0	3

Second-stage model

For differentiation of the substance/substance group *Bai Zhu* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bai Zhu	G041H0501721	62219	40	from supplier
PhytoComm	Bai Zhu	G041H0501721	62220	40	from supplier
PhytoComm	Bai Zhu	G041H0501822	62385	40	from supplier
PhytoComm	Bai Zhu	G041H0501822	62386	40	from supplier
PhytoComm	Bai Zhu	G041HS064SG1	62651	40	from supplier
PhytoComm	Bai Zhu	G041HS064SG1	62652	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Bai Zhu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Bai Zhu*.
- 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
PhytoComm	Bai Zhu	G041H0501721	62219 [†]	20
PhytoComm	Bai Zhu	G041H0501721	62220 [†]	20
PhytoComm	Bai Zhu	G041H0501822	62385 [†]	20
PhytoComm	Bai Zhu	G041H0501822	62386 [†]	20
PhytoComm	Bai Zhu	G041HS064SG1	62651 [†]	20
PhytoComm	Bai Zhu	G041HS064SG1	62652 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 8 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Bai Zhu*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Bai Zhu	G041H0501221	1
Phytocomm	Bai Zhu	g041h0501221	3
Phytocomm	Bai Zhu	G041H0501422	3
PhytoComm	Bai Zhu	G041H0501621	1

- 849 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	4	240	0	19 236
Type B	8	116	4	9789
Type C	2	1	7	847

The substance/substance group *Bai Zhu* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9842 % (> 99.9657 %)	100.0000 % (> 97.5000 %)
Type B	99.9367 % (> 99.9008 %)	96.6667 % (> 94.1667 %)
Type C	99.7158 % (> 99.1284 %)	n/a (n/a)

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai Zhu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Jie Geng	3.28	—
Jiao Gu Lan	8.79	—
Jin Yin Hua	9.90	—
Mu Dan Pi	11.53	—
Hong Jing Tian	12.00	—
Shan Yu Rou	13.15	—
Huang Qi	13.15	—
Shan Yao	13.45	—
Di Gu Pi	14.14	—
Chuan Xiong	14.40	—
Zhi Ke	15.21	—
Sang Zhi	16.46	—
Dan Shen	16.76	—
Gou Qi Zi	17.27	—
Chen Pi	17.32	—
Cang Zhu	17.76	—
Zi Hua Di Ding	18.03	—
Wu Wei Zi	18.34	—
Gua Lou	18.37	—
Yuan Zhi	18.48	—
Chuang Mu Xiang	19.14	—
Pi Pa Ye	19.61	—
Lian Qiao	19.65	—
Suan Zao Ren	19.90	—
Gan Cao	21.13	—
Qing Pi	21.18	—
Chai Hu	21.24	—
Tian Hua Fen	22.28	—
Yu Zhu	22.44	—
Ren Dong Teng	22.49	—
Hou Po	22.55	—
Dang Shen	22.79	—
Hong Hua	22.84	—
Ji Li	22.88	—
Qin Jiao	22.94	—
Chi Shao (Yao)	23.80	—
Mao Dong Qing	24.23	—
Bai Mao Gen	24.52	—
Lian Zi	24.55	—
Zhe Bei Mu	25.22	—
Ma Huang	25.99	—

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Substanz	Distance in main model	Distance in second-stage model
Chuan Lian Zi	26.05	—
Yan Hu Suo	26.11	—
Cang Er Zi	26.33	—
Ye Jiao Teng	26.33	—
Mai Men Dong	26.33	—
Sheng Jiang	26.77	—
Bai Xian Pi	26.87	—
Fu Zi	27.00	—
Yin Yang Huo	27.04	—
Bai Shao Yao	27.06	—
Long Yan Rou	27.24	—
(Huai) Niu Xi	27.62	—
Qiang Huo	27.72	—
Dang Gui Wei	27.91	—
Du Huo	28.16	—
Huang Bai	28.35	—
Shen Qu	28.99	—
San Qi	29.22	—
Huang Qin	29.33	—
Tai Zi Shen	29.46	—
Lai Fu Zi	29.64	—
Dan Dou Chi	29.67	—
He Huan Pi	30.22	—
Tu Fu Ling	30.79	—
Dang Gui	31.07	—
Rou Gui	31.11	—
Ji Xue Teng	31.20	—
Bai Zi Ren	31.66	—
Sang Ye	32.10	—
Mang Xiao	32.14	—
Ba Ji Tian	32.80	—
Du Zhong	33.04	—
Tian Men Dong	33.13	—
Gou Teng	33.84	—
Tao Ren	34.01	—
Huang Lian	34.80	—
Bai He	34.85	—
Ban Zhi Lian	35.16	—
Ling Zhi	35.37	—
Xiang Fu	35.56	—
Fu Ling	35.91	—
E Zhu	36.88	—
Da Zao	37.11	—
Ci Wu Jia	37.67	—
Gui Zhi	37.95	—
Yu Jin	38.60	—
Che Qian Zi	38.64	—
Huo Ma Ren	38.89	—
Yi Yi Ren	39.76	—
Ma Huang Gen	40.14	—
Fang Feng	40.76	—
Niu Bang Zi	40.99	—
Fo Shou	41.22	—
(Shi) Chang Pu	41.30	—
Sha Shen (Bei)	42.21	—
Mai Ya	42.24	—
Bai Bian Dou	42.91	—
Pu Gong Ying	42.96	—
Zi Su Zi	43.33	—

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Substanz	Distance in main model	Distance in second-stage model
Xie Bai	43.36	—
Zhi Mu	44.01	—
Ku Shen	45.64	—
Wu Yao	46.60	—
Wu Mei	46.96	—
Zhu Ru	47.75	—
Fu Shen	49.04	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62219	62219	0.00	3.28
62385	62385	0.00	4.78
62386	62386	0.00	4.98
62651	62651	0.00	9.12
62652	62652	0.00	8.79
62220	62220	0.00	3.99

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 2.3-2020-05

Validated substance/substance group **Bai Zi Ren**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60197-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bai Zi Ren; Biotae orientalis semen

Special notes

When selecting the *Bai Zi Ren* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bai Zi Ren	1	0	3

Second-stage model

For differentiation of the substance/substance group *Bai Zi Ren* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bai Zi Ren	G052HS187SK1	62659	40	from supplier
PhytoComm	Bai Zi Ren	G052HS187SK1	62660	40	from supplier

Validation samples

A total of 30 254 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 *Bai Zi Ren*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Bai Zi Ren*.
- 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
PhytoComm	Bai Zi Ren	G052HS187SK1	62659 [†]	20
PhytoComm	Bai Zi Ren	G052HS187SK1	62660 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 4 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Bai Zi Ren*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Bai Zi Ren	g052f110315	1
Phytocomm	Bai Zi Ren	g952f110315	1
Phytocomm	Bai Zi Ren	G052HS187	2

- 853 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	4	853

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8269 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai Zi Ren* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Lian Zi	6.05	—
Ji Li	7.76	—
Bai Shao Yao	10.34	—
Ling Zhi	10.47	—
Shen Qu	11.24	—
He Huan Pi	11.44	—
Huo Ma Ren	11.67	—
Tai Zi Shen	12.76	—
Di Gu Pi	12.86	—
Sheng Jiang	13.11	—
Yuan Zhi	14.16	—
Ci Wu Jia	14.53	—
Gua Lou	14.67	—
Shan Yao	14.77	—
Gui Zhi	14.82	—
Fu Xiao Mai	15.07	—
Zhu Ru	15.53	—
Tian Hua Fen	15.65	—
Pi Pa Ye	15.87	—
Zhe Bei Mu	15.91	—
Ren Dong Teng	16.26	—
Tao Ren	16.37	—
San Qi	17.05	—
Dang Shen	17.33	—
Ye Jiao Teng	17.33	—
Tu Fu Ling	17.37	—
Fu Ling	17.37	—
Bai Xian Pi	17.57	—
Chen Pi	17.97	—
Chuan Xiong	18.01	—
Yi Yi Ren	18.83	—
Lian Qiao	19.29	—
Tian Men Dong	19.62	—
Rou Gui	19.73	—
Gou Teng	20.65	—
Dang Gui Wei	21.56	—
Yu Jin	21.88	—
Fo Shou	22.58	—
Mao Dong Qing	22.81	—
Suan Zao Ren	23.21	—
Yu Zhu	23.53	—
Fu Zi	24.13	—
Cang Zhu	24.24	—
Ban Xia (Jiang)	24.59	—
Jiao Gu Lan	24.85	—
Dan Shen	25.28	—
Ji Xue Teng	25.57	—
Chai Hu	26.17	—
Dan Dou Chi	26.41	—
Hou Po	27.12	—
Da Zao	27.12	—
Ma Huang Gen	27.15	—

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Substanz	Distance in main model	Distance in second-stage model
Long Yan Rou	27.19	—
Dang Gui	27.28	—
Shan Yu Rou	28.55	—
Zhi Mu	29.15	—
Zhi Ke	29.32	—
Che Qian Zi	30.69	—
Jin Yin Hua	30.81	—
Hong Jing Tian	32.05	—
Yan Hu Suo	32.27	—
Gou Qi Zi	33.70	—
Yin Yang Huo	33.82	—
Ma Huang	35.04	—
Wu Wei Zi	35.41	—
Fu Shen	36.07	—
Qiang Huo	38.63	—
Huang Qin	39.41	—
Mu Dan Pi	40.74	—
Mang Xiao	42.72	—
Bai Zhu	42.76	—
Chuang Mu Xiang	43.35	—
Jie Geng	43.91	—
Qing Pi	44.33	—
Chuan Lian Zi	44.69	—
Sang Zhi	46.22	—
Du Zhong	46.39	—
Huang Lian	47.29	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62659	62659	0.00	6.30
62660	62660	0.00	6.05

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 2.3-2020-05

Validated substance/substance group **Ban Xia (Jiang)**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60019-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ban Xia (Jiang); Pinelliae rhizoma praeparatum cum zingibere

Special notes

When selecting the *Ban Xia (Jiang)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ban Xia (Jiang)	1	0	2

Second-stage model

For differentiation of the substance/substance group *Ban Xia (Jiang)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ban Xia (Jiang)	G191HS090SH1	62599	40	from supplier
PhytoComm	Ban Xia (Jiang)	G191HS090SH1	62600	40	from supplier

Validation samples

A total of 30 254 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 *Ban Xia (Jiang)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ban Xia (Jiang)*.
- 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
PhytoComm	Ban Xia (Jiang)	G191HS090SH1	62599 [†]	20
PhytoComm	Ban Xia (Jiang)	G191HS090SH1	62600 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

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

Supplier	Substance	Batch	Spectra
Phytocomm	Ban Xia (Jiang)	g191h0526121	1
Phytocomm	Ban Xia (Jiang)	G191H0526322	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	39	1	9877
Type C	0	0	2	855

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ban Xia (Jiang)* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Di Gu Pi	5.95	—
Gui Zhi	7.27	—
Sheng Jiang	7.47	—
Rou Gui	8.54	—
Bai Shao Yao	9.99	—
He Huan Pi	10.00	—
Fu Xiao Mai	10.56	—
Shen Qu	10.91	—
Zhu Ru	11.39	—
Zhe Bei Mu	11.51	—
Ji Xue Teng	12.11	—
Ci Wu Jia	12.46	—
Yi Yi Ren	12.57	—
Tai Zi Shen	12.71	—
Tao Ren	12.78	—
Gou Teng	13.56	—
Fu Ling	14.01	—
Ji Li	15.07	—
Bai Zi Ren	15.22	—
Fo Shou	15.28	—
Ye Jiao Teng	15.78	—
Huo Ma Ren	17.36	—
Lian Zi	17.62	—
Ling Zhi	17.86	—
Gua Lou	18.10	—
Long Yan Rou	18.85	—
Tian Hua Fen	19.10	—
Pi Pa Ye	19.16	—
Da Zao	19.40	—
Bai Xian Pi	19.41	—
Fu Shen	19.42	—
Ma Huang Gen	19.54	—
Yuan Zhi	20.92	—
Tian Men Dong	21.20	—
Lian Qiao	22.70	—
Chen Pi	23.10	—
Yan Hu Suo	24.65	—
Shan Yao	25.49	—
Yu Jin	27.15	—
Tu Fu Ling	27.48	—
Dang Shen	27.67	—
Chuan Xiong	28.00	—
Ren Dong Teng	28.43	—
Shan Yu Rou	30.62	—
Jin Yin Hua	30.64	—
Fu Zi	30.72	—
Zhi Ke	31.26	—
Huang Qin	31.32	—
Jiao Gu Lan	32.17	—
Dang Gui Wei	33.19	—
Dan Dou Chi	33.43	—
Dan Shen	33.56	—

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Substanz	Distance in main model	Distance in second-stage model
Yu Zhu	33.84	—
Yin Yang Huo	36.10	—
Dang Gui	36.18	—
Wu Wei Zi	36.48	—
Hou Po	38.07	—
San Qi	38.09	—
Ma Huang	38.10	—
Cang Zhu	38.88	—
Zhi Mu	40.32	—
Chai Hu	40.55	—
Mao Dong Qing	40.81	—
Mang Xiao	42.04	—
Bai Zhu	44.68	—
Che Qian Zi	46.28	—
Jie Geng	46.53	—
Sang Zhi	47.14	—
Hong Jing Tian	47.18	—
Qiang Huo	47.36	—
Huang Lian	47.63	—
Gou Qi Zi	49.58	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62599	62599	0.00	6.09
62600	62600	0.00	5.95

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 2.3-2020-05

Validated substance/substance group **Ban Zhi Lian**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60038-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ban Zhi Lian; Scutellariae barbatae herba

Special notes

When selecting the *Ban Zhi Lian* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ban Zhi Lian	1	0	2

Second-stage model

For differentiation of the substance/substance group *Ban Zhi Lian* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ban Zhi Lian	G224H0528821	62753	40	from supplier
PhytoComm	Ban Zhi Lian	G224H0528821	62754	40	from supplier

Validation samples

A total of 30 254 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 *Ban Zhi Lian*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ban Zhi Lian*.
- 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
PhytoComm	Ban Zhi Lian	G224H0528821	62753 [†]	20
PhytoComm	Ban Zhi Lian	G224H0528821	62754 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 4 spectra from 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Ban Zhi Lian*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ban Zhi Lian	G224H0528221	1
Phytocomm	Ban Zhi Lian	G224H0528521	2
PhytoComm	Ban Zhi Lian	G224H0528521	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	39	1	9877
Type C	0	0	4	853

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8269 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ban Zhi Lian* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sheng Jiang	15.25	—
Mai Ya	22.86	—
Sang Zhi	23.71	—
Fu Ling	25.16	—
Rou Gui	25.72	—
Mang Xiao	26.73	—
Bai Xian Pi	26.80	—
E Zhu	27.67	—
Di Gu Pi	28.02	—
Mu Dan Pi	28.87	—
Tian Hua Fen	29.72	—
Ji Xue Teng	30.24	—
San Qi	30.46	—
Yan Hu Suo	30.99	—
Chuan Lian Zi	31.50	—
Gui Zhi	31.69	—
Shan Yao	32.56	—
Ji Li	32.70	—
Ling Zhi	32.71	—
Zhu Ling	33.36	—
Gou Teng	33.45	—
Lian Zi	34.01	—
Ye Jiao Teng	34.03	—
Bai He	35.01	—
Jiang Huang	35.16	—
Bai Shao Yao	35.32	—
Long Dan (Cao)	35.62	—
Jie Geng	35.91	—
Dang Gui	36.10	—
Yi Yi Ren	36.28	—
Dan Dou Chi	36.79	—
He Huan Pi	37.04	—
Du Huo	37.12	—
Fo Shou	37.72	—
Yuan Zhi	37.91	—
Shen Qu	38.15	—
Zhi Ke	38.70	—
Tu Fu Ling	39.27	—
Tian Men Dong	39.45	—
Mao Dong Qing	39.54	—
(Bai) Dou Kou	39.57	—
Bai Bian Dou	40.24	—
Ren Dong Teng	40.34	—
Du Zhong	40.44	—
Ma Huang Gen	40.49	—
Sha Shen (Bei)	40.66	—
Mai Men Dong	40.98	—
Qin Jiao	41.07	—
Wang Bu Liu Xing	41.70	—
Yu Jin	41.73	—
Da Zao	42.11	—
(Shi) Chang Pu	43.42	—

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Substanz	Distance in main model	Distance in second-stage model
Qiang Huo	43.56	—
Sha Ren	43.76	—
Wu Wei Zi	43.82	—
Qing Pi	44.51	—
Chen Pi	44.62	—
Zi Su Zi	45.21	—
Bai Zhu	45.66	—
Ba Ji Tian	45.71	—
Huang Lian	46.19	—
Tai Zi Shen	46.45	—
Huang Qi	46.71	—
Zhu Ru	46.81	—
Lai Fu Zi	47.10	—
Fu Shen	47.38	—
Cang Er Zi	47.87	—
Jin Yin Hua	47.88	—
Xie Bai	47.96	—
Xiang Fu	48.00	—
Yin Yang Huo	48.31	—
Chai Hu	48.48	—
Dan Shen	48.99	—
Lian Qiao	49.00	—
(Huai) Niu Xi	49.70	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62754	62754	0.00	15.43
62753	62753	0.00	15.25

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Bu Gu Zhi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60023-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bu Gu Zhi; Psoraleae corylifoliae fructus

Special notes

When selecting the *Bu Gu Zhi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bu Gu Zhi	1	0	2

Second-stage model

For differentiation of the substance/substance group *Bu Gu Zhi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Bu Gu Zhi	G205H1247822	62487	40	from supplier
PhytoComm	Bu Gu Zhi	G205H1247822	62488	40	from supplier

Validation samples

A total of 30 254 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 *Bu Gu Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Bu Gu Zhi*.
- 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
PhytoComm	Bu Gu Zhi	G205H1247822	62487 [†]	20
PhytoComm	Bu Gu Zhi	G205H1247822	62488 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 5 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Bu Gu Zhi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Bu Gu Zhi	G205H1247222	2
Phytocomm	Bu Gu Zhi	g205h1247222	1
Phytocomm	Bu Gu Zhi	G205H1247421	2

- 852 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	5	852

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bu Gu Zhi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dan Zhu Ye	19.78	—
Sang Bai Pi	20.54	—
Jing Jie	21.05	—
Sha Ren	23.35	—
Tu Si Zi	24.15	—
Yu Xing Cao	24.87	—
Gu Sui Bu	26.40	—
Wu Zhu Yu	28.49	—
Sang Ji Shend	28.54	—
Gui Zhi	32.64	—
He Huan Pi	32.91	—
Wu Jia Pi	33.39	—
Fu Zi	33.95	—
Mang Xiao	36.54	—
He Shou Wu	37.36	—
Jin Qian Cao	37.81	—
Nü Zhen Zi	38.96	—
Ge Gen	39.19	—
Yin Chen Hao	40.70	—
Yu Jin	43.39	—
Du Zhong	43.62	—
Xian He Cao	43.83	—
(Bai) Dou Kou	44.24	—
Wu Yao	44.66	—
Jiang Huang	45.08	—
Ji Li	45.47	—
(Sheng) Di Huang	47.05	—
Hua Shi	48.10	—
Fang Feng	48.23	—
Chen Pi	48.60	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62487	62487	0.00	19.88
62488	62488	0.00	19.78

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Cang Er Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60054-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Cang Er Zi; Xanthii fructus

Special notes

When selecting the *Cang Er Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cang Er Zi	2	0	3

Second-stage model

For differentiation of the substance/substance group *Cang Er Zi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Cang Er Zi	G251H1401821	62503	40	from supplier
PhytoComm	Cang Er Zi	G251H1401821	62504	40	from supplier
PhytoComm	Cang Er Zi	G251H1401921	62755	40	from supplier
PhytoComm	Cang Er Zi	G251H1401921	62756	40	from supplier

Validation samples

A total of 30 254 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 *Cang Er Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Cang Er Zi*.
- 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
PhytoComm	Cang Er Zi	G251H1401821	62503 [†]	20
PhytoComm	Cang Er Zi	G251H1401821	62504 [†]	20
PhytoComm	Cang Er Zi	G251H1401921	62755 [†]	20
PhytoComm	Cang Er Zi	G251H1401921	62756 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 4 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Cang Er Zi*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Cang Er Zi	g251h1401021	1
Phytocomm	Cang Er Zi	G251H1401322	1
Phytocomm	Cang Er Zi	G251H1401521	1
PhytoComm	Cang Er Zi	G251H1401322	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cang Er Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cang Er Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	1	0	4	852

The substance/substance group *Cang Er Zi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.5349 % (> 98.9483 %)	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

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cang Er Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zi Su Zi	10.04	—
Shan Yao	11.06	—
Bai Bian Dou	14.53	—
E Zhu	16.57	—
Ji Li	18.09	—
Wu Wei Zi	19.53	—
San Qi	19.71	—
Niu Bang Zi	21.17	—
Wang Bu Liu Xing	21.89	—
Wu Mei	22.05	—
Sang Zhi	22.10	—
Chuan Lian Zi	22.35	—
Sha Shen (Bei)	22.39	—
Jiang Huang	22.99	—
Di Gu Pi	23.51	—
Xie Bai	23.52	—
Gui Zhi	23.86	—
Sheng Jiang	24.52	—
Jin Yin Hua	24.56	—
Yan Hu Suo	25.71	—
Ba Ji Tian	26.48	—
Qing Pi	27.55	—
Lai Fu Zi	27.58	—
Mang Xiao	27.77	—
Xiang Fu	27.86	—
Yi Mu Cao	28.48	—
Qiang Huo	28.80	—
Ku Shen	29.50	—
Tian Hua Fen	29.80	—
Zhi Ke	29.81	—
Chen Pi	29.82	—
Sha Ren	30.01	—
Jie Geng	30.02	—
(Bai) Dou Kou	30.89	—
(Huai) Niu Xi	30.90	—
Shan Yu Rou	31.46	—
Gua Lou	31.49	—
Jiao Gu Lan	31.81	—
Mao Dong Qing	31.99	—
Fang Feng	32.30	—
Huang Bai	32.30	—
Hou Po	32.66	—
Du Zhong	32.77	—

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Substanz	Distance in main model	Distance in second-stage model
Lian Qiao	32.84	—
Sang Ye	34.70	—
Zi Hua Di Ding	34.79	—
Zhi Zi	34.84	—
Du Huo	35.08	—
Dang Gui	35.09	—
Gan Cao	35.39	—
(Shi) Chang Pu	35.50	—
Suan Zao Ren	35.82	—
Xi Xian Cao	35.91	—
Long Dan (Cao)	36.01	—
Pu Gong Ying	36.16	—
Mu Dan Pi	36.42	—
Fu Zi	36.78	—
Chuan Xiong	37.04	—
Dan Dou Chi	37.11	—
Hong Hua	38.19	—
He Huan Pi	38.22	—
Tu Fu Ling	38.47	—
Chi Shao (Yao)	38.61	—
Dong Gua Zi	39.02	—
Huang Qi	39.03	—
Yuan Zhi	39.46	—
Dan Shen	39.50	—
Shen Qu	39.97	—
Bai Mao Gen	40.04	—
Ye Jiao Teng	40.08	—
Ren Dong Teng	40.27	—
Zhe Bei Mu	40.99	—
Nü Zhen Zi	41.09	—
Hong Jing Tian	41.27	—
Xin Yi	41.28	—
Fu Ling	42.07	—
Wu Yao	42.13	—
Huang Lian	42.20	—
Cang Zhu	42.66	—
Mai Men Dong	42.86	—
Bai Xian Pi	42.95	—
Bai Zhu	43.01	—
Lian Zi	43.14	—
Gou Qi Zi	43.15	—
Yin Yang Huo	44.11	—
Mai Ya	44.45	—
Yu Jin	44.52	—
Da Zao	44.56	—
Xian He Cao	44.94	—
Ling Zhi	46.51	—
Chai Hu	46.53	—
Huang Bo	46.59	—
Zhu Ling	48.60	—
Qin Jiao	49.93	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62504	62504	0.00	11.08
62755	62755	0.00	10.77
62503	62503	0.00	11.06
62756	62756	0.00	10.04

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Cang Zhu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60160-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Cang Zhu; Atractylodis rhizoma

Special notes

When selecting the *Cang Zhu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cang Zhu	1	0	1

Second-stage model

For differentiation of the substance/substance group *Cang Zhu* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Cang Zhu	G042HS301SG1	62653	40	from supplier
PhytoComm	Cang Zhu	G042HS301SG1	62654	40	from supplier

Validation samples

A total of 30 254 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 *Cang Zhu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Cang Zhu*.
- 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
PhytoComm	Cang Zhu	G042HS301SG1	62653 [†]	20
PhytoComm	Cang Zhu	G042HS301SG1	62654 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Cang Zhu*.
- 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
Phytocomm	Cang Zhu	g042h1402221	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	1	856

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8367 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cang Zhu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yuan Zhi	6.27	—
Shan Yao	7.41	—
Pi Pa Ye	8.82	—
Chen Pi	8.98	—
Lian Qiao	9.97	—
Gou Qi Zi	10.11	—
Chuan Xiong	10.92	—
Suan Zao Ren	12.05	—
Dang Shen	12.12	—
Chuang Mu Xiang	12.37	—
Jiao Gu Lan	12.45	—
Bai Shao Yao	12.85	—
San Qi	12.90	—
Ji Li	13.34	—
Shen Qu	13.65	—
Yu Zhu	13.85	—
Bai Zi Ren	14.35	—
Lian Zi	14.90	—
Jin Yin Hua	15.35	—
Mao Dong Qing	16.57	—
Dang Gui Wei	16.74	—
Dan Shen	17.21	—
Ren Dong Teng	17.49	—
Shan Yu Rou	17.83	—
Mu Dan Pi	17.84	—
Zhe Bei Mu	18.18	—
Hou Po	18.40	—
Tai Zi Shen	18.57	—
Hong Jing Tian	19.07	—
Ling Zhi	19.25	—
Gua Lou	19.45	—
Dang Gui	19.84	—
Huo Ma Ren	20.85	—
Tian Hua Fen	20.87	—
Di Gu Pi	21.28	—
Fu Zi	21.69	—
Fu Ling	21.88	—
Chai Hu	22.16	—
Wu Wei Zi	22.88	—
He Huan Pi	23.65	—
Zhi Ke	23.72	—
Ci Wu Jia	24.24	—
Sheng Jiang	24.33	—
Gui Zhi	24.43	—
Long Yan Rou	24.75	—
Tu Fu Ling	24.91	—
Bai Zhu	24.98	—
Dan Dou Chi	25.38	—
Ye Jiao Teng	25.45	—
Gou Teng	26.13	—
Zhi Mu	27.05	—
Da Zao	27.38	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Xian Pi	27.68	—
Zhu Ru	28.19	—
Ji Xue Teng	28.62	—
Qing Pi	29.32	—
Yan Hu Suo	29.43	—
Yin Yang Huo	29.58	—
Gan Cao	29.98	—
Tao Ren	30.09	—
Rou Gui	30.48	—
Qiang Huo	30.58	—
Tian Men Dong	30.70	—
Che Qian Zi	30.90	—
Fu Xiao Mai	31.14	—
Fo Shou	31.59	—
Yu Jin	31.92	—
Huang Qin	32.48	—
Zi Hua Di Ding	32.51	—
Yi Yi Ren	32.70	—
Ma Huang	32.74	—
Cang Er Zi	33.82	—
Ma Huang Gen	34.78	—
Jie Geng	35.60	—
Sang Zhi	36.17	—
Du Zhong	37.74	—
Ban Xia (Jiang)	37.88	—
Chi Shao (Yao)	39.55	—
Huang Lian	41.51	—
Mang Xiao	43.24	—
Chuan Lian Zi	43.58	—
Mai Men Dong	45.28	—
Hong Hua	45.64	—
Fu Shen	48.06	—
Huang Bai	48.21	—
Sang Ye	49.32	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62654	62654	0.00	6.83
62653	62653	0.00	6.27

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 2.3-2020-05

Validated substance/substance group **Chai Hu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60010-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chai Hu; Bupleuri radix

Special notes

When selecting the *Chai Hu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chai Hu	1	0	3

Second-stage model

For differentiation of the substance/substance group *Chai Hu* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Chai Hu	G055HS233SK1	62661	40	from supplier
PhytoComm	Chai Hu	G055HS233SK1	62662	40	from supplier

Validation samples

A total of 30 254 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 *Chai Hu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Chai Hu*.
- 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
PhytoComm	Chai Hu	G055HS233SK1	62661 [†]	20
PhytoComm	Chai Hu	G055HS233SK1	62662 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 8 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Chai Hu*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Chai Hu	G055H1055123	1
Phytocomm	Chai Hu	g055h1055123	1
Phytocomm	Chai Hu	G055H1055422	5
PhytoComm	Chai Hu	G055H1055322	1

- 849 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	38	2	9877
Type C	0	0	8	849

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	95.0000 % (> 87.5000 %)
Type C	100.0000 % (> 98.8253 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chai Hu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ji Li	5.62	—
Mao Dong Qing	6.55	—
Yuan Zhi	7.51	—
Ling Zhi	7.72	—
Shen Qu	8.54	—
Hou Po	9.42	—
Dan Dou Chi	9.82	—
Lian Zi	9.85	—
Bai Xian Pi	10.17	—
Yu Jin	11.16	—
Tu Fu Ling	11.71	—
Lian Qiao	11.87	—
Qiang Huo	12.07	—
Ren Dong Teng	12.56	—
Chuan Xiong	13.86	—
Pi Pa Ye	14.04	—
Yin Yang Huo	14.04	—
Shan Yao	14.19	—
Dan Shen	14.35	—
Che Qian Zi	14.77	—
Jiao Gu Lan	14.82	—
Fu Zi	15.42	—
Bai Shao Yao	15.60	—
Fu Ling	16.26	—
Jin Yin Hua	17.22	—
Hong Jing Tian	17.47	—
Ye Jiao Teng	17.49	—
Sheng Jiang	17.60	—
Cang Zhu	18.05	—
Chen Pi	18.22	—
Gua Lou	18.82	—
Qing Pi	19.11	—
Rou Gui	19.65	—
Yan Hu Suo	19.66	—
Gui Zhi	20.20	—
He Huan Pi	20.60	—
Yi Yi Ren	21.32	—
Huo Ma Ren	21.40	—
Gou Teng	21.78	—
Du Zhong	21.79	—
Tian Hua Fen	21.97	—
Di Gu Pi	22.75	—
Mu Dan Pi	22.76	—
Ma Huang Gen	22.78	—
Bai Zi Ren	22.79	—
Gou Qi Zi	23.22	—
Zhe Bei Mu	23.33	—
Suan Zao Ren	23.73	—
Wu Wei Zi	24.44	—
Ji Xue Teng	24.69	—
Tai Zi Shen	25.97	—
Tao Ren	26.89	—

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Substanz	Distance in main model	Distance in second-stage model
Zhu Ru	27.08	—
Zi Hua Di Ding	27.31	—
Ma Huang	27.55	—
Fu Xiao Mai	27.84	—
Yu Zhu	28.66	—
San Qi	28.99	—
Tian Men Dong	29.50	—
Zhi Ke	29.61	—
Da Zao	29.82	—
Huang Lian	30.04	—
Ci Wu Jia	30.21	—
Long Yan Rou	30.70	—
Dang Gui Wei	31.17	—
Fo Shou	32.37	—
Ban Xia (Jiang)	32.85	—
Dang Shen	33.10	—
Chuang Mu Xiang	33.12	—
Huang Bai	33.64	—
Sang Zhi	34.03	—
Chuan Lian Zi	36.04	—
Dang Gui	36.31	—
Shan Yu Rou	36.69	—
Jie Geng	37.43	—
Huang Qin	38.60	—
Chi Shao (Yao)	38.65	—
Mang Xiao	38.68	—
Cang Er Zi	39.99	—
Wang Bu Liu Xing	40.14	—
Bai Zhu	40.41	—
Fu Shen	40.50	—
Zi Su Zi	41.36	—
Bai Bian Dou	41.46	—
Pu Gong Ying	45.49	—
Sang Ye	46.27	—
Gan Cao	47.87	—
Bai Mao Gen	48.08	—
Ban Zhi Lian	48.39	—
Zhi Mu	49.82	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62661	62661	0.00	6.49
62662	62662	0.00	5.62

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 2.3-2020-05

Validated substance/substance group **Che Qian Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60255-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Che Qian Zi; Plantaginis semen

Special notes

When selecting the *Che Qian Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Che Qian Zi	1	0	4

Second-stage model

For differentiation of the substance/substance group *Che Qian Zi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Che Qian Zi	G192HS120SH1	62607	40	from supplier
PhytoComm	Che Qian Zi	G192HS120SH1	62608	40	from supplier

Validation samples

A total of 30 254 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 *Che Qian Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Che Qian Zi*.
- 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
PhytoComm	Che Qian Zi	G192HS120SH1	62607 [†]	20
PhytoComm	Che Qian Zi	G192HS120SH1	62608 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 6 spectra from 6 *Apo-Ident* customers from 4 batches from the substance/substance group *Che Qian Zi*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Che Qian Zi	410704805	1
Phytocomm	Che Qian Zi	G192H0723421	2
PhytoComm	Che Qian Zi	G192H0723321	2
PhytoComm	Che Qian Zi	G192H0723621	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	6	851

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8258 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Che Qian Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hou Po	5.57	—
Yu Jin	7.51	—
Ling Zhi	8.91	—
Ren Dong Teng	8.96	—
Yin Yang Huo	8.98	—
Chai Hu	9.70	—
Dan Dou Chi	10.31	—
Bai Xian Pi	10.57	—
Yan Hu Suo	11.11	—
Shen Qu	12.03	—
Mao Dong Qing	12.35	—
Ji Li	12.36	—
Du Zhong	12.86	—
Qiang Huo	13.60	—
Yuan Zhi	13.61	—
Pi Pa Ye	14.18	—
Chuan Xiong	14.61	—
Shan Yao	15.12	—
Ye Jiao Teng	15.38	—
Dan Shen	17.18	—
Tu Fu Ling	17.40	—
Ma Huang Gen	17.44	—
Lian Zi	17.71	—
Lian Qiao	17.80	—
He Huan Pi	19.30	—
Ji Xue Teng	20.09	—
Rou Gui	20.11	—
Qing Pi	20.17	—
Gou Teng	20.29	—
Chen Pi	20.41	—
Jiao Gu Lan	20.64	—
Hong Jing Tian	20.94	—
Ma Huang	21.37	—
Sheng Jiang	21.98	—
Yi Yi Ren	22.18	—
Mu Dan Pi	22.25	—
Jin Yin Hua	22.74	—
Huo Ma Ren	22.79	—
Tian Hua Fen	22.82	—
Fu Ling	23.16	—
Fu Zi	23.19	—
Bai Shao Yao	23.49	—
Gui Zhi	24.06	—
Zi Hua Di Ding	24.08	—
Huang Lian	25.10	—
Gua Lou	25.76	—
Wu Wei Zi	26.88	—
Tao Ren	28.54	—
Tai Zi Shen	29.44	—
Bai Zi Ren	29.60	—
Di Gu Pi	29.71	—
Cang Zhu	30.47	—

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Substanz	Distance in main model	Distance in second-stage model
Zhe Bei Mu	30.74	—
Fu Xiao Mai	31.01	—
Da Zao	31.10	—
Zhi Ke	31.50	—
Suan Zao Ren	31.55	—
Huang Bai	32.73	—
Ban Xia (Jiang)	33.37	—
Gou Qi Zi	35.00	—
Zhu Ru	35.49	—
Fo Shou	36.41	—
Fu Shen	36.47	—
Ci Wu Jia	36.52	—
San Qi	38.16	—
Mang Xiao	38.43	—
Wang Bu Liu Xing	38.46	—
Pu Gong Ying	38.80	—
Sang Zhi	39.56	—
Yu Zhu	39.90	—
Tian Men Dong	40.81	—
Huang Qin	40.99	—
Xi Xian Cao	41.87	—
Chi Shao (Yao)	42.39	—
Jie Geng	42.42	—
Long Yan Rou	43.18	—
Dang Gui	43.23	—
Jiang Huang	43.33	—
Dang Gui Wei	43.65	—
Shan Yu Rou	44.06	—
Sang Ye	44.53	—
Dang Shen	45.22	—
Ban Zhi Lian	46.22	—
Zi Su Zi	47.53	—
Chuang Mu Xiang	48.00	—
Chuan Lian Zi	48.24	—
Cang Er Zi	48.35	—
Bai Bian Dou	48.41	—
E Zhu	48.55	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62608	62608	0.00	5.57
62607	62607	0.00	5.79

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 2.3-2020-05

Validated substance/substance group **Chen Pi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60009-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chen Pi; Citri reticulatae pericarpium

Special notes

When selecting the *Chen Pi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chen Pi	3	0	2

Second-stage model

For differentiation of the substance/substance group *Chen Pi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Chen Pi	G073H1128821	62377	40	from supplier
PhytoComm	Chen Pi	G073H1128821	62378	40	from supplier
PhytoComm	Chen Pi	G073HS254RR1	62445	40	from supplier
PhytoComm	Chen Pi	G073HS254RR1	62446	40	from supplier
PhytoComm	Chen Pi	G073HS254SG1	62669	40	from supplier
PhytoComm	Chen Pi	G073HS254SG1	62670	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Chen Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Chen Pi*.
- 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
PhytoComm	Chen Pi	G073H1128821	62377 [†]	20
PhytoComm	Chen Pi	G073H1128821	62378 [†]	20
PhytoComm	Chen Pi	G073HS254RR1	62445 [†]	20
PhytoComm	Chen Pi	G073HS254RR1	62446 [†]	20
PhytoComm	Chen Pi	G073HS254SG1	62669 [†]	20
PhytoComm	Chen Pi	G073HS254SG1	62670 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 4 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Chen Pi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Chen Pi	G073H1128222	1
Phytocomm	Chen Pi	g07h1128221	1
Phytocomm	Chen Pi	g073h1128222	1
PhytoComm	Chen Pi	G073H1128222	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	240	0	19 240
Type B	0	120	0	9797
Type C	0	0	4	853

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9281 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8269 %)	n/a (n/a)

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chen Pi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chuan Xiong	6.84	—
Yu Zhu	7.61	—
Gua Lou	7.84	—
Gou Qi Zi	7.88	—
Cang Zhu	8.29	—
Fo Shou	9.63	—
Yuan Zhi	10.25	—
Pi Pa Ye	10.39	—
Fang Feng	10.62	—
Dang Gui Wei	11.02	—
Bai Shao Yao	11.43	—
Ye Jiao Teng	11.63	—
Da Zao	12.10	—
Long Yan Rou	12.55	—
Ren Dong Teng	12.95	—
Shen Qu	12.97	—
Wu Yao	13.31	—
Gu Sui Bu	13.58	—
Shan Yao	14.19	—
Tian Men Dong	14.19	—
Zhe Bei Mu	14.21	—
San Qi	14.58	—
Hong Jing Tian	14.84	—
Dang Shen	14.88	—
Tao Ren	15.50	—
Lian Qiao	15.53	—
Lian Zi	16.03	—
Tai Zi Shen	16.34	—
Ji Li	16.94	—
Jin Yin Hua	17.05	—
Bai Zi Ren	17.58	—
Tu Fu Ling	17.69	—
Yu Jin	17.81	—
Dan Shen	18.12	—
Fu Zi	18.19	—
He Huan Pi	18.53	—
Jiao Gu Lan	18.73	—
Ci Wu Jia	18.74	—
Dang Gui	19.07	—
Di Gu Pi	19.13	—
Chuang Mu Xiang	19.20	—

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Substanz	Distance in main model	Distance in second-stage model
Ma Huang	19.30	—
Ban Xia (Jiang)	19.81	—
Rou Gui	20.17	—
Huo Ma Ren	20.53	—
Gui Zhi	20.56	—
Gou Teng	20.71	—
Hou Po	20.77	—
Bai Zhu	21.11	—
Qiang Huo	21.29	—
Xian He Cao	21.31	—
Shan Yu Rou	21.48	—
Jie Geng	21.67	—
Sha Ren	21.96	—
Sang Bai Pi	22.15	—
Tian Hua Fen	22.17	—
Ju Hua	22.20	—
Chai Hu	22.24	—
Yin Chen Hao	22.27	—
Mao Dong Qing	22.29	—
Zhi Ke	22.44	—
Jiang Huang	23.67	—
Yin Yang Huo	23.82	—
Ling Zhi	23.88	—
Bai Xian Pi	24.15	—
Wu Wei Zi	24.35	—
Fu Ling	24.40	—
Ji Xue Teng	24.43	—
Sheng Jiang	24.66	—
Fu Xiao Mai	24.68	—
Sang Ji Shend	24.84	—
Wu Zhu Yu	25.02	—
He Shou Wu	25.16	—
Du Huo	25.20	—
Gan Cao	25.35	—
Mu Dan Pi	25.41	—
Nü Zhen Zi	25.51	—
Dan Dou Chi	25.52	—
Huang Qin	26.51	—
Che Qian Zi	27.06	—
Suan Zao Ren	27.10	—
(Shi) Chang Pu	27.66	—
Zhu Ru	28.41	—
Huang Bo	28.68	—
Yan Hu Suo	28.91	—
Ma Huang Gen	29.46	—
Sang Zhi	30.15	—
Zi Hua Di Ding	30.36	—
Xu Duan	31.32	—
Yi Yi Ren	31.97	—
Zhi Mu	32.21	—
Dan Zhu Ye	32.56	—
Fu Shen	32.57	—
Mang Xiao	32.66	—
Yi Mu Cao	32.93	—
Qing Pi	33.19	—
Chi Shao (Yao)	33.26	—
Ge Gen	34.25	—
Xiang Fu	34.35	—
Xie Bai	34.88	—

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Substanz	Distance in main model	Distance in second-stage model
Ba Ji Tian	35.55	—
Huang Qi	36.22	—
(Bai) Dou Kou	36.84	—
Hu Zhang	37.37	—
Bu Gu Zhi	38.43	—
Mai Men Dong	38.45	—
Huang Lian	38.83	—
Ku Shen	38.93	—
Bai Mao Gen	39.05	—
E Zhu	39.53	—
Cang Er Zi	39.71	—
Zi Su Zi	39.78	—
Zhi Shi	41.86	—
Chuan Lian Zi	42.29	—
Xin Yi	42.38	—
Du Zhong	43.84	—
Niu Bang Zi	48.13	—
Sang Ye	49.11	—
Hong Hua	49.44	—
Xia Ku Cao	49.72	—
(Huai) Niu Xi	50.04	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62378	62378	0.00	11.72
62670	62670	0.00	6.84
62669	62669	0.00	6.99
62445	62445	0.00	7.61
62377	62377	0.00	10.62
62446	62446	0.00	8.06

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 2.3-2020-05

Validated substance/substance group **Chi Shao (Yao)**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60014-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chi Shao (Yao); Paeoniae radix rubra

Special notes

When selecting the *Chi Shao (Yao)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chi Shao (Yao)	2	0	4

Second-stage model

For differentiation of the substance/substance group *Chi Shao (Yao)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Chi Shao (Yao)	G180H0705821	62363	40	from supplier
PhytoComm	Chi Shao (Yao)	G180H0705821	62364	40	from supplier
PhytoComm	Chi Shao (Yao)	G180H0705822	62481	40	from supplier
PhytoComm	Chi Shao (Yao)	G180H0705822	62482	40	from supplier

Validation samples

A total of 30 254 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 *Chi Shao (Yao)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Chi Shao (Yao)*.
- 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
PhytoComm	Chi Shao (Yao)	G180H0705821	62363 [†]	20
PhytoComm	Chi Shao (Yao)	G180H0705821	62364 [†]	20
PhytoComm	Chi Shao (Yao)	G180H0705822	62481 [†]	20
PhytoComm	Chi Shao (Yao)	G180H0705822	62482 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 4 spectra from 3 *Apo-Ident* customers from 4 batches from the substance/substance group *Chi Shao (Yao)*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Chi Shao (Yao)	g180h0705122	1
Phytocomm	Chi Shao (Yao)	G180H0705321	1
Phytocomm	Chi Shao (Yao)	G189H0705321	1
Phytocomm	Chi Shao (Yao)	G180H0705422	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Chi Shao (Yao)* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chi Shao (Yao)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	2	2	853

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8269 %)	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.)

[†]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*.

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chi Shao (Yao)* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Huang Qi	11.23	—
Gan Cao	25.64	—
Yuan Zhi	25.69	—
Bai Mao Gen	26.43	—
(Huai) Niu Xi	27.92	—
Mu Dan Pi	28.01	—
Zhi Ke	30.32	—
Jie Geng	30.67	—
Du Huo	31.22	—
Xiang Fu	31.39	—
Di Gu Pi	31.85	—
Bai Zhu	32.06	—
Chen Pi	32.10	—
Sang Zhi	32.45	—
Wu Yao	35.06	—
Gou Qi Zi	35.79	—
Gua Lou	35.98	—
Ban Zhi Lian	36.76	—
Lian Qiao	37.27	—
Shan Yao	37.92	—
Huang Qin	38.28	—
Dang Gui	38.47	—
(Shi) Chang Pu	38.97	—
Shan Yu Rou	39.27	—
Qing Pi	40.25	—
Dan Shen	40.58	—
Mang Xiao	40.61	—
Fu Zi	41.43	—
Ju Hua	42.45	—
Tian Hua Fen	42.55	—
Wu Wei Zi	43.09	—
Huang Lian	43.39	—
Zi Hua Di Ding	43.49	—
Jin Yin Hua	43.54	—
Da Zao	44.01	—
Chuan Xiong	44.74	—
Yin Yang Huo	45.72	—
Cang Er Zi	46.38	—
Pu Gong Ying	46.92	—
Mao Dong Qing	47.05	—
Long Yan Rou	47.48	—
Ma Huang	47.63	—
San Qi	47.92	—
Qin Jiao	48.18	—
Sha Shen (Bei)	48.24	—

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Substanz	Distance in main model	Distance in second-stage model
Fang Feng	48.29	—
Jiao Gu Lan	48.31	—
Ku Shen	48.54	—
Ye Jiao Teng	48.86	—
Gou Teng	49.00	—
Lian Zi	49.39	—
Niu Bang Zi	49.53	—
Gui Zhi	49.79	—
Chai Hu	50.02	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62363	62363	0.00	11.76
62364	62364	0.00	11.23
62482	62482	0.00	18.48
62481	62481	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 2.3-2020-05

Validated substance/substance group **Chuan Lian Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60078-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chuan Lian Zi; Meliae toosendan fructus

Special notes

When selecting the *Chuan Lian Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chuan Lian Zi	1	0	1

Second-stage model

For differentiation of the substance/substance group *Chuan Lian Zi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Chuan Lian Zi	G157H0306821	62355	40	from supplier
PhytoComm	Chuan Lian Zi	G157H0306821	62356	40	from supplier

Validation samples

A total of 30 254 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 *Chuan Lian Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Chuan Lian Zi*.
- 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
PhytoComm	Chuan Lian Zi	G157H0306821	62355 [†]	20
PhytoComm	Chuan Lian Zi	G157H0306821	62356 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 batches from the substance/substance group *Chuan Lian Zi*.
- 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
Phytocomm	Chuan Lian Zi	G157H0306421	1
PhytoComm	Chuan Lian Zi	G157H0306421	2

- 854 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	1	40	0	9876
Type C	3	0	3	851

The substance/substance group *Chuan Lian Zi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	99.9842 % (> 99.9484 %)	100.0000 % (> 85.0000 %)
Type C	99.7209 % (> 99.1349 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chuan Lian Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sheng Jiang	10.98	—
San Qi	11.33	—
Di Gu Pi	11.69	—
Mai Ya	15.67	—
Sang Zhi	15.71	—
Lai Fu Zi	15.83	—
Jie Geng	16.91	—
E Zhu	17.76	—
Bai He	18.10	—
Tian Hua Fen	19.26	—
Dang Gui	20.32	—
Mai Men Dong	21.73	—
Long Dan (Cao)	22.04	—
Ji Li	23.40	—
Ba Ji Tian	24.18	—
Mu Dan Pi	24.59	—
Du Huo	25.16	—
Bai Bian Dou	25.28	—
Mang Xiao	25.47	—
Da Zao	26.11	—
Cang Er Zi	26.63	—
Qin Jiao	27.04	—
Yan Hu Suo	27.18	—
Ban Zhi Lian	27.34	—
Zi Su Zi	28.53	—
Bai Zhu	29.01	—
Jiang Huang	30.29	—
Shan Yao	30.92	—
Qing Pi	32.12	—
Sha Shen (Bei)	32.40	—
Huang Qi	32.45	—
(Huai) Niu Xi	32.80	—
Xie Bai	33.50	—
Zhu Ling	34.50	—
(Shi) Chang Pu	35.40	—
Gui Zhi	35.78	—
Fu Ling	37.81	—
Xiang Fu	37.83	—
Rou Gui	37.84	—
Fang Feng	38.25	—
Niu Bang Zi	38.62	—
Lian Zi	39.16	—
Yi Yi Ren	41.15	—
Sha Ren	41.55	—
Chen Pi	41.88	—
Bai Xian Pi	42.39	—
(Bai) Dou Kou	42.61	—
Gua Lou	43.48	—
Yuan Zhi	43.90	—
Wang Bu Liu Xing	45.13	—
Bai Shao Yao	45.52	—
Tu Fu Ling	45.54	—

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Substanz	Distance in main model	Distance in second-stage model
Qiang Huo	45.96	—
Tian Men Dong	46.04	—
Ku Shen	46.31	—
Wu Wei Zi	46.64	—
Chai Hu	46.84	—
He Huan Pi	47.02	—
Bai Mao Gen	47.61	—
Ren Dong Teng	47.75	—
Ye Jiao Teng	48.33	—
Ma Huang Gen	48.48	—
Chi Shao (Yao)	49.66	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62356	62356	0.00	10.98
62355	62355	0.00	11.69

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 2.3-2020-05

Validated substance/substance group **Chuan Xiong**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60013-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chuan Xiong; Ligustici wallichii radix

Special notes

When selecting the *Chuan Xiong* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chuan Xiong	2	0	3

Second-stage model

For differentiation of the substance/substance group *Chuan Xiong* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Chuan Xiong	G136HS031RR2	62457	40	from supplier
PhytoComm	Chuan Xiong	G136HS031RR2	62458	40	from supplier
PhytoComm	Chuan Xiong	G136HS031SH1	62689	40	from supplier
PhytoComm	Chuan Xiong	G136HS031SH1	62690	40	from supplier

Validation samples

A total of 30 254 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 *Chuan Xiong*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Chuan Xiong*.
- 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
PhytoComm	Chuan Xiong	G136HS031RR2	62457 [†]	20
PhytoComm	Chuan Xiong	G136HS031RR2	62458 [†]	20
PhytoComm	Chuan Xiong	G136HS031SH1	62689 [†]	20
PhytoComm	Chuan Xiong	G136HS031SH1	62690 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 6 spectra from 6 *Apo-Ident* customers from 3 batches from the substance/substance group *Chuan Xiong*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Chuan Xiong	G136H0305221	1
Phytocomm	Chuan Xiong	g136h0305121	1
Phytocomm	Chuan Xiong	G136H0305421	2
PhytoComm	Chuan Xiong	G136H0305221	2

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Chuan Xiong* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chuan Xiong* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	79	1	9837
Type C	0	0	6	851

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	98.7500 % (> 95.0000 %)
Type C	100.0000 % (> 98.8258 %)	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.)

[†]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*.

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chuan Xiong* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pi Pa Ye	4.94	—
Shan Yao	5.67	—
Shen Qu	6.60	—
San Qi	6.72	—
Dang Shen	7.81	—
Dang Gui	7.88	—
Ren Dong Teng	8.71	—
Yuan Zhi	8.76	—
Cang Zhu	8.87	—
Hong Jing Tian	9.44	—
Lian Qiao	9.57	—
Chen Pi	9.65	—
Shan Yu Rou	9.78	—
Jin Yin Hua	10.24	—
Dan Shen	10.60	—
Ji Li	11.15	—
Hou Po	11.70	—
Gou Qi Zi	11.71	—
Dang Gui Wei	11.92	—
Gua Lou	12.04	—
Bai Shao Yao	12.20	—
Zhe Bei Mu	12.43	—
Lian Zi	12.46	—
Fu Zi	12.73	—
Ling Zhi	13.59	—
Jiao Gu Lan	14.04	—
Mao Dong Qing	14.31	—
Tian Hua Fen	14.51	—
Yu Zhu	15.02	—
Tai Zi Shen	15.11	—
Chai Hu	15.34	—
Dan Dou Chi	15.47	—
Bai Zi Ren	15.88	—
Huo Ma Ren	17.10	—
Ye Jiao Teng	17.31	—
He Huan Pi	17.41	—
Di Gu Pi	17.85	—
Yin Yang Huo	18.15	—
Bai Xian Pi	18.28	—
Tu Fu Ling	18.30	—
Fu Ling	18.46	—
Gou Teng	19.00	—
Che Qian Zi	19.18	—
Chuang Mu Xiang	19.21	—
Zhi Ke	19.23	—

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Substanz	Distance in main model	Distance in second-stage model
Gui Zhi	19.35	—
Ma Huang	19.87	—
Zhi Mu	20.13	—
Sheng Jiang	20.23	—
Ci Wu Jia	20.32	—
Ji Xue Teng	20.39	—
Mu Dan Pi	20.42	—
Yu Jin	20.91	—
Qiang Huo	21.00	—
Wu Wei Zi	21.27	—
Tao Ren	21.37	—
Yan Hu Suo	21.41	—
Long Yan Rou	21.57	—
Da Zao	21.67	—
Rou Gui	22.92	—
Ma Huang Gen	23.16	—
Suan Zao Ren	23.78	—
Fo Shou	23.96	—
Qing Pi	24.70	—
Zi Hua Di Ding	24.74	—
Zhu Ru	25.12	—
Huang Qin	25.34	—
Gan Cao	25.77	—
Ban Xia (Jiang)	27.03	—
Bai Zhu	27.41	—
Yi Yi Ren	27.69	—
Tian Men Dong	28.55	—
Fu Xiao Mai	29.38	—
Sang Zhi	31.80	—
Jie Geng	32.63	—
Huang Lian	32.86	—
Du Zhong	32.92	—
Chi Shao (Yao)	36.26	—
Cang Er Zi	37.33	—
Fu Shen	38.50	—
Huang Bai	39.84	—
Chuan Lian Zi	40.27	—
Mai Men Dong	40.45	—
Mang Xiao	40.80	—
Hong Hua	41.83	—
Bai Mao Gen	46.61	—
Sang Ye	48.43	—
Zi Su Zi	48.76	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62690	62690	0.00	4.94
62689	62689	0.00	5.53
62458	62458	0.00	6.72
62457	62457	0.00	7.38

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 2.3-2020-05

Validated substance/substance group **Chuang Mu Xiang**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50323-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chuang Mu Xiang; Vladimira radix

Special notes

When selecting the *Chuang Mu Xiang* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chuang Mu Xiang	1	0	3

Second-stage model

For differentiation of the substance/substance group *Chuang Mu Xiang* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Chuang Mu Xiang	G219HS046SK1	62643	40	from supplier
PhytoComm	Chuang Mu Xiang	G219HS046SK1	62644	40	from supplier

Validation samples

A total of 30 254 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 *Chuang Mu Xiang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Chuang Mu Xiang*.
- 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
PhytoComm	Chuang Mu Xiang	G219HS046SK1	62643 [†]	20
PhytoComm	Chuang Mu Xiang	G219HS046SK1	62644 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 5 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Chuang Mu Xiang*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Chuang Mu Xiang	G219H0309322	1
Phytocomm	Chuang Mu Xiang	g219h0309321	1
Phytocomm	Chuang Mu Xiang	g219h0309322	1
Phytocomm	Chuang Mu Xiang	G219H0309521	2

- 852 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	5	852

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chuang Mu Xiang* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chen Pi	9.87	—
Chuan Xiong	12.50	—
Gou Qi Zi	13.55	—
Cang Zhu	14.10	—
Yuan Zhi	14.28	—
Dang Shen	14.32	—
Shan Yao	15.20	—
Pi Pa Ye	17.02	—
Mu Dan Pi	17.30	—
Shan Yu Rou	17.46	—
Long Yan Rou	18.04	—
Hong Jing Tian	18.05	—
Bai Shao Yao	18.16	—
Yu Zhu	18.49	—
Jin Yin Hua	18.72	—
Suan Zao Ren	18.87	—
Jiao Gu Lan	19.75	—
Lian Zi	20.11	—
Bai Zhu	20.17	—
Lian Qiao	20.27	—
Dang Gui Wei	20.28	—
Dan Shen	21.49	—
Shen Qu	22.32	—
Zhe Bei Mu	22.54	—
San Qi	22.75	—
Ji Li	22.95	—
Gua Lou	22.98	—
Di Gu Pi	23.46	—
Ren Dong Teng	23.91	—
Tai Zi Shen	24.07	—
Chai Hu	24.56	—
Zhi Ke	25.20	—
Jie Geng	25.60	—
Gan Cao	25.71	—
Mao Dong Qing	25.71	—
Da Zao	27.06	—
Bai Zi Ren	27.17	—
Wu Wei Zi	27.22	—
Hou Po	27.25	—
Ci Wu Jia	28.38	—
Dang Gui	28.54	—
Zi Hua Di Ding	28.77	—
Ling Zhi	29.00	—
Tu Fu Ling	30.11	—
He Huan Pi	30.18	—
Bai Xian Pi	30.79	—
Dan Dou Chi	31.12	—
Fu Zi	31.78	—
Gou Teng	32.29	—
Tao Ren	32.34	—
Gui Zhi	32.35	—
Ye Jiao Teng	32.46	—

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Substanz	Distance in main model	Distance in second-stage model
Cang Er Zi	32.56	—
Tian Men Dong	32.72	—
Huo Ma Ren	32.81	—
Sheng Jiang	32.91	—
Fo Shou	33.10	—
Tian Hua Fen	33.20	—
Sang Zhi	33.91	—
Yin Yang Huo	33.96	—
Zhi Mu	34.07	—
Ji Xue Teng	34.32	—
Qing Pi	34.50	—
Huang Qin	34.81	—
Rou Gui	35.03	—
Fu Ling	35.42	—
Yan Hu Suo	35.53	—
Mai Men Dong	35.92	—
Ma Huang	36.42	—
Qiang Huo	37.49	—
Chi Shao (Yao)	38.92	—
Che Qian Zi	38.99	—
Yu Jin	39.99	—
Zhu Ru	41.00	—
Ma Huang Gen	41.24	—
Hong Hua	41.42	—
Mang Xiao	42.84	—
Fu Xiao Mai	43.09	—
Huang Qi	43.17	—
Yi Yi Ren	44.40	—
Du Zhong	45.14	—
Ban Xia (Jiang)	45.17	—
Niu Bang Zi	45.34	—
Huang Lian	46.10	—
Chuan Lian Zi	47.50	—
Sang Ye	48.97	—
Lai Fu Zi	49.06	—
Bai Mao Gen	49.26	—
Huang Bai	50.19	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62643	62643	0.00	9.87
62644	62644	0.00	9.91

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 2.3-2020-05

Validated substance/substance group **Ci Wu Jia**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60354-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ci Wu Jia; Eleutherococci radix

Special notes

When selecting the *Ci Wu Jia* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ci Wu Jia	1	0	0

Second-stage model

For differentiation of the substance/substance group *Ci Wu Jia* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ci Wu Jia	G302HS422SH1	62623	40	from supplier
PhytoComm	Ci Wu Jia	G302HS422SH1	62624	40	from supplier

Validation samples

A total of 30 254 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 *Ci Wu Jia*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ci Wu Jia*.
- 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
PhytoComm	Ci Wu Jia	G302HS422SH1	62623 [†]	20
PhytoComm	Ci Wu Jia	G302HS422SH1	62624 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Ci Wu Jia*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	73	7	19 400
Type B	0	33	7	9877
Type C	0	0	0	857

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	91.2500 % (> 87.5000 %)
Type B	100.0000 % (> 99.9285 %)	82.5000 % (> 75.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ci Wu Jia* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

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

Substance	Distance in main model	Distance in second-stage model
Sheng Jiang	2.90	—
He Huan Pi	3.46	—
Fu Xiao Mai	4.24	—
Tao Ren	4.66	—
Gui Zhi	4.82	—
Di Gu Pi	7.72	—
Zhu Ru	8.20	—
Fu Ling	8.22	—
Yi Yi Ren	8.80	—
Ban Xia (Jiang)	8.98	—
Bai Zi Ren	9.51	—
Rou Gui	9.90	—
Gou Teng	9.91	—
Lian Zi	10.27	—
Ji Li	10.48	—
Huo Ma Ren	10.55	—
Ling Zhi	11.43	—
Bai Shao Yao	12.16	—
Tai Zi Shen	12.98	—
Zhe Bei Mu	13.53	—
Shen Qu	13.62	—
Bai Xian Pi	13.96	—
Ma Huang Gen	15.82	—
Ji Xue Teng	16.11	—
Tian Hua Fen	16.35	—
Fo Shou	16.74	—
Ye Jiao Teng	17.01	—
Gua Lou	18.70	—
Tian Men Dong	19.90	—
Ren Dong Teng	20.77	—
Yu Jin	20.83	—
Chen Pi	21.02	—
Fu Shen	21.50	—
Tu Fu Ling	21.78	—
Yuan Zhi	22.34	—
Chuan Xiong	22.93	—
Shan Yao	23.04	—
Long Yan Rou	23.43	—
Pi Pa Ye	23.71	—
Da Zao	24.39	—
Lian Qiao	24.92	—
Dan Dou Chi	26.96	—
Dang Shen	27.64	—
Yan Hu Suo	27.95	—
Dan Shen	28.53	—
Mao Dong Qing	29.94	—
Fu Zi	31.70	—
Jiao Gu Lan	31.72	—
Chai Hu	32.11	—
San Qi	33.37	—
Dang Gui Wei	34.23	—
Yu Zhu	34.31	—
Zhi Ke	34.36	—
Yin Yang Huo	34.56	—
Shan Yu Rou	34.89	—
Hong Jing Tian	36.30	—
Jin Yin Hua	36.40	—
Cang Zhu	37.62	—
Ma Huang	37.99	—

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Substanz	Distance in main model	Distance in second-stage model
Dang Gui	38.22	—
Wu Wei Zi	38.29	—
Hou Po	38.68	—
Huang Qin	40.49	—
Mang Xiao	40.68	—
Che Qian Zi	40.89	—
Zhi Mu	41.98	—
Qiang Huo	43.16	—
Suan Zao Ren	45.29	—
Huang Lian	47.91	—
Jie Geng	48.00	—
Sang Zhi	48.54	—
Bai Zhu	48.66	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62624	62624	0.00	2.90
62623	62623	0.00	3.12

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 2.3-2020-05

Validated substance/substance group **Da Huang**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60140-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Da Huang; Rhei radix et rhizoma

Special notes

When selecting the *Da Huang* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Da Huang	1	0	3

Second-stage model

For differentiation of the substance/substance group *Da Huang* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Da Huang	G212H0320822	62495	40	from supplier
PhytoComm	Da Huang	G212H0320822	62496	40	from supplier

Validation samples

A total of 30 254 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 *Da Huang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Da Huang*.
- 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
PhytoComm	Da Huang	G212H0320822	62495 [†]	20
PhytoComm	Da Huang	G212H0320822	62496 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 7 spectra from 5 *Apo-Ident* customers from 3 batches from the substance/substance group *Da Huang*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Da Huang	G212H0320321	2
Phytocomm	Da Huang	g212h0320023	1
Phytocomm	Da Huang	G212H0320521	3
PhytoComm	Da Huang	G212H0320321	1

- 850 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	1	6	850

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8255 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Da Huang* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hua Shi	36.25	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62495	62495	0.00	36.28
62496	62496	0.00	36.25

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Da Zao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60055-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Da Zao; Zizyphi jujubae fructus

Special notes

When selecting the *Da Zao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Da Zao	2	0	2

Second-stage model

For differentiation of the substance/substance group *Da Zao* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Da Zao	G129HS019RT1	62455	40	from supplier
PhytoComm	Da Zao	G129HS019RT1	62456	40	from supplier
PhytoComm	Da Zao	G129H0316821	62539	40	from supplier
PhytoComm	Da Zao	G129H0316821	62540	40	from supplier

Validation samples

A total of 30 254 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 *Da Zao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Da Zao*.
- 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
PhytoComm	Da Zao	G129HS019RT1	62455 [†]	20
PhytoComm	Da Zao	G129HS019RT1	62456 [†]	20
PhytoComm	Da Zao	G129H0316821	62539 [†]	20
PhytoComm	Da Zao	G129H0316821	62540 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 4 spectra from 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Da Zao*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Da Zao	g129h0316221	1
Phytocomm	Da Zao	G129H0316521	3

- 853 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Da Zao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Da Zao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	1	3	853

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8269 %)	n/a (n/a)

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

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Da Zao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Gua Lou	13.85	—
Long Yan Rou	13.91	—
Tian Men Dong	14.57	—
Dang Gui	15.24	—
Chen Pi	16.73	—
Rou Gui	18.20	—
Dang Shen	18.53	—
Di Gu Pi	19.49	—
Fu Xiao Mai	20.45	—
Bai Shao Yao	20.89	—
Ji Li	21.36	—
Ye Jiao Teng	21.68	—
Yu Zhu	21.70	—
Yuan Zhi	21.73	—
Tai Zi Shen	21.98	—
Fo Shou	22.00	—
Chuan Xiong	22.08	—
Shen Qu	22.81	—
He Huan Pi	22.90	—
Jie Geng	22.94	—
Ban Xia (Jiang)	23.10	—
Fu Shen	23.21	—
Long Dan (Cao)	23.50	—
Mai Men Dong	23.55	—
Gou Teng	24.91	—
Gui Zhi	25.16	—
Tao Ren	25.41	—
Sheng Jiang	26.15	—
Mang Xiao	26.22	—
Pi Pa Ye	26.25	—
Fu Ling	26.39	—
Qin Jiao	26.90	—
Du Huo	27.07	—
Bai Zhu	27.19	—
Huang Qi	27.68	—
Mu Dan Pi	27.73	—
Bai Xian Pi	28.49	—
Lian Zi	28.98	—
Zhe Bei Mu	29.18	—
Huang Qin	29.38	—
Dang Gui Wei	29.39	—
Cang Zhu	29.96	—
Ma Huang Gen	30.10	—
Ji Xue Teng	30.20	—
Shan Yu Rou	30.44	—
Mai Ya	30.96	—
Sang Zhi	31.05	—
Ci Wu Jia	31.25	—

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Substanz	Distance in main model	Distance in second-stage model
Yi Yi Ren	31.62	—
Ma Huang	31.76	—
Tu Fu Ling	32.04	—
Ling Zhi	33.30	—
San Qi	33.31	—
Bai Zi Ren	33.95	—
Bai Mao Gen	34.03	—
Lian Qiao	34.07	—
Zhu Ru	34.09	—
(Huai) Niu Xi	35.27	—
Chuan Lian Zi	35.38	—
Gou Qi Zi	36.23	—
Ba Ji Tian	36.52	—
Ren Dong Teng	36.91	—
Huo Ma Ren	37.10	—
Shan Yao	37.46	—
Jiao Gu Lan	37.55	—
Zhi Ke	37.73	—
Zhi Mu	38.15	—
Sha Shen (Bei)	38.63	—
Lai Fu Zi	38.79	—
Chuang Mu Xiang	39.71	—
Dan Shen	40.07	—
Tian Hua Fen	40.64	—
Yin Yang Huo	40.91	—
Bai He	41.01	—
E Zhu	41.36	—
Fang Feng	43.01	—
Bai Bian Dou	43.20	—
Hong Jing Tian	43.47	—
Fu Zi	43.89	—
Yan Hu Suo	44.62	—
Jin Yin Hua	44.76	—
Yu Jin	44.90	—
Dan Dou Chi	45.05	—
Wu Wei Zi	45.60	—
Gan Cao	46.87	—
Chi Shao (Yao)	47.12	—
Mao Dong Qing	49.52	—
Hou Po	49.63	—
Zhu Ling	50.04	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62539	62539	0.00	15.54
62540	62540	0.00	15.24
62455	62455	0.00	13.91
62456	62456	0.00	13.85

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 2.3-2020-05

Validated substance/substance group **Dan Dou Chi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60794-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dan Dou Chi; Sojae semen praeparatum

Special notes

When selecting the *Dan Dou Chi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dan Dou Chi	1	0	1

Second-stage model

For differentiation of the substance/substance group *Dan Dou Chi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Dan Dou Chi	G232HS239SK1	62713	40	from supplier
PhytoComm	Dan Dou Chi	G232HS239SK1	62714	40	from supplier

Validation samples

A total of 30 254 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 *Dan Dou Chi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Dan Dou Chi*.
- 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
PhytoComm	Dan Dou Chi	G232HS239SK1	62713 [†]	20
PhytoComm	Dan Dou Chi	G232HS239SK1	62714 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Dan Dou Chi*.
- 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
Phytocomm	Dan Dou Chi	G232HS239	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	3	76	4	19 397
Type B	0	37	3	9877
Type C	0	0	1	856

The substance/substance group *Dan Dou Chi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9881 % (> 99.9698 %)	95.0000 % (> 91.2500 %)
Type B	100.0000 % (> 99.9285 %)	92.5000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8367 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dan Dou Chi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Xian Pi	3.19	—
Ling Zhi	6.67	—
Ye Jiao Teng	8.50	—
Ren Dong Teng	8.80	—
Lian Zi	9.13	—
Mao Dong Qing	9.32	—
Tu Fu Ling	9.53	—
Yuan Zhi	10.83	—
Yu Jin	10.83	—
Yin Yang Huo	11.19	—
Hou Po	11.72	—
Chai Hu	11.74	—
Rou Gui	12.95	—
Shen Qu	14.11	—
Qiang Huo	15.28	—
Che Qian Zi	15.29	—
Ji Li	16.19	—
Ji Xue Teng	17.26	—
Gou Teng	17.36	—
He Huan Pi	17.59	—
Sheng Jiang	17.67	—
Dan Shen	17.76	—
Ma Huang Gen	18.58	—
Gui Zhi	18.90	—
Shan Yao	19.22	—
Huo Ma Ren	19.56	—
Yan Hu Suo	19.71	—
Lian Qiao	19.81	—
Pi Pa Ye	19.87	—
Chuan Xiong	20.20	—
Chen Pi	21.02	—
Fu Ling	21.34	—
Jiao Gu Lan	21.52	—
Jin Yin Hua	21.56	—
Bai Shao Yao	21.57	—
Yi Yi Ren	22.56	—
Gua Lou	23.49	—
Ma Huang	23.57	—
Fu Zi	23.59	—
Du Zhong	24.11	—
Tao Ren	24.67	—
Zhi Ke	24.75	—
Zhe Bei Mu	24.86	—
Tian Hua Fen	24.96	—
Di Gu Pi	25.00	—
Hong Jing Tian	25.68	—
Qing Pi	26.24	—
Cang Zhu	26.96	—
Mu Dan Pi	27.58	—
Zi Hua Di Ding	28.15	—
Long Yan Rou	29.45	—
Tai Zi Shen	29.56	—

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Substanz	Distance in main model	Distance in second-stage model
Wu Wei Zi	30.06	—
Bai Zi Ren	30.11	—
Ci Wu Jia	30.42	—
Huang Lian	30.43	—
Fu Xiao Mai	31.10	—
Gou Qi Zi	31.10	—
Fo Shou	31.35	—
Fu Shen	32.41	—
Tian Men Dong	32.88	—
Da Zao	33.07	—
Ban Xia (Jiang)	33.56	—
Yu Zhu	33.81	—
Zhu Ru	36.25	—
Dang Shen	36.52	—
Suan Zao Ren	36.74	—
Dang Gui Wei	37.88	—
Sang Zhi	38.29	—
Ban Zhi Lian	38.40	—
Mang Xiao	38.45	—
San Qi	38.52	—
Huang Bai	39.53	—
Dang Gui	41.45	—
Chuang Mu Xiang	41.59	—
Huang Qin	42.29	—
Jie Geng	42.34	—
Chuan Lian Zi	42.52	—
Chi Shao (Yao)	44.27	—
Shan Yu Rou	45.22	—
Bai Bian Dou	45.77	—
Wang Bu Liu Xing	45.98	—
Zi Su Zi	46.84	—
Bai Zhu	47.09	—
Pu Gong Ying	47.68	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62713	62713	0.00	3.19
62714	62714	0.00	4.03

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 2.3-2020-05

Validated substance/substance group **Dan Shen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60030-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dan Shen; Salviae miltiorrhizae radix

Special notes

When selecting the *Dan Shen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dan Shen	1	0	4

Second-stage model

For differentiation of the substance/substance group *Dan Shen* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Dan Shen	G214HS059SG1	62573	40	from supplier
PhytoComm	Dan Shen	G214HS059SG1	62574	40	from supplier

Validation samples

A total of 30 254 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 *Dan Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Dan Shen*.
- 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
PhytoComm	Dan Shen	G214HS059SG1	62573 [†]	20
PhytoComm	Dan Shen	G214HS059SG1	62574 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

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

Supplier	Substance	Batch	Spectra
Phytocomm	Dan Shen	G214H0441121	1
Phytocomm	Dan Shen	G214H0441221	1
Phytocomm	Dan Shen	G214H0441322	1
Phytocomm	Dan Shen	g214h0441121	1
Phytocomm	Dan Shen	G214H0441522	1
PhytoComm	Dan Shen	G214H0441221	2
PhytoComm	Dan Shen	G214H0441322	1
PhytoComm	Dan Shen	G214H0441522	1

- 848 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	79	1	19 400
Type B	4	39	1	9873
Type C	0	0	9	848

The substance/substance group *Dan Shen* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	98.7500 % (> 95.0000 %)
Type B	99.9604 % (> 99.9247 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8251 %)	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.)

[†]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*.

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dan Shen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zi Hua Di Ding	4.27	—
Mu Dan Pi	6.54	—
Hou Po	10.46	—
Jin Yin Hua	10.75	—
Yin Yang Huo	11.26	—
Hong Jing Tian	11.41	—
Zhi Ke	11.69	—
Ye Jiao Teng	11.94	—
Qiang Huo	11.95	—
Jiao Gu Lan	12.46	—
Huang Bai	15.16	—
Chai Hu	15.49	—
Ma Huang	15.69	—
Chuan Xiong	15.99	—
Bai Xian Pi	17.25	—
Yu Jin	17.26	—
Shan Yao	17.31	—
Dan Dou Chi	17.38	—
Mao Dong Qing	17.94	—
Ji Xue Teng	18.08	—
Ren Dong Teng	18.25	—
Pi Pa Ye	18.30	—
Qing Pi	18.34	—
Huang Lian	18.99	—
Du Zhong	19.32	—
Yuan Zhi	19.58	—
Wu Wei Zi	19.70	—
Bai Shao Yao	19.81	—
Fu Zi	20.27	—
Lian Zi	21.08	—
Yan Hu Suo	21.12	—
Che Qian Zi	21.53	—
Di Gu Pi	21.99	—
Gua Lou	22.61	—
Gou Qi Zi	22.63	—
Shen Qu	23.55	—
Lian Qiao	24.43	—
Tu Fu Ling	24.81	—
He Huan Pi	25.18	—
Ji Li	25.18	—
Cang Zhu	25.33	—
Ling Zhi	26.24	—
Chi Shao (Yao)	28.08	—
Gou Teng	28.65	—
Chen Pi	28.86	—

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Substanz	Distance in main model	Distance in second-stage model
Rou Gui	28.86	—
Pu Gong Ying	28.86	—
Shan Yu Rou	29.74	—
Bai Zhu	30.31	—
Tao Ren	30.71	—
Sang Ye	30.90	—
Huang Qin	31.45	—
Cang Er Zi	32.07	—
Huo Ma Ren	32.27	—
Zhe Bei Mu	32.72	—
Ban Zhi Lian	32.80	—
Gan Cao	33.64	—
Bai Mao Gen	34.51	—
Da Zao	34.60	—
Gui Zhi	34.72	—
Ma Huang Gen	34.94	—
Chuang Mu Xiang	35.73	—
Jie Geng	35.79	—
Tian Hua Fen	36.17	—
Sang Zhi	37.00	—
Sheng Jiang	37.47	—
Tai Zi Shen	37.48	—
Hong Hua	37.68	—
San Qi	37.73	—
Dang Gui	38.90	—
Long Yan Rou	39.34	—
Dang Gui Wei	39.69	—
Yu Zhu	39.77	—
Mang Xiao	40.32	—
Dang Shen	40.86	—
Ci Wu Jia	41.26	—
Wu Yao	41.28	—
Suan Zao Ren	41.96	—
Bai Zi Ren	42.16	—
Xi Xian Cao	43.43	—
Ban Xia (Jiang)	43.46	—
Fu Ling	43.81	—
Jiang Huang	44.79	—
Fu Shen	45.23	—
Yi Yi Ren	45.41	—
(Shi) Chang Pu	45.82	—
Fo Shou	46.26	—
E Zhu	46.53	—
Chuan Lian Zi	47.31	—
Du Huo	48.81	—
Wu Mei	49.06	—
Niu Bang Zi	49.31	—
Yi Mu Cao	49.74	—
Huang Qi	49.75	—

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

Identity according to identity test using NIR spectroscopy

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

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62574	62574	0.00	7.48
62573	62573	0.00	4.27

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 2.3-2020-05

Validated substance/substance group **Dan Zhu Ye**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60147-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dan Zhu Ye; Lophatheri gracilis herba

Special notes

When selecting the *Dan Zhu Ye* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dan Zhu Ye	2	0	1

Second-stage model

For differentiation of the substance/substance group *Dan Zhu Ye* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Dan Zhu Ye	G046H1105621	62105	40	from supplier
PhytoComm	Dan Zhu Ye	G046H1105621	62106	40	from supplier
PhytoComm	Dan Zhu Ye	G046H1105821	62581	40	from supplier
PhytoComm	Dan Zhu Ye	G046H1105821	62582	40	from supplier

Validation samples

A total of 30 254 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 *Dan Zhu Ye*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Dan Zhu Ye*.
- 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
PhytoComm	Dan Zhu Ye	G046H1105621	62105 [†]	20
PhytoComm	Dan Zhu Ye	G046H1105621	62106 [†]	20
PhytoComm	Dan Zhu Ye	G046H1105821	62581 [†]	20
PhytoComm	Dan Zhu Ye	G046H1105821	62582 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 2 spectra from 2 *Apo-Ident* customers from 1 batches from the substance/substance group *Dan Zhu Ye*.
- 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
Phytocomm	Dan Zhu Ye	G046H1105321	2

- 855 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dan Zhu Ye* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dan Zhu Ye* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	14	0	2	841

The substance/substance group *Dan Zhu Ye* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	98.1279 % (> 97.5430 %)	n/a (n/a)

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

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dan Zhu Ye* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
He Shou Wu	9.96	—
Jing Jie	10.50	—
Sang Bai Pi	12.29	—
Sha Ren	12.63	—
Bu Gu Zhi	15.13	—
Yin Chen Hao	15.78	—
Du Zhong	16.39	—
Gu Sui Bu	16.51	—
Sang Ji Shend	17.02	—
Xian He Cao	17.45	—
Nü Zhen Zi	21.92	—
Wu Zhu Yu	21.95	—
He Huan Pi	22.90	—
Gou Teng	25.39	—
Jin Qian Cao	25.92	—
Qiang Huo	27.00	—
Yu Jin	29.43	—
Pu Gong Ying	30.67	—
Huang Bo	30.89	—
Chen Pi	31.62	—
Zhi Shi	31.88	—
Yi Mu Cao	32.01	—
Wu Jia Pi	33.74	—
Gui Zhi	33.96	—
Sang Ye	34.36	—
Ge Gen	35.37	—
Fu Zi	36.00	—
Yu Xing Cao	36.38	—
Fang Feng	36.72	—
Jiang Huang	38.09	—
Hong Jing Tian	38.34	—
Hu Zhang	40.06	—
Xia Ku Cao	40.54	—
Bai Hua She She Cao	40.58	—
Xuan Shen	41.45	—
Xin Yi	41.46	—
(Bai) Dou Kou	42.75	—
Ji Li	43.62	—
Wu Yao	44.14	—
Han Lian Cao	44.22	—
Mang Xiao	44.59	—
Tu Si Zi	46.90	—
Xu Duan	47.59	—
Qing Hao	49.12	—
Hua Shi	49.50	—
Shan Yao	49.70	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62582	62582	0.00	12.29
62581	62581	0.00	12.49
62105	62105	0.00	9.96
62106	62106	0.00	10.50

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Dang Gui**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60003-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dang Gui; Angelicae sinensis radix

Special notes

When selecting the *Dang Gui* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dang Gui	2	0	4

Second-stage model

For differentiation of the substance/substance group *Dang Gui* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Dang Gui	G022H1306822	62413	40	from supplier
PhytoComm	Dang Gui	G022H1306822	62414	40	from supplier
PhytoComm	Dang Gui	G022HS290SK1	62649	40	from supplier
PhytoComm	Dang Gui	G022HS290SK1	62650	40	from supplier

Validation samples

A total of 30 254 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 *Dang Gui*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Dang Gui*.
- 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
PhytoComm	Dang Gui	G022H1306822	62413 [†]	20
PhytoComm	Dang Gui	G022H1306822	62414 [†]	20
PhytoComm	Dang Gui	G022HS290SK1	62649 [†]	20
PhytoComm	Dang Gui	G022HS290SK1	62650 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 12 spectra from 5 *Apo-Ident* customers from 5 batches from the substance/substance group *Dang Gui*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Dang Gui	g022h1306121	3
Phytocomm	Dang Gui	G022H1306422	3
PhytoComm	Dang Gui	G13-0784	1
PhytoComm	Dang Gui	G022H1306121	1
PhytoComm	Dang Gui	G022H1306621	4

- 845 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dang Gui* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dang Gui* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	1	5	7	844

The substance/substance group *Dang Gui* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.9225 % (> 99.3349 %)	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

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dang Gui* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dang Gui Wei	6.75	—
Mu Dan Pi	8.36	—
Dang Shen	8.78	—
Chuan Xiong	9.01	—
Gou Qi Zi	9.45	—
Sang Zhi	11.15	—
Cang Zhu	11.62	—
San Qi	12.03	—
Yuan Zhi	12.36	—
Shan Yu Rou	12.50	—
Yu Zhu	12.52	—
Du Huo	13.69	—
Gua Lou	13.74	—
Di Gu Pi	14.18	—
Lian Qiao	14.32	—
Ba Ji Tian	14.69	—
Tai Zi Shen	14.95	—
Bai Shao Yao	15.09	—
Pi Pa Ye	15.31	—
Ye Jiao Teng	15.65	—
Chen Pi	15.84	—
Jie Geng	16.08	—
Zhe Bei Mu	16.58	—
Jiao Gu Lan	17.53	—
He Huan Pi	17.76	—
Ren Dong Teng	17.81	—
Zhi Ke	18.30	—
Jin Yin Hua	18.70	—
Long Yan Rou	18.72	—
Bai Mao Gen	18.86	—
Shan Yao	19.15	—
Ci Wu Jia	19.73	—
Tian Hua Fen	19.84	—
(Huai) Niu Xi	20.33	—
Zhi Mu	20.47	—
Ji Li	20.72	—
Huang Qi	20.78	—
Fo Shou	21.70	—
Hou Po	21.97	—
Chuang Mu Xiang	22.17	—
Qin Jiao	22.45	—
Tao Ren	22.48	—
Ma Huang	22.58	—

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Substanz	Distance in main model	Distance in second-stage model
Da Zao	22.68	—
Chuan Lian Zi	23.16	—
Gan Cao	23.60	—
Bai Zi Ren	23.69	—
Shen Qu	23.90	—
Huang Qin	23.93	—
Fang Feng	24.06	—
Hong Jing Tian	24.32	—
Long Dan (Cao)	24.42	—
Sha Shen (Bei)	24.58	—
E Zhu	25.01	—
Gou Teng	25.34	—
Fu Zi	25.35	—
Bai Zhu	25.62	—
Lian Zi	25.92	—
Wu Wei Zi	26.20	—
Huo Ma Ren	26.46	—
Ban Xia (Jiang)	26.72	—
Rou Gui	26.72	—
Ji Xue Teng	26.78	—
Tian Men Dong	28.31	—
Mang Xiao	28.51	—
Sheng Jiang	28.75	—
(Shi) Chang Pu	29.68	—
Fu Ling	29.82	—
Dan Shen	29.95	—
Yin Yang Huo	30.58	—
Mai Ya	30.62	—
Gui Zhi	30.84	—
Suan Zao Ren	31.38	—
Yan Hu Suo	31.83	—
Lai Fu Zi	31.88	—
Mai Men Dong	32.15	—
Xie Bai	32.42	—
Qing Pi	32.59	—
Zhu Ru	33.04	—
Che Qian Zi	33.16	—
Tu Fu Ling	33.27	—
Yi Yi Ren	33.88	—
Mao Dong Qing	34.36	—
Ling Zhi	34.41	—
Zi Hua Di Ding	35.41	—
Bai Xian Pi	35.57	—
Xian He Cao	35.69	—
Fu Xiao Mai	36.13	—
Chai Hu	36.85	—
Dan Dou Chi	37.09	—
Wu Yao	37.48	—
Zi Su Zi	38.18	—
Ju Hua	38.28	—
Qiang Huo	38.76	—
Jiang Huang	39.22	—
Ban Zhi Lian	39.45	—
Xiang Fu	39.54	—
Chi Shao (Yao)	39.58	—
Zhu Ling	40.86	—
Fu Shen	41.21	—
Sha Ren	41.37	—
Bai He	41.88	—

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Substanz	Distance in main model	Distance in second-stage model
Yu Jin	42.26	—
Hong Hua	42.49	—
Ma Huang Gen	43.76	—
Huang Lian	44.35	—
Cang Er Zi	44.84	—
(Bai) Dou Kou	45.21	—
Bai Bian Dou	46.11	—
Ku Shen	46.54	—
Niu Bang Zi	50.11	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62650	62650	0.00	6.91
62649	62649	0.00	6.75
62414	62414	0.00	8.36
62413	62413	0.00	8.59

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 2.3-2020-05

Validated substance/substance group **Dang Gui Wei**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60308-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dang Gui Wei; Angelicae sinensis radix extremas

Special notes

When selecting the *Dang Gui Wei* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dang Gui Wei	1	0	0

Second-stage model

For differentiation of the substance/substance group *Dang Gui Wei* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Dang Gui Wei	G312HS291SK1	62621	40	from supplier
PhytoComm	Dang Gui Wei	G312HS291SK1	62622	40	from supplier

Validation samples

A total of 30 254 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 *Dang Gui Wei*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Dang Gui Wei*.
- 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
PhytoComm	Dang Gui Wei	G312HS291SK1	62621 [†]	20
PhytoComm	Dang Gui Wei	G312HS291SK1	62622 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Dang Gui Wei*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dang Gui Wei* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

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

Substance	Distance in main model	Distance in second-stage model
Dang Shen	7.60	—
Chen Pi	7.62	—
Yuan Zhi	7.99	—
Bai Shao Yao	8.06	—
Gua Lou	8.60	—
Yu Zhu	8.68	—
Chuan Xiong	9.70	—
Pi Pa Ye	10.21	—
Fo Shou	10.57	—
Dang Gui	10.65	—
Cang Zhu	10.98	—
San Qi	11.06	—
Tai Zi Shen	12.61	—
Ye Jiao Teng	13.14	—
Zhe Bei Mu	13.27	—
Gou Qi Zi	13.58	—
Shen Qu	13.66	—
Di Gu Pi	14.07	—
Ren Dong Teng	15.03	—
Shan Yao	15.83	—
Ji Li	15.83	—
He Huan Pi	15.91	—
Da Zao	16.32	—
Lian Qiao	16.39	—
Tian Men Dong	16.42	—
Ci Wu Jia	16.76	—
Bai Zi Ren	16.77	—
Long Yan Rou	17.53	—
Tao Ren	17.88	—
Lian Zi	18.14	—
Rou Gui	19.30	—
Tian Hua Fen	19.71	—
Shan Yu Rou	19.82	—
Huo Ma Ren	20.60	—
Tu Fu Ling	20.75	—
Jiao Gu Lan	20.92	—
Gou Teng	21.26	—
Gui Zhi	22.64	—
Zhi Ke	22.77	—
Sheng Jiang	22.98	—
Ma Huang	23.31	—
Fu Zi	23.33	—
Fu Ling	23.35	—
Ban Xia (Jiang)	23.36	—
Jin Yin Hua	23.36	—
Hong Jing Tian	23.51	—
Chuang Mu Xiang	23.54	—
Zhi Mu	23.91	—
Bai Zhu	24.79	—
Ling Zhi	24.82	—
Ji Xue Teng	25.15	—
Hou Po	25.49	—
Dan Shen	25.62	—
Fu Xiao Mai	26.02	—
Jie Geng	26.35	—
Bai Xian Pi	26.59	—
Zhu Ru	26.72	—
Huang Qin	27.35	—
Wu Wei Zi	27.93	—

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Substanz	Distance in main model	Distance in second-stage model
Mao Dong Qing	28.07	—
Yi Yi Ren	29.15	—
Gan Cao	29.49	—
Yin Yang Huo	29.60	—
Suan Zao Ren	29.83	—
Che Qian Zi	31.78	—
Chai Hu	31.85	—
Dan Dou Chi	31.89	—
Ma Huang Gen	32.11	—
Mu Dan Pi	32.66	—
Yan Hu Suo	33.39	—
Yu Jin	35.88	—
Sang Zhi	35.88	—
Mai Men Dong	36.50	—
Fu Shen	37.05	—
Qiang Huo	37.59	—
Chi Shao (Yao)	39.19	—
Zi Hua Di Ding	40.96	—
Qing Pi	41.70	—
Mang Xiao	42.62	—
Huang Lian	45.41	—
Chuan Lian Zi	47.84	—
Huang Qi	48.16	—
Cang Er Zi	48.56	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62622	62622	0.00	7.60
62621	62621	0.00	7.60

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 2.3-2020-05

Validated substance/substance group **Dang Shen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60000-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dang Shen; Codonopsis pilosulae radix

Special notes

When selecting the *Dang Shen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dang Shen	2	0	4

Second-stage model

For differentiation of the substance/substance group *Dang Shen* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Dang Shen	G077HS352RQ1	62369	40	from supplier
PhytoComm	Dang Shen	G077HS352RQ1	62370	40	from supplier
PhytoComm	Dang Shen	G077HS352SG1	62673	40	from supplier
PhytoComm	Dang Shen	G077HS352SG1	62674	40	from supplier

Validation samples

A total of 30 254 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 *Dang Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Dang Shen*.
- 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
PhytoComm	Dang Shen	G077HS352RQ1	62369 [†]	20
PhytoComm	Dang Shen	G077HS352RQ1	62370 [†]	20
PhytoComm	Dang Shen	G077HS352SG1	62673 [†]	20
PhytoComm	Dang Shen	G077HS352SG1	62674 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 8 spectra from 5 *Apo-Ident* customers from 4 batches from the substance/substance group *Dang Shen*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Dang Shen	G077H2001022	1
Phytocomm	Dang Shen	g077h2001222	2
Phytocomm	Dang Shen	G077H2001521	2
PhytoComm	Dang Shen	G077H2001521	2
PhytoComm	Dang Shen	G077H2001621	1

- 849 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dang Shen* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dang Shen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	1	76	4	9836
Type C	0	0	8	849

The substance/substance group *Dang Shen* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	99.9842 % (> 99.9483 %)	95.0000 % (> 91.2500 %)
Type C	100.0000 % (> 98.8253 %)	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

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dang Shen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yuan Zhi	5.51	—
Chen Pi	8.06	—
Bai Shao Yao	8.40	—
Dang Gui Wei	8.43	—
Fo Shou	8.62	—
Tian Men Dong	9.72	—
Chuan Xiong	10.01	—
Pi Pa Ye	11.32	—
Di Gu Pi	13.03	—
San Qi	13.33	—
Dang Gui	13.34	—
Gua Lou	13.40	—
Ye Jiao Teng	13.41	—
Shen Qu	14.59	—
Shan Yao	14.99	—
Yu Zhu	15.55	—
Cang Zhu	15.76	—
Zhi Mu	16.24	—
He Huan Pi	16.63	—
Da Zao	17.10	—
Tai Zi Shen	17.26	—
Ji Li	17.39	—
Ci Wu Jia	17.47	—
Rou Gui	17.56	—
Shan Yu Rou	17.82	—
Lian Zi	17.95	—
Ren Dong Teng	18.86	—
Gou Qi Zi	20.02	—
Fu Xiao Mai	20.08	—
Bai Zi Ren	20.43	—
Chuang Mu Xiang	20.50	—
Tao Ren	20.77	—
Zhe Bei Mu	21.07	—
Lian Qiao	21.29	—
Gui Zhi	21.42	—
Tu Fu Ling	21.50	—
Jie Geng	21.72	—
Fu Ling	21.79	—
Tian Hua Fen	22.26	—
Long Yan Rou	23.11	—
Huo Ma Ren	23.14	—
Sheng Jiang	23.60	—
Ling Zhi	24.84	—

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Substanz	Distance in main model	Distance in second-stage model
Gou Teng	24.92	—
Mai Men Dong	25.50	—
Jiao Gu Lan	25.52	—
Ban Xia (Jiang)	25.76	—
Zhu Ru	26.72	—
Bai Xian Pi	27.40	—
Bai Zhu	28.43	—
Zhi Ke	28.73	—
Suan Zao Ren	29.03	—
Ji Xue Teng	29.35	—
Jin Yin Hua	29.80	—
Yi Yi Ren	29.81	—
Fu Zi	30.03	—
Mao Dong Qing	30.04	—
Dan Shen	30.89	—
Huang Qin	31.28	—
Hou Po	31.65	—
Ma Huang	31.77	—
Gan Cao	32.12	—
Hong Jing Tian	32.27	—
Wu Wei Zi	32.67	—
Ma Huang Gen	34.73	—
Mu Dan Pi	35.30	—
Che Qian Zi	36.84	—
Yin Yang Huo	36.86	—
Dan Dou Chi	37.44	—
Fu Shen	38.17	—
Chai Hu	38.23	—
Yu Jin	38.93	—
Yan Hu Suo	38.95	—
Sang Zhi	41.82	—
Mang Xiao	43.24	—
Chi Shao (Yao)	44.17	—
Qiang Huo	44.89	—
Huang Qi	48.54	—
Chuan Lian Zi	48.80	—
Qing Pi	49.02	—
Zi Hua Di Ding	49.95	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62370	62370	0.00	9.73
62674	62674	0.00	5.51
62369	62369	0.00	9.78
62673	62673	0.00	5.75

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 2.3-2020-05

Validated substance/substance group **Di Fu Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002264-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Di Fu Zi; Kochiae scopariae fructus

Special notes

When selecting the *Di Fu Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Di Fu Zi	1	0	1

Second-stage model

For differentiation of the substance/substance group *Di Fu Zi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Di Fu Zi	G131H0605921	62737	40	from supplier
PhytoComm	Di Fu Zi	G131H0605921	62738	40	from supplier

Validation samples

A total of 30 254 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 *Di Fu Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Di Fu Zi*.
- 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
PhytoComm	Di Fu Zi	G131H0605921	62737 [†]	20
PhytoComm	Di Fu Zi	G131H0605921	62738 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Di Fu Zi*.
- 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
Phytocomm	Di Fu Zi	G131H0605122	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	1	856

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8367 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Di Fu Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Guang Huo Xiang	30.42	—
Hua Shi	45.99	—
Wu Mei	56.22	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62738	62738	0.00	30.86
62737	62737	0.00	30.42

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Di Gu Pi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60036-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Di Gu Pi; Lycii chinensis radicis cortex

Special notes

When selecting the *Di Gu Pi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Di Gu Pi	3	0	2

Second-stage model

For differentiation of the substance/substance group *Di Gu Pi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Di Gu Pi	G149H0601622	62211	40	from supplier
PhytoComm	Di Gu Pi	G149H0601622	62212	40	from supplier
PhytoComm	Di Gu Pi	G149H0601821	62347	40	from supplier
PhytoComm	Di Gu Pi	G149H0601821	62348	40	from supplier
PhytoComm	Di Gu Pi	G149HS101SK1	62691	40	from supplier
PhytoComm	Di Gu Pi	G149HS101SK1	62692	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Di Gu Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Di Gu Pi*.
- 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
PhytoComm	Di Gu Pi	G149H0601622	62211 [†]	20
PhytoComm	Di Gu Pi	G149H0601622	62212 [†]	20
PhytoComm	Di Gu Pi	G149H0601821	62347 [†]	20
PhytoComm	Di Gu Pi	G149H0601821	62348 [†]	20
PhytoComm	Di Gu Pi	G149HS101SK1	62691 [†]	20
PhytoComm	Di Gu Pi	G149HS101SK1	62692 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 4 spectra from 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Di Gu Pi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Di Gu Pi	g149h060112	1
Phytocomm	Di Gu Pi	G149H0601421	1
PhytoComm	Di Gu Pi	G149H0601421	2

- 853 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	239	1	19 240
Type B	2	118	2	9795
Type C	6	1	3	847

The substance/substance group *Di Gu Pi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	99.5833 % (> 98.3333 %)
Type B	99.9763 % (> 99.9403 %)	98.3333 % (> 95.8333 %)
Type C	99.5556 % (> 98.9690 %)	n/a (n/a)

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Di Gu Pi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sheng Jiang	4.88	—
He Huan Pi	4.92	—
Gui Zhi	5.78	—
Ci Wu Jia	6.24	—
Ban Xia (Jiang)	8.11	—
Bai Shao Yao	8.89	—
Sang Zhi	9.17	—
Fu Xiao Mai	9.23	—
Tao Ren	9.39	—
Yi Yi Ren	10.20	—
Rou Gui	10.50	—
Zhu Ru	10.58	—
Jie Geng	10.71	—
Bai Zi Ren	10.83	—
Shen Qu	10.92	—
Zhe Bei Mu	11.00	—
Lian Zi	12.55	—
Ji Li	12.85	—
Fu Ling	13.01	—
Tai Zi Shen	13.20	—
Gou Teng	13.83	—
Ling Zhi	14.29	—
Ye Jiao Teng	14.54	—
Huo Ma Ren	14.71	—
Fo Shou	14.94	—
Bai Zhu	15.64	—
Tian Hua Fen	15.75	—
Gua Lou	16.16	—
Bai Xian Pi	16.32	—
Ji Xue Teng	16.90	—
Qing Pi	17.35	—
Pi Pa Ye	18.61	—
Huang Qi	18.87	—
Yuan Zhi	19.29	—
Shan Yao	19.43	—
Tian Men Dong	20.33	—
Ma Huang Gen	20.44	—
Qin Jiao	20.84	—
Long Yan Rou	21.08	—
Du Huo	21.26	—
San Qi	21.71	—

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Substanz	Distance in main model	Distance in second-stage model
Chen Pi	21.94	—
Mu Dan Pi	22.18	—
Tu Fu Ling	22.30	—
Lian Qiao	22.96	—
Bai Mao Gen	23.11	—
Da Zao	23.29	—
Yu Jin	23.31	—
Fu Shen	23.50	—
Chi Shao (Yao)	23.61	—
Ren Dong Teng	24.00	—
Chuan Lian Zi	24.12	—
Chuan Xiong	24.33	—
Bai He	25.05	—
Dang Gui	25.12	—
Lai Fu Zi	25.35	—
Dang Shen	25.68	—
Qiang Huo	26.02	—
Cang Er Zi	26.90	—
Mai Men Dong	27.49	—
Yan Hu Suo	27.50	—
Wu Wei Zi	28.69	—
Ban Zhi Lian	28.93	—
Chai Hu	29.13	—
Fu Zi	29.34	—
Jin Yin Hua	29.63	—
Shan Yu Rou	30.58	—
E Zhu	30.88	—
Mang Xiao	30.90	—
Xiang Fu	31.33	—
Zhi Ke	31.54	—
Dan Dou Chi	31.57	—
(Huai) Niu Xi	31.63	—
(Shi) Chang Pu	31.69	—
Jiao Gu Lan	31.77	—
Ba Ji Tian	31.91	—
Dan Shen	32.07	—
Mai Ya	32.10	—
Zi Su Zi	32.49	—
Ku Shen	32.58	—
Niu Bang Zi	32.65	—
Dang Gui Wei	33.06	—
Yu Zhu	34.00	—
Cang Zhu	34.41	—
Mao Dong Qing	35.65	—
Gan Cao	35.98	—
Huang Qin	36.04	—
Hou Po	36.35	—
Zhi Mu	36.63	—
Yin Yang Huo	36.86	—
Pu Gong Ying	36.91	—
Sha Shen (Bei)	37.27	—
Gou Qi Zi	38.57	—
Ma Huang	38.59	—
Huang Lian	39.70	—
Che Qian Zi	39.99	—
Jiang Huang	41.35	—
Du Zhong	41.96	—
Xie Bai	42.64	—
Long Dan (Cao)	42.83	—

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Substanz	Distance in main model	Distance in second-stage model
Suan Zao Ren	43.60	—
Fang Feng	43.72	—
Hong Jing Tian	43.82	—
Zi Hua Di Ding	44.10	—
Bai Bian Dou	44.50	—
Wu Yao	45.32	—
Dong Gua Zi	45.65	—
Yi Mu Cao	47.81	—
(Bai) Dou Kou	48.08	—
Zhu Ling	48.72	—
Huang Bai	48.73	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62692	62692	0.00	4.88
62691	62691	0.00	5.25
62211	62211	0.00	9.90
62348	62348	0.00	9.47
62212	62212	0.00	9.33
62347	62347	0.00	9.17

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 2.3-2020-05

Validated substance/substance group **Dong Gua Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60202-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dong Gua Zi; Benincasae hispidae semen

Special notes

When selecting the *Dong Gua Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dong Gua Zi	1	0	1

Second-stage model

For differentiation of the substance/substance group *Dong Gua Zi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Dong Gua Zi	G049H0551822	62513	40	from supplier
PhytoComm	Dong Gua Zi	G049H0551822	62514	40	from supplier

Validation samples

A total of 30 254 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 *Dong Gua Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Dong Gua Zi*.
- 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
PhytoComm	Dong Gua Zi	G049H0551822	62513 [†]	20
PhytoComm	Dong Gua Zi	G049H0551822	62514 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Dong Gua Zi*.
- 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
Phytocomm	Dong Gua Zi	G049H0551221	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	1	856

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8367 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dong Gua Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Shan Yao	29.21	—
Ku Shen	29.39	—
Shen Qu	34.05	—
Mang Xiao	40.49	—
Zhi Zi	40.68	—
Di Gu Pi	45.42	—
Sang Zhi	47.07	—
Cang Er Zi	47.11	—
Bai Bian Dou	47.21	—
Wu Wei Zi	47.69	—
Zi Su Zi	47.78	—
Bai Shao Yao	47.91	—
San Qi	48.79	—
Gan Cao	50.26	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62514	62514	0.00	29.56
62513	62513	0.00	29.21

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 2.3-2020-05

Validated substance/substance group **Du Huo**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50259-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Du Huo; Angelicae pubescentis radix

Special notes

When selecting the *Du Huo* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Du Huo	1	0	2

Second-stage model

For differentiation of the substance/substance group *Du Huo* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Du Huo	G021H1610821	62391	40	from supplier
PhytoComm	Du Huo	G021H1610821	62392	40	from supplier

Validation samples

A total of 30 254 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 *Du Huo*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Du Huo*.
- 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
PhytoComm	Du Huo	G021H1610821	62391 [†]	20
PhytoComm	Du Huo	G021H1610821	62392 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Du Huo*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Du Huo	g021h610221	1
Phytocomm	Du Huo	G021H1610421	2

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	2	0	3	852

The substance/substance group *Du Huo* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.8802 % (> 99.2942 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Du Huo* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Mu Dan Pi	10.22	—
Dang Gui	12.04	—
Bai Mao Gen	14.22	—
Fang Feng	16.26	—
(Shi) Chang Pu	16.32	—
Ba Ji Tian	19.41	—
Huang Qi	20.69	—
Sang Zhi	21.10	—
Ju Hua	22.31	—
Di Gu Pi	23.52	—
Chen Pi	23.58	—
(Huai) Niu Xi	24.19	—
Wu Yao	24.37	—
Qing Pi	24.51	—
Ji Li	25.29	—
Tian Hua Fen	25.73	—
Xiang Fu	26.64	—
Jie Geng	29.03	—
Xian He Cao	29.05	—
E Zhu	30.09	—
Xie Bai	30.72	—
Gui Zhi	31.36	—
Mang Xiao	31.60	—
Bai Zhu	32.53	—
Qin Jiao	33.15	—
Gua Lou	33.26	—
Shan Yao	33.50	—
Jiang Huang	34.36	—
Sha Ren	34.51	—
He Huan Pi	35.45	—
Zhi Ke	35.65	—
Yu Jin	35.68	—
Sha Shen (Bei)	36.18	—
Yan Hu Suo	37.29	—
Chi Shao (Yao)	38.39	—
Chuan Lian Zi	38.97	—
Zi Su Zi	38.97	—
Lai Fu Zi	39.09	—
(Bai) Dou Kou	39.51	—
Ku Shen	39.68	—
Da Zao	39.92	—
Gu Sui Bu	40.59	—
Qiang Huo	41.01	—
Sheng Jiang	41.62	—
Yuan Zhi	42.27	—
Long Dan (Cao)	42.68	—
He Shou Wu	43.70	—
Sang Ji Shend	44.90	—
Hong Jing Tian	45.98	—
Niu Bang Zi	46.25	—
Wu Wei Zi	46.28	—
Cang Er Zi	46.62	—

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Substanz	Distance in main model	Distance in second-stage model
Pu Gong Ying	47.00	—
Fu Zi	48.15	—
San Qi	49.15	—
Mai Men Dong	49.15	—
Sang Bai Pi	49.54	—
Mai Ya	49.80	—
Tu Fu Ling	49.82	—
Mao Dong Qing	50.00	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62392	62392	0.00	10.22
62391	62391	0.00	10.50

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Du Zhong**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60214-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Du Zhong; Eucommiae ulmoidis cortex

Special notes

When selecting the *Du Zhong* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Du Zhong	3	0	4

Second-stage model

For differentiation of the substance/substance group *Du Zhong* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Du Zhong	G101H0736821	62335	40	from supplier
PhytoComm	Du Zhong	G101H0736821	62336	40	from supplier
PhytoComm	Du Zhong	G101HS133SH1	62579	40	from supplier
PhytoComm	Du Zhong	G101HS133SH1	62580	40	from supplier
PhytoComm	Du Zhong	G101HS133SP1	62729	40	from supplier
PhytoComm	Du Zhong	G101HS133SP1	62730	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Du Zhong*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Du Zhong*.
- 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
PhytoComm	Du Zhong	G101H0736821	62335 [†]	20
PhytoComm	Du Zhong	G101H0736821	62336 [†]	20
PhytoComm	Du Zhong	G101HS133SH1	62579 [†]	20
PhytoComm	Du Zhong	G101HS133SH1	62580 [†]	20
PhytoComm	Du Zhong	G101HS133SP1	62729 [†]	20
PhytoComm	Du Zhong	G101HS133SP1	62730 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 8 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Du Zhong*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Du Zhong	g101h0736021	1
Phytocomm	Du Zhong	G101H0736321	1
Phytocomm	Du Zhong	g101h076521	1
Phytocomm	Du Zhong	G101H0736522	5

- 849 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	240	0	19 240
Type B	1	118	2	9796
Type C	0	0	8	849

The substance/substance group *Du Zhong* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.5000 %)
Type B	99.9921 % (> 99.9561 %)	98.3333 % (> 95.8333 %)
Type C	100.0000 % (> 98.8253 %)	n/a (n/a)

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Du Zhong* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Mao Dong Qing	4.57	—
Yu Jin	4.76	—
Ling Zhi	7.90	—
Qiang Huo	8.14	—
Hou Po	9.25	—
Bai Xian Pi	10.60	—
Zi Hua Di Ding	10.93	—
Yin Yang Huo	11.20	—
Jing Jie	13.00	—
Dan Dou Chi	13.22	—
Yan Hu Suo	13.31	—
Sang Bai Pi	13.50	—
Qing Pi	13.68	—
Dan Zhu Ye	13.78	—
Jiao Gu Lan	14.32	—
Mu Dan Pi	14.60	—
Shan Yao	14.61	—
Shen Qu	14.94	—
Ye Jiao Teng	15.52	—
Che Qian Zi	16.35	—
Chai Hu	17.45	—
Pi Pa Ye	17.92	—
Dan Shen	17.96	—
Ji Li	18.46	—
Ren Dong Teng	18.47	—
Sha Ren	19.07	—
Tu Fu Ling	19.10	—
Huang Bai	19.31	—
Chuan Xiong	19.34	—
Hong Jing Tian	19.42	—
Lian Zi	19.97	—
Wu Jia Pi	20.10	—
Huang Lian	20.77	—
Ji Xue Teng	20.92	—
Yuan Zhi	21.29	—
Nü Zhen Zi	21.57	—
Ma Huang	21.62	—
Pu Gong Ying	21.77	—
Zhi Ke	22.00	—
Jin Yin Hua	23.44	—
Yin Chen Hao	23.54	—

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Substanz	Distance in main model	Distance in second-stage model
Xi Xian Cao	23.93	—
Lian Qiao	25.29	—
Bai Shao Yao	26.21	—
Wu Wei Zi	26.30	—
Sang Ji Shend	26.34	—
Ma Huang Gen	26.37	—
Di Gu Pi	26.40	—
Bu Gu Zhi	26.50	—
He Huan Pi	26.84	—
He Shou Wu	27.88	—
Gua Lou	28.08	—
Gou Teng	28.24	—
Rou Gui	29.06	—
Fu Zi	29.19	—
Xian He Cao	30.09	—
Sheng Jiang	30.63	—
Chen Pi	30.79	—
Xuan Shen	30.99	—
Jin Qian Cao	31.01	—
Cang Zhu	31.06	—
Sang Ye	31.27	—
Gui Zhi	31.79	—
Gou Qi Zi	32.04	—
Wang Bu Liu Xing	32.07	—
Yi Mu Cao	33.03	—
Yi Yi Ren	35.01	—
Huo Ma Ren	35.39	—
E Zhu	35.90	—
Wu Zhu Yu	36.52	—
Zhi Shi	36.97	—
Wu Mei	37.18	—
Tian Hua Fen	37.40	—
Fu Ling	37.84	—
Gu Sui Bu	37.87	—
Jiang Huang	37.88	—
Ban Zhi Lian	38.21	—
Mang Xiao	38.75	—
Qing Hao	38.81	—
Cang Er Zi	39.10	—
Huang Bo	39.16	—
Ge Gen	39.21	—
Da Zao	39.33	—
Tao Ren	39.51	—
Zhe Bei Mu	40.30	—
Yu Xing Cao	40.84	—
Chi Shao (Yao)	41.26	—
Sang Zhi	41.36	—
Xin Yi	41.94	—
Hong Hua	42.13	—
Suan Zao Ren	42.16	—
Bai Zi Ren	42.43	—
Jie Geng	42.57	—
Shan Yu Rou	42.63	—
Tai Zi Shen	43.35	—
Huang Qin	43.78	—
Fu Shen	44.64	—
Zi Su Zi	44.72	—
Ban Xia (Jiang)	45.21	—
Chuan Lian Zi	45.33	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Mao Gen	45.93	—
Bai Bian Dou	46.43	—
San Qi	46.85	—
Bai Zhu	47.80	—
Xia Ku Cao	47.90	—
Ci Wu Jia	48.11	—
Wu Yao	48.59	—
Hu Zhang	48.75	—
Dang Gui	49.25	—
Zhu Ru	49.28	—
Hua Shi	49.55	—
Yu Zhu	49.71	—
Dang Shen	49.78	—
Sha Shen (Bei)	49.87	—
Chuang Mu Xiang	50.03	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62729	62729	0.00	4.92
62580	62580	0.00	4.69
62336	62336	0.00	13.45
62335	62335	0.00	13.00
62579	62579	0.00	4.57
62730	62730	0.00	4.76

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 2.3-2020-05

Validated substance/substance group **E Zhu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50344-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

E Zhu; Curcumae zedoariae rhizoma

Special notes

When selecting the *E Zhu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
E Zhu	1	0	2

Second-stage model

For differentiation of the substance/substance group *E Zhu* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	E Zhu	G083H1110821	62515	40	from supplier
PhytoComm	E Zhu	G083H1110821	62516	40	from supplier

Validation samples

A total of 30 254 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 *E Zhu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *E Zhu*.
- 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
PhytoComm	E Zhu	G083H1110821	62515 [†]	20
PhytoComm	E Zhu	G083H1110821	62516 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 4 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *E Zhu*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	E Zhu	H1110021	1
Phytocomm	E Zhu	h1110021	1
PhytoComm	E Zhu	G083H1110222	2

- 853 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	1	0	4	852

The substance/substance group *E Zhu* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.8450 % (> 99.2584 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *E Zhu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ji Li	15.57	—
Cang Er Zi	16.32	—
Jiang Huang	17.76	—
Sha Shen (Bei)	18.60	—
(Bai) Dou Kou	22.56	—
Gui Zhi	23.13	—
Sha Ren	23.45	—
Yan Hu Suo	24.02	—
He Huan Pi	24.77	—
Mang Xiao	24.99	—
Niu Bang Zi	26.07	—
Chuan Lian Zi	26.16	—
Bai Bian Dou	26.89	—
Wang Bu Liu Xing	29.37	—
Ba Ji Tian	29.88	—
Lai Fu Zi	30.07	—
Sang Zhi	30.07	—
Zi Su Zi	30.50	—
Sheng Jiang	30.58	—
San Qi	31.15	—
Mu Dan Pi	31.20	—
Shan Yao	32.44	—
Chen Pi	32.84	—
Zhu Ling	33.04	—
Di Gu Pi	34.88	—
Du Huo	35.15	—
Yuan Zhi	37.12	—
Yu Jin	37.73	—
(Huai) Niu Xi	38.50	—
Mai Ya	38.52	—
Fu Ling	40.14	—
Xiang Fu	40.47	—
Dang Gui	40.56	—
Rou Gui	40.80	—
Xie Bai	41.14	—
Xian He Cao	41.58	—
Wu Yao	41.72	—
Long Dan (Cao)	41.75	—
Fang Feng	42.61	—
Huang Lian	42.87	—
Jie Geng	43.89	—
Tian Hua Fen	44.12	—
Da Zao	44.79	—
Ban Zhi Lian	45.20	—
Du Zhong	45.84	—
(Shi) Chang Pu	46.08	—
Qing Pi	46.15	—
Zhi Ke	46.19	—
Bai Xian Pi	47.34	—
Qiang Huo	47.35	—
Xin Yi	48.15	—
Xi Xian Cao	48.50	—

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Substanz	Distance in main model	Distance in second-stage model
Lian Zi	48.82	—
Fu Zi	49.16	—
Huang Qi	49.59	—
Dan Dou Chi	49.73	—
Hong Jing Tian	49.86	—
Tu Fu Ling	49.91	—
Gou Teng	50.02	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62515	62515	0.00	15.57
62516	62516	0.00	15.92

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 2.3-2020-05

Validated substance/substance group **Fang Feng**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50261-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fang Feng; Saposhnikovia radix

Special notes

When selecting the *Fang Feng* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Fang Feng	1	0	3

Second-stage model

For differentiation of the substance/substance group *Fang Feng* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Fang Feng	G217H0728821	62307	40	from supplier
PhytoComm	Fang Feng	G217H0728821	62308	40	from supplier

Validation samples

A total of 30 254 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 *Fang Feng*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Fang Feng*.
- 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
PhytoComm	Fang Feng	G217H0728821	62307 [†]	20
PhytoComm	Fang Feng	G217H0728821	62308 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 7 spectra from 5 *Apo-Ident* customers from 3 batches from the substance/substance group *Fang Feng*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Fang Feng	g217h0728923	1
Phytocomm	Fang Feng	G217H0728521	3
Phytocomm	Fang Feng	g217h0728221	1
PhytoComm	Fang Feng	G217H0728521	2

- 850 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	2	0	7	848

The substance/substance group *Fang Feng* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.7674 % (> 99.1802 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fang Feng* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chen Pi	11.82	—
Ju Hua	13.27	—
Du Huo	15.28	—
Dang Gui	20.94	—
Mu Dan Pi	22.45	—
Wu Yao	22.65	—
Ba Ji Tian	23.48	—
Xie Bai	23.81	—
He Huan Pi	23.97	—
Gu Sui Bu	24.31	—
Bai Mao Gen	24.73	—
(Shi) Chang Pu	25.28	—
Huang Qi	26.02	—
Qiang Huo	26.93	—
Gui Zhi	26.99	—
Sang Zhi	28.12	—
Ji Li	28.61	—
Qing Pi	29.55	—
Hong Jing Tian	30.47	—
Xian He Cao	30.54	—
Jiang Huang	30.63	—
Mang Xiao	30.79	—
Gua Lou	31.05	—
Sha Ren	32.21	—
Yu Jin	33.25	—
Di Gu Pi	33.99	—
(Huai) Niu Xi	34.24	—
Sang Ji Shend	34.41	—
E Zhu	35.02	—
He Shou Wu	35.21	—
Xiang Fu	36.01	—
Jie Geng	36.03	—
Tian Hua Fen	36.69	—
Wu Zhu Yu	37.56	—
Ku Shen	37.59	—
Shan Yao	37.79	—
Yan Hu Suo	38.01	—
Sang Bai Pi	38.32	—
Zi Su Zi	39.66	—
Zhi Ke	40.05	—
Huang Bo	40.74	—
Yin Chen Hao	41.43	—
Lai Fu Zi	42.30	—
Xu Duan	42.47	—
Da Zao	42.86	—
Sheng Jiang	43.35	—
(Bai) Dou Kou	43.78	—
Bai Zhu	44.00	—
Niu Bang Zi	44.43	—
Nü Zhen Zi	45.44	—
Yi Mu Cao	46.17	—
Cang Er Zi	46.84	—

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Substanz	Distance in main model	Distance in second-stage model
Chuan Lian Zi	46.93	—
Yuan Zhi	46.97	—
Ge Gen	46.98	—
Xin Yi	47.08	—
Chi Shao (Yao)	47.37	—
Qin Jiao	48.12	—
Fu Zi	48.28	—
Bai Bian Dou	48.36	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62307	62307	0.00	11.82
62308	62308	0.00	12.49

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 2.3-2020-05

Validated substance/substance group **Fo Shou**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60119-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fo Shou; Citri sarcodactylis fructus

Special notes

When selecting the *Fo Shou* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Fo Shou	1	0	0

Second-stage model

For differentiation of the substance/substance group *Fo Shou* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Fo Shou	G307HS159RQ1	62419	40	from supplier
PhytoComm	Fo Shou	G307HS159RQ1	62420	40	from supplier

Validation samples

A total of 30 254 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 *Fo Shou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Fo Shou*.
- 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
PhytoComm	Fo Shou	G307HS159RQ1	62419 [†]	20
PhytoComm	Fo Shou	G307HS159RQ1	62420 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Fo Shou*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	1	79	1	19 399
Type B	0	39	1	9877
Type C	0	0	0	857

The substance/substance group *Fo Shou* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9960 % (> 99.9777 %)	98.7500 % (> 95.0000 %)
Type B	100.0000 % (> 99.9285 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fo Shou* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

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

Substance	Distance in main model	Distance in second-stage model
Gua Lou	4.49	—
Chen Pi	7.34	—
Tian Men Dong	8.96	—
Ye Jiao Teng	9.11	—
Tao Ren	10.99	—
Bai Shao Yao	11.59	—
Tai Zi Shen	12.09	—
Rou Gui	12.60	—
He Huan Pi	12.70	—
Dang Shen	13.10	—
Di Gu Pi	13.33	—
Shen Qu	13.71	—
Da Zao	14.07	—
Yu Zhu	14.42	—
Zhe Bei Mu	14.71	—
Ci Wu Jia	14.89	—
Long Yan Rou	14.89	—
Ban Xia (Jiang)	15.15	—
Lian Zi	15.46	—
Gui Zhi	15.79	—
Yuan Zhi	16.29	—
Pi Pa Ye	16.55	—
Sheng Jiang	16.96	—
Ji Li	17.05	—
Bai Zi Ren	17.37	—
Chuan Xiong	17.49	—
Dang Gui Wei	17.66	—
Fu Xiao Mai	17.83	—
Gou Teng	18.09	—
Bai Xian Pi	18.31	—
Tu Fu Ling	18.91	—
Fu Ling	19.29	—
San Qi	20.49	—
Ren Dong Teng	21.26	—
Ling Zhi	21.68	—
Huo Ma Ren	21.83	—
Shan Yao	22.32	—
Cang Zhu	22.37	—
Ji Xue Teng	22.41	—
Ma Huang Gen	23.38	—
Zhu Ru	23.48	—
Lian Qiao	24.39	—
Ma Huang	24.42	—
Dang Gui	25.53	—
Yi Yi Ren	25.65	—
Tian Hua Fen	25.72	—
Fu Shen	26.34	—
Dan Shen	27.10	—
Shan Yu Rou	27.57	—
Zhi Ke	27.62	—
Jiao Gu Lan	28.21	—
Fu Zi	28.23	—
Bai Zhu	28.27	—
Gou Qi Zi	29.38	—
Jie Geng	29.70	—
Huang Qin	30.61	—
Hong Jing Tian	30.63	—
Dan Dou Chi	31.31	—
Yin Yang Huo	31.73	—

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Substanz	Distance in main model	Distance in second-stage model
Yu Jin	32.02	—
Jin Yin Hua	33.14	—
Mao Dong Qing	33.36	—
Zhi Mu	33.48	—
Chai Hu	33.84	—
Yan Hu Suo	35.63	—
Hou Po	36.24	—
Wu Wei Zi	36.86	—
Chuang Mu Xiang	38.45	—
Sang Zhi	38.79	—
Gan Cao	40.12	—
Mang Xiao	40.93	—
Suan Zao Ren	41.40	—
Che Qian Zi	42.36	—
Qiang Huo	42.44	—
Mai Men Dong	43.25	—
Chi Shao (Yao)	46.74	—
Chuan Lian Zi	46.78	—
Mu Dan Pi	47.02	—
Huang Lian	47.95	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62420	62420	0.00	4.49
62419	62419	0.00	6.48

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Fu Ling**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50260-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fu Ling; Poriae cocos sclerotium

Special notes

When selecting the *Fu Ling* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Fu Ling	2	0	4

Second-stage model

For differentiation of the substance/substance group *Fu Ling* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Fu Ling	G200HS211RT1	62429	40	from supplier
PhytoComm	Fu Ling	G200HS211RT1	62430	40	from supplier
PhytoComm	Fu Ling	G200HS211SH1	62597	40	from supplier
PhytoComm	Fu Ling	G200HS211SH1	62598	40	from supplier

Validation samples

A total of 30 254 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 *Fu Ling*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Fu Ling*.
- 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
PhytoComm	Fu Ling	G200HS211RT1	62429 [†]	20
PhytoComm	Fu Ling	G200HS211RT1	62430 [†]	20
PhytoComm	Fu Ling	G200HS211SH1	62597 [†]	20
PhytoComm	Fu Ling	G200HS211SH1	62598 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

Type C Spectra of independent samples not included in the database structure. *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 5 batches from the substance/substance group *Fu Ling*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phyto Comm	Fu Ling	G200H1019522	1
Phytocomm	Fu Ling	G200H1019221	1
Phytocomm	Fu Ling	G200H1019321	1
Phytocomm	Fu Ling	g200h1019321	3
Phytocomm	Fu Ling	G200H1019522	2
PhytoComm	Fu Ling	G200H1019221	1
PhytoComm	Fu Ling	G200H1019321	1
PhytoComm	Fu Ling	G200H1019522	1
PhytoComm	Fu Ling	G200H1019622	1

- 845 spectra from 12 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Fu Ling* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Fu Ling* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	12	845

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8248 %)	n/a (n/a)

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fu Ling* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yi Yi Ren	8.74	—
Gui Zhi	8.95	—
Sheng Jiang	9.10	—
Rou Gui	9.36	—
Gou Teng	12.66	—
Ma Huang Gen	13.46	—
Fu Xiao Mai	13.76	—
Ji Xue Teng	13.87	—
Zhu Ru	14.23	—
Fu Shen	14.75	—
He Huan Pi	14.88	—
Bai Xian Pi	15.47	—
Ci Wu Jia	15.87	—
Lian Zi	16.23	—
Ling Zhi	16.73	—
Ji Li	17.27	—
Tao Ren	17.33	—
Ren Dong Teng	17.83	—
Huo Ma Ren	19.25	—
Di Gu Pi	21.40	—
Tai Zi Shen	21.81	—
Bai Zi Ren	21.93	—
Bai Shao Yao	22.25	—
Ye Jiao Teng	22.92	—
Fo Shou	22.94	—
Shen Qu	24.29	—
Zhe Bei Mu	25.04	—
Chen Pi	25.18	—
Tian Men Dong	25.26	—
Dan Dou Chi	25.74	—
Ban Xia (Jiang)	25.92	—
Yu Jin	26.01	—
Long Yan Rou	29.17	—
Tu Fu Ling	29.25	—
Mao Dong Qing	29.97	—
Gua Lou	30.65	—
Tian Hua Fen	30.89	—
Da Zao	30.95	—
Shan Yao	31.07	—
Chai Hu	31.49	—
Yuan Zhi	31.76	—

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Substanz	Distance in main model	Distance in second-stage model
Dan Shen	32.39	—
Chuan Xiong	33.36	—
Lian Qiao	34.84	—
Dang Shen	35.80	—
Mang Xiao	36.01	—
Pi Pa Ye	36.13	—
Yin Yang Huo	36.24	—
Yan Hu Suo	36.35	—
Jiao Gu Lan	37.12	—
Dang Gui Wei	39.73	—
Hong Jing Tian	41.14	—
Yu Zhu	41.83	—
San Qi	42.02	—
Zhi Ke	42.52	—
Che Qian Zi	42.75	—
Jie Geng	43.55	—
Fu Zi	43.75	—
Qiang Huo	44.88	—
Mai Men Dong	45.08	—
Shan Yu Rou	45.12	—
Cang Zhu	45.52	—
Sang Zhi	46.21	—
Chuan Lian Zi	46.72	—
Bai Zhu	46.73	—
Wu Wei Zi	48.12	—
Huang Qin	48.87	—
Huang Lian	49.35	—
Hou Po	49.81	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62597	62597	0.00	9.28
62430	62430	0.00	8.74
62598	62598	0.00	8.95
62429	62429	0.00	9.53

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Fu Shen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60004-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fu Shen; Poriae cocos sclerotium paradicis

Special notes

When selecting the *Fu Shen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Fu Shen	1	0	2

Second-stage model

For differentiation of the substance/substance group *Fu Shen* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Fu Shen	G201HS212SH1	62617	40	from supplier
PhytoComm	Fu Shen	G201HS212SH1	62618	40	from supplier

Validation samples

A total of 30 254 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 *Fu Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Fu Shen*.
- 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
PhytoComm	Fu Shen	G201HS212SH1	62617 [†]	20
PhytoComm	Fu Shen	G201HS212SH1	62618 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 4 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Fu Shen*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Fu Shen	g201h1021321	1
Phytocomm	Fu Shen	G201H1021321	1
Phytocomm	Fu Shen	G201H1021422	2

- 853 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	1	0	4	852

The substance/substance group *Fu Shen* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.8837 % (> 99.2972 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fu Shen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yi Yi Ren	6.69	—
Ma Huang Gen	7.64	—
Rou Gui	11.61	—
Fu Ling	13.07	—
Gui Zhi	13.36	—
Fu Xiao Mai	13.63	—
Sheng Jiang	14.03	—
Ji Xue Teng	18.11	—
Ban Xia (Jiang)	18.47	—
Gou Teng	19.13	—
Zhu Ru	20.06	—
Di Gu Pi	22.58	—
Long Yan Rou	24.48	—
Bai Xian Pi	24.96	—
He Huan Pi	25.98	—
Ling Zhi	26.55	—
Bai Zi Ren	26.63	—
Bai Shao Yao	26.80	—
Lian Zi	27.20	—
Fo Shou	27.45	—
Ji Li	28.25	—
Tian Men Dong	29.61	—
Da Zao	29.95	—
Tao Ren	30.05	—
Shen Qu	30.80	—
Ye Jiao Teng	31.15	—
Huo Ma Ren	31.79	—
Chen Pi	32.60	—
Tai Zi Shen	32.88	—
Ci Wu Jia	33.08	—
Gua Lou	36.64	—
Yuan Zhi	37.59	—
Zhe Bei Mu	37.79	—
Tu Fu Ling	38.60	—
Ren Dong Teng	39.00	—
Mang Xiao	39.72	—
Pi Pa Ye	40.10	—
Yu Jin	41.08	—
Dan Dou Chi	41.20	—
Chuan Xiong	41.87	—
Dang Shen	42.82	—
Tian Hua Fen	43.12	—
Dan Shen	43.88	—
Lian Qiao	44.63	—
Yan Hu Suo	44.71	—
Shan Yu Rou	45.16	—
Shan Yao	45.51	—
Jiao Gu Lan	48.05	—
Huang Qin	50.54	—

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

stance/substance group *Fu Shen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62618	62618	0.00	6.69
62617	62617	0.00	7.18

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 2.3-2020-05

Validated substance/substance group **Fu Xiao Mai**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60081-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fu Xiao Mai; Triticum aestivum semen levis

Special notes

When selecting the *Fu Xiao Mai* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Fu Xiao Mai	2	0	0

Second-stage model

For differentiation of the substance/substance group *Fu Xiao Mai* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Fu Xiao Mai	G244HS021RT1	62423	40	from supplier
PhytoComm	Fu Xiao Mai	G244HS021RT1	62424	40	from supplier
PhytoComm	Fu Xiao Mai	G244HS021SK1	62631	40	from supplier
PhytoComm	Fu Xiao Mai	G244HS021SK1	62632	40	from supplier

Validation samples

A total of 30 254 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 *Fu Xiao Mai*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Fu Xiao Mai*.
- 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
PhytoComm	Fu Xiao Mai	G244HS021RT1	62423 [†]	20
PhytoComm	Fu Xiao Mai	G244HS021RT1	62424 [†]	20
PhytoComm	Fu Xiao Mai	G244HS021SK1	62631 [†]	20
PhytoComm	Fu Xiao Mai	G244HS021SK1	62632 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

Type C Spectra of independent samples not included in the database structure. *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 *Fu Xiao Mai*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	7	153	7	19 313
Type B	7	67	13	9830
Type C	0	0	0	857

The substance/substance group *Fu Xiao Mai* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9815 % (> 99.9631 %)	95.6250 % (> 93.7500 %)
Type B	99.9288 % (> 99.8929 %)	83.7500 % (> 80.0000 %)
Type C	100.0000 % (> 98.8345 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fu Xiao Mai* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yi Yi Ren	2.71	—
Zhu Ru	3.67	—
Rou Gui	6.07	—
Sheng Jiang	6.59	—
Fu Ling	7.37	—
Gui Zhi	7.46	—
Di Gu Pi	8.03	—
Bai Shao Yao	8.75	—
He Huan Pi	9.06	—
Ci Wu Jia	9.11	—
Ji Li	10.97	—
Fu Shen	11.40	—
Ban Xia (Jiang)	11.88	—
Lian Zi	12.26	—
Tao Ren	12.68	—
Shen Qu	12.73	—
Bai Zi Ren	13.08	—
Ma Huang Gen	13.56	—
Ling Zhi	14.40	—
Gou Teng	15.80	—
Ji Xue Teng	15.99	—
Zhe Bei Mu	16.67	—
Gua Lou	17.21	—
Bai Xian Pi	18.60	—
Huo Ma Ren	18.68	—
Yuan Zhi	19.42	—
Tian Hua Fen	19.59	—
Ye Jiao Teng	19.97	—
Tai Zi Shen	20.41	—
Fo Shou	20.57	—
Shan Yao	20.59	—
Pi Pa Ye	22.24	—
Yu Jin	22.60	—
Tian Men Dong	22.61	—
Chen Pi	24.74	—
Long Yan Rou	24.87	—
Tu Fu Ling	25.62	—
Ren Dong Teng	26.40	—
Da Zao	26.47	—
Lian Qiao	27.84	—
Dang Shen	28.14	—
Chuan Xiong	29.20	—
Shan Yu Rou	31.39	—
Yan Hu Suo	32.25	—
San Qi	33.75	—
Fu Zi	34.34	—
Jiao Gu Lan	35.90	—
Zhi Mu	36.05	—
Dan Dou Chi	36.46	—
Dang Gui Wei	36.66	—
Mao Dong Qing	36.87	—
Dan Shen	36.93	—

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Substanz	Distance in main model	Distance in second-stage model
Jin Yin Hua	37.92	—
Zhi Ke	38.62	—
Yu Zhu	39.44	—
Wu Wei Zi	39.49	—
Chai Hu	39.57	—
Suan Zao Ren	40.14	—
Mang Xiao	41.06	—
Huang Qin	41.15	—
Dang Gui	41.37	—
Yin Yang Huo	41.87	—
Hou Po	42.75	—
Che Qian Zi	43.28	—
Cang Zhu	43.55	—
Jie Geng	48.04	—
Mai Men Dong	49.92	—
Ma Huang	49.97	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62424	62424	0.00	2.71
62631	62631	0.00	4.31
62423	62423	0.00	4.68
62632	62632	0.00	2.72

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 2.3-2020-05

Validated substance/substance group **Fu Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50884-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fu Zi; Aconiti radix lateralis praep.

Special notes

When selecting the *Fu Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Fu Zi	2	0	3

Second-stage model

For differentiation of the substance/substance group *Fu Zi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Fu Zi	G005H0801723	62225	40	from supplier
PhytoComm	Fu Zi	G005H0801723	62226	40	from supplier
PhytoComm	Fu Zi	G005HS158SP1	62699	40	from supplier
PhytoComm	Fu Zi	G005HS158SP1	62700	40	from supplier

Validation samples

A total of 30 254 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 *Fu Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Fu Zi*.
- 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
PhytoComm	Fu Zi	G005H0801723	62225 [†]	20
PhytoComm	Fu Zi	G005H0801723	62226 [†]	20
PhytoComm	Fu Zi	G005HS158SP1	62699 [†]	20
PhytoComm	Fu Zi	G005HS158SP1	62700 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 4 spectra from 3 *Apo-Ident* customers from 4 batches from the substance/substance group *Fu Zi*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
phytocomm	Fu Zi	g005h0801322	1
Phytocomm	Fu Zi	G005H0801322	1
Phytocomm	Fu Zi	G005H0801524	1
Phytocomm	Fu Zi	g005h0801122	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	157	3	19 320
Type B	1	75	5	9836
Type C	1	0	4	852

The substance/substance group *Fu Zi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	98.1250 % (> 96.2500 %)
Type B	99.9842 % (> 99.9483 %)	93.7500 % (> 90.0000 %)
Type C	99.8837 % (> 99.2972 %)	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

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fu Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Shan Yao	3.68	—
Pi Pa Ye	4.24	—
Ren Dong Teng	7.19	—
Lian Qiao	7.68	—
Ji Li	8.25	—
Gui Zhi	9.13	—
Hou Po	9.68	—
Tian Hua Fen	9.82	—
Jin Yin Hua	10.16	—
Gua Lou	10.20	—
Chuan Xiong	10.44	—
Bai Zi Ren	10.60	—
Shen Qu	10.69	—
Huo Ma Ren	11.28	—
Bai Shao Yao	12.56	—
Yan Hu Suo	13.24	—
Jiang Huang	13.46	—
Ji Xue Teng	13.70	—
Yuan Zhi	14.00	—
Che Qian Zi	14.27	—
Tai Zi Shen	14.29	—
Jiao Gu Lan	14.62	—
He Huan Pi	14.76	—
Lian Zi	14.97	—
Cang Zhu	15.29	—
Zhe Bei Mu	15.52	—
Ling Zhi	15.76	—
Dan Shen	15.86	—
Chen Pi	15.93	—
Wu Yao	16.23	—
Chai Hu	16.35	—
Fu Ling	16.83	—
Tu Fu Ling	17.05	—
Yu Jin	17.15	—
Tao Ren	17.39	—
Sha Ren	17.88	—
Dan Dou Chi	18.30	—
San Qi	18.54	—
Mao Dong Qing	18.56	—
Ma Huang	18.59	—
Gou Teng	18.61	—
Ye Jiao Teng	18.82	—
Wu Wei Zi	18.84	—
Yin Yang Huo	18.93	—

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Substanz	Distance in main model	Distance in second-stage model
Hong Jing Tian	19.01	—
Bai Xian Pi	19.27	—
Hu Zhang	19.61	—
Qing Pi	19.85	—
Sheng Jiang	19.93	—
Di Gu Pi	20.76	—
Qiang Huo	21.31	—
Mu Dan Pi	21.53	—
Yu Zhu	21.72	—
Xin Yi	21.79	—
Dang Gui	21.91	—
Sang Ye	21.93	—
Zhu Ru	21.95	—
Ban Xia (Jiang)	22.21	—
Gou Qi Zi	22.38	—
Shan Yu Rou	22.57	—
Ci Wu Jia	22.86	—
Dang Shen	23.09	—
Xiang Fu	23.43	—
Da Zao	23.82	—
(Shi) Chang Pu	24.26	—
Dang Gui Wei	24.26	—
Gu Sui Bu	24.69	—
(Bai) Dou Kou	24.82	—
Suan Zao Ren	25.41	—
Yi Yi Ren	25.52	—
Zhi Ke	25.59	—
Ma Huang Gen	25.63	—
Xi Xian Cao	25.66	—
Huang Bo	25.97	—
Rou Gui	26.64	—
Huang Qin	27.00	—
Huang Lian	27.26	—
Yi Mu Cao	27.62	—
Pu Gong Ying	28.21	—
Zi Hua Di Ding	28.84	—
Fo Shou	28.88	—
Han Lian Cao	29.15	—
Fu Xiao Mai	29.40	—
Wu Zhu Yu	29.65	—
Du Zhong	30.14	—
Xu Duan	30.37	—
Chuang Mu Xiang	30.47	—
Gan Cao	31.07	—
Bai Hua She She Cao	32.15	—
Xian He Cao	32.21	—
Cang Er Zi	32.57	—
Long Yan Rou	33.11	—
Sang Zhi	34.51	—
Zhi Mu	34.73	—
Sang Ji Shend	34.74	—
Bai Zhu	35.33	—
Tian Men Dong	35.94	—
Dan Zhu Ye	36.09	—
E Zhu	36.43	—
Nü Zhen Zi	36.90	—
Xie Bai	36.96	—
Ju Hua	37.00	—
Chi Shao (Yao)	37.28	—

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Substanz	Distance in main model	Distance in second-stage model
Du Huo	37.44	—
Sang Bai Pi	37.44	—
Mang Xiao	37.94	—
Niu Bang Zi	38.24	—
Fu Shen	38.48	—
Wang Bu Liu Xing	38.54	—
Xia Ku Cao	40.31	—
Fang Feng	40.72	—
Huang Bai	40.82	—
He Shou Wu	40.91	—
Ku Shen	41.03	—
Yin Chen Hao	41.41	—
Jie Geng	41.53	—
Bai Mao Gen	42.91	—
Zi Su Zi	43.13	—
Chuan Lian Zi	46.60	—
Zhi Shi	47.40	—
Hong Hua	47.61	—
Ge Gen	48.02	—
Wu Mei	49.54	—
Rou Cong Rong	49.69	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62699	62699	0.00	3.94
62226	62226	0.00	9.13
62700	62700	0.00	3.68
62225	62225	0.00	9.64

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Gan Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60011-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gan Cao; Glycyrrhizae radix

Special notes

When selecting the *Gan Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Gan Cao	2	0	3

Second-stage model

For differentiation of the substance/substance group *Gan Cao* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Gan Cao	G119H0521822	62341	40	from supplier
PhytoComm	Gan Cao	G119H0521822	62342	40	from supplier
PhytoComm	Gan Cao	G119H0521823	62533	40	from supplier
PhytoComm	Gan Cao	G119H0521823	62534	40	from supplier

Validation samples

A total of 30 254 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 *Gan Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Gan Cao*.
- 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
PhytoComm	Gan Cao	G119H0521822	62341 [†]	20
PhytoComm	Gan Cao	G119H0521822	62342 [†]	20
PhytoComm	Gan Cao	G119H0521823	62533 [†]	20
PhytoComm	Gan Cao	G119H0521823	62534 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 18 spectra from 7 *Apo-Ident* customers from 6 batches from the substance/substance group *Gan Cao*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Gan Cao	g119h0521121	1
Phytocomm	Gan Cao	G119H0521121	1
Phytocomm	Gan Cao	G119H0521522	8
PhytoComm	Gan Cao	G119H0521121	4
PhytoComm	Gan Cao	G119H0521524	1
PhytoComm	Gan Cao	G119H0521822	2
PhytoComm	Gan Cao	G119H0521823	1

- 839 spectra from 13 *Apo-Ident* customers from a total of 513 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Gan Cao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Gan Cao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	12	6	839

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8244 %)	n/a (n/a)

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gan Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chi Shao (Yao)	19.34	—
Zhi Ke	20.60	—
Mu Dan Pi	20.71	—
Bai Zhu	21.18	—
Zi Hua Di Ding	22.05	—
Shan Yu Rou	22.44	—
Gou Qi Zi	23.08	—
Lian Qiao	24.94	—
Yuan Zhi	25.16	—
Chuan Xiong	27.10	—
Xiang Fu	27.27	—
Shan Yao	27.60	—
Huang Bai	28.46	—
Jiao Gu Lan	28.56	—
Dang Gui	28.86	—
Hong Jing Tian	29.10	—
Wu Wei Zi	29.57	—
Huang Qin	29.63	—
Chen Pi	30.00	—
Hong Hua	30.15	—
Jin Yin Hua	31.01	—
Di Gu Pi	31.21	—
Chuang Mu Xiang	31.66	—
Cang Zhu	31.98	—
Ma Huang	32.92	—
Hou Po	32.97	—
Niu Bang Zi	32.99	—
San Qi	33.89	—
Fu Zi	33.96	—
Yin Yang Huo	34.12	—
Wu Yao	34.54	—
Pu Gong Ying	35.38	—
Sang Zhi	35.56	—
Ye Jiao Teng	36.02	—
Yu Zhu	36.94	—
Dang Gui Wei	37.06	—
He Huan Pi	37.82	—
Yan Hu Suo	37.92	—
Jie Geng	38.41	—
Dan Shen	38.50	—
Zhe Bei Mu	38.63	—

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Substanz	Distance in main model	Distance in second-stage model
Zhi Mu	39.11	—
(Huai) Niu Xi	39.82	—
Tai Zi Shen	39.99	—
Long Yan Rou	40.10	—
Qiang Huo	40.67	—
Qing Pi	40.83	—
Cang Er Zi	40.85	—
Tao Ren	42.43	—
Chai Hu	42.95	—
Huang Qi	43.03	—
Ren Dong Teng	43.14	—
Huang Lian	43.38	—
Gua Lou	43.64	—
Gou Teng	43.64	—
Pi Pa Ye	44.31	—
Sang Ye	44.58	—
Bai Mao Gen	44.82	—
Mao Dong Qing	45.26	—
Dang Shen	46.04	—
Gui Zhi	46.25	—
Ku Shen	46.26	—
Mang Xiao	47.71	—
Dan Dou Chi	48.91	—
Suan Zao Ren	49.02	—
Lian Zi	49.88	—
Du Huo	50.83	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62341	62341	0.00	20.06
62533	62533	0.00	21.39
62534	62534	0.00	21.18
62342	62342	0.00	19.34

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 2.3-2020-05

Validated substance/substance group **Ge Gen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60050-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ge Gen; Puerariae radix

Special notes

When selecting the *Ge Gen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ge Gen	1	0	3

Second-stage model

For differentiation of the substance/substance group *Ge Gen* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ge Gen	G206H1301822	62489	40	from supplier
PhytoComm	Ge Gen	G206H1301822	62490	40	from supplier

Validation samples

A total of 30 254 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 *Ge Gen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ge Gen*.
- 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
PhytoComm	Ge Gen	G206H1301822	62489 [†]	20
PhytoComm	Ge Gen	G206H1301822	62490 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 5 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Ge Gen*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ge Gen	G206H1301221	2
Phytocomm	Ge Gen	G206H1301422	2
PhytoComm	Ge Gen	G206H1301323	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	5	852

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ge Gen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zhi Shi	23.70	—
Sang Ji Shend	24.33	—
Jing Jie	37.77	—
Dan Zhu Ye	39.24	—
Sang Bai Pi	39.40	—
Gu Sui Bu	39.91	—
Gou Teng	40.71	—
He Shou Wu	41.36	—
Hong Jing Tian	42.78	—
Xian He Cao	43.86	—
Pu Gong Ying	44.44	—
Qiang Huo	45.26	—
He Huan Pi	49.27	—
Du Zhong	50.32	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62490	62490	0.00	23.70
62489	62489	0.00	23.76

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 2.3-2020-05

Validated substance/substance group **Gou Qi Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60094-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gou Qi Zi; Lycii chinensis fructus

Special notes

When selecting the *Gou Qi Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Gou Qi Zi	1	0	2

Second-stage model

For differentiation of the substance/substance group *Gou Qi Zi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Gou Qi Zi	G150HS171SK1	62615	40	from supplier
PhytoComm	Gou Qi Zi	G150HS171SK1	62616	40	from supplier

Validation samples

A total of 30 254 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 *Gou Qi Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Gou Qi Zi*.
- 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
PhytoComm	Gou Qi Zi	G150HS171SK1	62615 [†]	20
PhytoComm	Gou Qi Zi	G150HS171SK1	62616 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 6 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Gou Qi Zi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Gou Qi Zi	g150h0913221	1
Phytocomm	Gou Qi Zi	G150H0913422	4
PhytoComm	Gou Qi Zi	G150H0913221	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	6	851

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8258 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gou Qi Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chen Pi	9.54	—
Yu Zhu	10.66	—
Chuan Xiong	11.77	—
Hong Jing Tian	12.06	—
Long Yan Rou	12.45	—
Dang Gui Wei	13.05	—
Gua Lou	13.60	—
Cang Zhu	13.98	—
Dang Gui	16.18	—
Zhi Ke	16.41	—
Chuang Mu Xiang	16.48	—
Ma Huang	16.57	—
Shan Yu Rou	17.09	—
San Qi	17.56	—
Jin Yin Hua	17.88	—
Yuan Zhi	18.84	—
Lian Qiao	19.00	—
Gan Cao	19.28	—
Hou Po	19.65	—
Ren Dong Teng	19.92	—
Di Gu Pi	19.92	—
Jiao Gu Lan	19.96	—
Tai Zi Shen	20.15	—
Pi Pa Ye	20.48	—
Mu Dan Pi	20.75	—
Dang Shen	20.85	—
Ye Jiao Teng	21.45	—
Zi Hua Di Ding	21.73	—
Tao Ren	22.07	—
Huang Qin	22.14	—
He Huan Pi	22.18	—
Dan Shen	22.55	—
Fu Zi	22.71	—
Shan Yao	22.86	—
Da Zao	23.31	—
Bai Shao Yao	23.42	—
Yin Yang Huo	23.48	—
Zhe Bei Mu	23.71	—
Yan Hu Suo	24.37	—
Wu Wei Zi	25.14	—
Bai Zhu	25.32	—
Ci Wu Jia	26.25	—
Shen Qu	26.75	—
Lian Zi	26.78	—
Gou Teng	26.82	—
Jie Geng	27.08	—
Ji Li	27.55	—
Ji Xue Teng	27.78	—
Bai Zi Ren	28.48	—
Tian Hua Fen	28.49	—
Fo Shou	29.43	—
Chai Hu	30.62	—

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Substanz	Distance in main model	Distance in second-stage model
Tu Fu Ling	31.23	—
Ban Xia (Jiang)	31.37	—
Huo Ma Ren	31.60	—
Bai Xian Pi	31.75	—
Sang Zhi	32.53	—
Chi Shao (Yao)	32.60	—
Dan Dou Chi	32.73	—
Rou Gui	32.76	—
Gui Zhi	32.82	—
Che Qian Zi	32.96	—
Qiang Huo	33.20	—
Mao Dong Qing	34.30	—
Sheng Jiang	34.55	—
Zhi Mu	34.68	—
Suan Zao Ren	35.19	—
Qing Pi	36.72	—
Fu Ling	36.75	—
Tian Men Dong	37.05	—
Hong Hua	38.01	—
Ling Zhi	38.25	—
Huang Lian	38.91	—
Yu Jin	39.40	—
Huang Qi	40.18	—
Zhu Ru	41.20	—
Cang Er Zi	41.51	—
Yi Yi Ren	41.62	—
Mai Men Dong	42.24	—
Huang Bai	43.02	—
Ma Huang Gen	43.09	—
Fu Xiao Mai	43.12	—
Fu Shen	43.61	—
Mang Xiao	43.80	—
Du Zhong	46.69	—
Sang Ye	47.53	—
Wu Yao	50.09	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62615	62615	0.00	9.54
62616	62616	0.00	9.98

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Gou Teng**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60097-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gou Teng; Uncariae ramulus cum uncis

Special notes

When selecting the *Gou Teng* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Gou Teng	2	0	2

Second-stage model

For differentiation of the substance/substance group *Gou Teng* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Gou Teng	G247H1210822	62313	40	from supplier
PhytoComm	Gou Teng	G247H1210822	62314	40	from supplier
PhytoComm	Gou Teng	G247HS288SG1	62629	40	from supplier
PhytoComm	Gou Teng	G247HS288SG1	62630	40	from supplier

Validation samples

A total of 30 254 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 *Gou Teng*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Gou Teng*.
- 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
PhytoComm	Gou Teng	G247H1210822	62313 [†]	20
PhytoComm	Gou Teng	G247H1210822	62314 [†]	20
PhytoComm	Gou Teng	G247HS288SG1	62629 [†]	20
PhytoComm	Gou Teng	G247HS288SG1	62630 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Gou Teng*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Gou Teng	g247h1210122	1
Phytocomm	Gou Teng	G247H1210422	2

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Gou Teng* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Gou Teng* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	77	3	9837
Type C	2	0	3	852

The substance/substance group *Gou Teng* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	96.2500 % (> 92.5000 %)
Type C	99.5349 % (> 98.9489 %)	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.)

[†]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*.

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gou Teng* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Rou Gui	3.10	—
Gui Zhi	5.91	—
Yi Yi Ren	6.57	—
Ma Huang Gen	6.84	—
Ji Xue Teng	7.80	—
Huo Ma Ren	7.94	—
Fu Ling	8.29	—
Sheng Jiang	8.63	—
He Huan Pi	9.99	—
Fu Shen	10.00	—
Fu Xiao Mai	10.22	—
Ci Wu Jia	10.90	—
Tai Zi Shen	11.41	—
Tao Ren	12.19	—
Ban Xia (Jiang)	12.39	—
Ling Zhi	12.99	—
Bai Shao Yao	13.19	—
Ren Dong Teng	13.46	—
Bai Xian Pi	13.74	—
Lian Zi	14.72	—
Di Gu Pi	15.62	—
Ye Jiao Teng	15.95	—
Fo Shou	16.00	—
Ji Li	16.23	—
Zhe Bei Mu	16.67	—
Shen Qu	17.96	—
Bai Zi Ren	18.32	—
Zhu Ru	18.77	—
Tian Men Dong	20.49	—
Dan Dou Chi	20.88	—
Tian Hua Fen	20.88	—
Yu Jin	21.25	—
Chen Pi	21.32	—
Nü Zhen Zi	21.49	—
Tu Fu Ling	21.83	—
Huang Bo	22.08	—
Yi Mu Cao	22.69	—
Da Zao	23.45	—
Chuan Xiong	23.67	—
Dan Zhu Ye	24.04	—
Yan Hu Suo	24.06	—
Dan Shen	24.26	—
Long Yan Rou	25.35	—
Lian Qiao	25.48	—
Pu Gong Ying	25.58	—

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Substanz	Distance in main model	Distance in second-stage model
Yin Chen Hao	25.79	—
Jing Jie	25.97	—
Qing Hao	26.06	—
Gua Lou	26.10	—
Pi Pa Ye	27.64	—
Shan Yao	28.17	—
Mao Dong Qing	28.31	—
Chai Hu	28.66	—
Yin Yang Huo	28.92	—
Yuan Zhi	29.41	—
Qiang Huo	29.46	—
Hong Jing Tian	31.03	—
Jiao Gu Lan	31.18	—
Ma Huang	32.84	—
Fu Zi	33.01	—
Dang Shen	34.04	—
Zhi Ke	34.13	—
Yu Zhu	34.63	—
Jin Yin Hua	35.41	—
Zhi Shi	36.02	—
Mang Xiao	37.40	—
Sha Ren	38.15	—
Cang Zhu	38.19	—
Wu Zhu Yu	38.38	—
Wu Wei Zi	38.47	—
Hou Po	38.50	—
Che Qian Zi	38.50	—
Dang Gui Wei	38.73	—
Xin Yi	39.40	—
Sang Ji Shend	40.72	—
San Qi	41.08	—
Huang Qin	41.10	—
Shan Yu Rou	41.38	—
Huang Lian	43.23	—
Xuan Shen	43.76	—
Xian He Cao	43.97	—
Sang Zhi	44.34	—
Dang Gui	45.13	—
Jin Qian Cao	45.48	—
Rou Cong Rong	45.50	—
Jie Geng	46.12	—
Xia Ku Cao	46.46	—
Hu Zhang	46.65	—
Xu Duan	46.89	—
Wu Jia Pi	47.54	—
Han Lian Cao	47.60	—
Du Zhong	48.73	—
Bai Hua She She Cao	49.92	—

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

Identity according to identity test using NIR spectroscopy

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

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62313	62313	0.00	21.49
62629	62629	0.00	5.91
62314	62314	0.00	22.54
62630	62630	0.00	3.10

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Gu Sui Bu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002263-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gu Sui Bu; Drynariae rhizoma

Special notes

When selecting the *Gu Sui Bu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Gu Sui Bu	1	0	3

Second-stage model

For differentiation of the substance/substance group *Gu Sui Bu* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Gu Sui Bu	G094H1011921	62779	40	from supplier
PhytoComm	Gu Sui Bu	G094H1011921	62780	40	from supplier

Validation samples

A total of 30 254 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 *Gu Sui Bu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Gu Sui Bu*.
- 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
PhytoComm	Gu Sui Bu	G094H1011921	62779 [†]	20
PhytoComm	Gu Sui Bu	G094H1011921	62780 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 6 spectra from 5 *Apo-Ident* customers from 4 batches from the substance/substance group *Gu Sui Bu*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Gu Sui Bu	G094H1011221	2
Phytocomm	Gu Sui Bu	g094h1011023	1
Phytocomm	Gu Sui Bu	g094h1011221	1
PhytoComm	Gu Sui Bu	G094H1011221	1
PhytoComm	Gu Sui Bu	G094H1011522	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	3	0	6	848

The substance/substance group *Gu Sui Bu* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.4574 % (> 98.8703 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gu Sui Bu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
He Huan Pi	13.23	—
Xian He Cao	15.54	—
Sang Bai Pi	17.24	—
He Shou Wu	17.35	—
Yu Jin	18.08	—
Gui Zhi	19.58	—
Fu Zi	20.18	—
Chen Pi	21.44	—
Dan Zhu Ye	22.02	—
Sang Ji Shend	23.15	—
Wu Yao	23.47	—
Jiang Huang	24.19	—
Bu Gu Zhi	26.44	—
Ji Li	26.81	—
Nü Zhen Zi	28.33	—
Fang Feng	28.42	—
Huang Bo	29.58	—
Sha Ren	29.89	—
Yin Chen Hao	30.44	—
(Bai) Dou Kou	30.87	—
Hu Zhang	31.42	—
Yi Mu Cao	32.53	—
Wu Zhu Yu	32.78	—
Qiang Huo	34.10	—
Mang Xiao	34.95	—
Ge Gen	36.37	—
Shan Yao	36.76	—
E Zhu	36.99	—
Xia Ku Cao	38.91	—
Hong Jing Tian	39.38	—
Xiang Fu	39.68	—
Jing Jie	40.70	—
Xi Xian Cao	42.53	—
Ju Hua	43.36	—
Qing Pi	45.79	—
Xu Duan	46.44	—
Mu Dan Pi	47.41	—
Huang Lian	47.66	—
Xin Yi	47.81	—
Zhi Shi	47.90	—
Zi Su Zi	48.20	—
(Shi) Chang Pu	49.28	—
Gou Teng	49.35	—
Du Zhong	50.61	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62780	62780	0.00	13.23
62779	62779	0.00	13.49

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 2.3-2020-05

Validated substance/substance group **Gua Lou**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60128-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gua Lou; Trichosanthis fructus

Special notes

When selecting the *Gua Lou* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Gua Lou	2	0	2

Second-stage model

For differentiation of the substance/substance group *Gua Lou* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Gua Lou	G241H1096821	62317	40	from supplier
PhytoComm	Gua Lou	G241H1096821	62318	40	from supplier
PhytoComm	Gua Lou	G241HS202SK1	62547	40	from supplier
PhytoComm	Gua Lou	G241HS202SK1	62548	40	from supplier

Validation samples

A total of 30 254 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 *Gua Lou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Gua Lou*.
- 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
PhytoComm	Gua Lou	G241H1096821	62317 [†]	20
PhytoComm	Gua Lou	G241H1096821	62318 [†]	20
PhytoComm	Gua Lou	G241HS202SK1	62547 [†]	20
PhytoComm	Gua Lou	G241HS202SK1	62548 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Gua Lou*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Gua Lou	G241H1096521	1
Phytocomm	Gua Lou	g241h1096321	1
Phytocomm	Gua Lou	G241H1096321	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	1	159	1	19 319
Type B	1	80	0	9836
Type C	0	0	3	854

The substance/substance group *Gua Lou* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9921 % (> 99.9737 %)	99.3750 % (> 97.5000 %)
Type B	99.9842 % (> 99.9483 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8280 %)	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.)

[†]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*.

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gua Lou* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fo Shou	4.26	—
Chen Pi	6.55	—
Bai Shao Yao	7.59	—
Ye Jiao Teng	8.48	—
Tai Zi Shen	9.44	—
Dang Gui Wei	9.57	—
Shen Qu	9.72	—
Tian Men Dong	10.17	—
Tao Ren	10.27	—
Dang Shen	10.60	—
He Huan Pi	10.77	—
Yuan Zhi	11.08	—
Zhe Bei Mu	11.15	—
Di Gu Pi	11.21	—
Ci Wu Jia	11.49	—
Pi Pa Ye	11.84	—
Ji Li	12.12	—
Yu Zhu	12.83	—
Rou Gui	13.54	—
Ban Xia (Jiang)	13.85	—
Bai Zi Ren	13.94	—
Da Zao	14.01	—
Lian Zi	14.83	—
Chuan Xiong	15.04	—
Qing Pi	15.63	—
Niu Bang Zi	15.80	—
Shan Yao	15.98	—
Ku Shen	16.08	—
San Qi	16.49	—
Sang Zhi	16.57	—
Ren Dong Teng	16.67	—
Gou Teng	16.98	—
Tu Fu Ling	17.17	—
Gui Zhi	17.34	—
Fu Ling	17.82	—
Sheng Jiang	17.86	—
Huo Ma Ren	18.22	—
(Shi) Chang Pu	18.27	—
Cang Zhu	18.37	—
Lian Qiao	18.49	—
Tian Hua Fen	19.38	—
Zhu Ru	19.98	—
Fu Xiao Mai	20.16	—
Xie Bai	20.39	—
(Huai) Niu Xi	20.45	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Xian Pi	20.65	—
Ling Zhi	20.71	—
Ji Xue Teng	21.00	—
Dang Gui	21.24	—
Long Yan Rou	21.28	—
Yi Mu Cao	21.70	—
Xiang Fu	22.10	—
Fu Zi	22.43	—
Yi Yi Ren	22.84	—
Ma Huang	23.01	—
Jiao Gu Lan	24.10	—
Shan Yu Rou	24.51	—
Gou Qi Zi	24.63	—
Yan Hu Suo	24.71	—
Zhi Ke	25.12	—
Ma Huang Gen	25.24	—
Dan Shen	25.46	—
Jie Geng	25.92	—
Bai Zhu	26.47	—
Jiang Huang	26.62	—
Cang Er Zi	26.80	—
Zi Su Zi	26.83	—
Huang Qin	27.20	—
Jin Yin Hua	27.37	—
Yin Yang Huo	28.14	—
Huang Qi	28.21	—
Bai Mao Gen	28.61	—
(Bai) Dou Kou	28.88	—
Zhi Mu	29.29	—
Hong Jing Tian	29.38	—
Mao Dong Qing	29.78	—
Hou Po	30.04	—
Wu Yao	30.21	—
Fu Shen	30.24	—
Yu Jin	30.30	—
Dan Dou Chi	30.50	—
Wu Wei Zi	30.51	—
Fang Feng	30.74	—
Chai Hu	31.41	—
Du Huo	31.98	—
Sha Ren	32.47	—
Huang Bo	32.86	—
Pu Gong Ying	33.91	—
Mang Xiao	34.02	—
Chuang Mu Xiang	34.27	—
Xu Duan	34.32	—
Nü Zhen Zi	34.48	—
Qiang Huo	34.86	—
Che Qian Zi	35.11	—
Gan Cao	35.17	—
Sha Shen (Bei)	36.05	—
Xian He Cao	36.13	—
E Zhu	37.13	—
Dong Gua Zi	37.50	—
Suan Zao Ren	37.61	—
Mu Dan Pi	39.84	—
Chuan Lian Zi	39.96	—
Ba Ji Tian	40.24	—
Chi Shao (Yao)	40.52	—

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Substanz	Distance in main model	Distance in second-stage model
Qin Jiao	41.17	—
Xin Yi	42.19	—
Ju Hua	42.87	—
Mai Men Dong	42.98	—
Gu Sui Bu	43.06	—
Huang Lian	43.87	—
Wu Zhu Yu	44.09	—
Sang Ye	44.93	—
Wang Bu Liu Xing	45.41	—
Bai Bian Dou	45.97	—
Sang Ji Shend	46.68	—
Lai Fu Zi	47.51	—
Wu Mei	48.26	—
Zi Hua Di Ding	48.75	—
Xi Xian Cao	49.25	—
Zhi Zi	49.30	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62548	62548	0.00	4.26
62547	62547	0.00	5.24
62318	62318	0.00	16.06
62317	62317	0.00	15.63

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 2.3-2020-05

Validated substance/substance group **Guang Huo Xiang**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 61079-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Guang Huo Xiang; Pogostemonis herba

Special notes

When selecting the *Guang Huo Xiang* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Guang Huo Xiang	1	0	1

Second-stage model

For differentiation of the substance/substance group *Guang Huo Xiang* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Guang Huo Xiang	G007H2005822	62589	40	from supplier
PhytoComm	Guang Huo Xiang	G007H2005822	62590	40	from supplier

Validation samples

A total of 30 254 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 *Guang Huo Xiang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Guang Huo Xiang*.
- 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
PhytoComm	Guang Huo Xiang	G007H2005822	62589 [†]	20
PhytoComm	Guang Huo Xiang	G007H2005822	62590 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 2 spectra from 2 *Apo-Ident* customers from 1 batches from the substance/substance group *Guang Huo Xiang*.
- 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
Phytocomm	Guang Huo Xiang	G007H2005521	2

- 855 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	2	855

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Guang Huo Xiang* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ai Ye	24.39	—
Xuan Shen	34.92	—
Jue Ming Zi	37.11	—
Pu Gong Ying	41.14	—
Hua Shi	44.96	—
Shu Di (Huang)	46.32	—
Wu Mei	49.24	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62590	62590	0.00	24.39
62589	62589	0.00	25.83

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 2.3-2020-05

Validated substance/substance group **Gui Zhi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60189-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gui Zhi; Cinnamomi cassiae ramulus

Special notes

When selecting the *Gui Zhi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Gui Zhi	2	0	4

Second-stage model

For differentiation of the substance/substance group *Gui Zhi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Gui Zhi	G070H1001624	62103	40	from supplier
PhytoComm	Gui Zhi	G070H1001624	62104	40	from supplier
PhytoComm	Gui Zhi	G070HS205SH1	62563	40	from supplier
PhytoComm	Gui Zhi	G070HS205SH1	62564	40	from supplier

Validation samples

A total of 30 254 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 *Gui Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Gui Zhi*.
- 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
PhytoComm	Gui Zhi	G070H1001624	62103 [†]	20
PhytoComm	Gui Zhi	G070H1001624	62104 [†]	20
PhytoComm	Gui Zhi	G070HS205SH1	62563 [†]	20
PhytoComm	Gui Zhi	G070HS205SH1	62564 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

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

Supplier	Substance	Batch	Spectra
Phytocomm	Gui Zhi	G070H1001221	2
Phytocomm	Gui Zhi	g070h1001422	1
Phytocomm	Gui Zhi	G070H100422	1
Phytocomm	Gui Zhi	G070H1001523	2

- 851 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Gui Zhi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Gui Zhi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	1	77	3	9836
Type C	3	1	5	848

The substance/substance group *Gui Zhi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	99.9921 % (> 99.9562 %)	96.2500 % (> 92.5000 %)
Type C	99.4684 % (> 98.8814 %)	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

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gui Zhi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sheng Jiang	4.97	—
Rou Gui	5.27	—
Gou Teng	7.09	—
Ban Xia (Jiang)	7.14	—
Yi Yi Ren	7.55	—
Fu Ling	7.82	—
Tao Ren	8.37	—
He Huan Pi	8.39	—
Di Gu Pi	8.72	—
Ci Wu Jia	8.76	—
Fu Xiao Mai	9.95	—
Jiang Huang	10.89	—
Zhu Ru	11.36	—
Tai Zi Shen	11.42	—
Fu Zi	11.49	—
Ma Huang Gen	11.72	—
Ji Li	13.42	—
Bai Zi Ren	13.44	—
Ji Xue Teng	13.47	—
Huo Ma Ren	13.71	—
Lian Zi	14.29	—
Bai Xian Pi	14.52	—
Ling Zhi	14.74	—
Bai Shao Yao	15.05	—
Shen Qu	15.52	—
Sha Ren	15.74	—
Wu Yao	16.45	—
Zhe Bei Mu	16.51	—
Fu Shen	16.57	—
Fo Shou	16.57	—
Ye Jiao Teng	17.06	—
Tian Men Dong	17.32	—
Long Yan Rou	18.44	—
Gua Lou	19.08	—
Da Zao	20.63	—
Chen Pi	20.92	—
Ren Dong Teng	21.50	—
Tian Hua Fen	22.33	—
Shan Yao	22.54	—
Xiang Fu	22.95	—
Qing Pi	23.23	—
Tu Fu Ling	23.56	—
Chuan Xiong	23.98	—

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Substanz	Distance in main model	Distance in second-stage model
Yuan Zhi	24.10	—
Qiang Huo	24.29	—
Xin Yi	24.31	—
Yu Jin	24.75	—
Hu Zhang	24.78	—
(Bai) Dou Kou	25.19	—
Huang Bo	25.79	—
Pi Pa Ye	25.87	—
Yi Mu Cao	25.94	—
Lian Qiao	26.88	—
Dang Shen	27.32	—
Dan Dou Chi	27.42	—
Gu Sui Bu	27.67	—
Dan Shen	27.73	—
Yan Hu Suo	27.80	—
Sang Ye	27.84	—
Pu Gong Ying	28.12	—
Huang Lian	28.75	—
Xi Xian Cao	29.96	—
(Shi) Chang Pu	30.57	—
Cang Er Zi	31.00	—
Nü Zhen Zi	31.33	—
Niu Bang Zi	31.61	—
Yu Zhu	32.00	—
Jiao Gu Lan	33.00	—
Mao Dong Qing	33.02	—
E Zhu	33.55	—
Ju Hua	34.04	—
Yin Yang Huo	34.14	—
Zhi Ke	34.15	—
Chai Hu	34.36	—
Sang Ji Shend	34.75	—
Hong Jing Tian	34.80	—
Dang Gui Wei	34.93	—
Du Zhong	35.01	—
Ma Huang	35.02	—
Xian He Cao	35.85	—
Shan Yu Rou	36.06	—
Cang Zhu	36.67	—
San Qi	36.88	—
Jin Yin Hua	37.19	—
Sang Bai Pi	37.56	—
Han Lian Cao	38.22	—
Huang Qin	38.23	—
Bai Hua She She Cao	38.35	—
Xu Duan	38.41	—
Fang Feng	38.51	—
Mang Xiao	38.53	—
Xie Bai	38.54	—
Xia Ku Cao	38.87	—
Wu Zhu Yu	39.56	—
Wang Bu Liu Xing	40.77	—
Wu Wei Zi	40.97	—
He Shou Wu	40.99	—
Zi Su Zi	41.04	—
Dang Gui	41.06	—
Dan Zhu Ye	42.03	—
Hou Po	42.19	—
Du Huo	43.26	—

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Substanz	Distance in main model	Distance in second-stage model
Mu Dan Pi	43.80	—
Ku Shen	43.82	—
Yin Chen Hao	43.90	—
Jie Geng	44.21	—
Bai Zhu	44.44	—
Sang Zhi	45.65	—
Zhi Mu	46.24	—
Che Qian Zi	46.99	—
Bu Gu Zhi	48.57	—
Wu Mei	49.34	—
Bai Mao Gen	49.34	—
Gou Qi Zi	49.68	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62104	62104	0.00	10.89
62563	62563	0.00	5.27
62564	62564	0.00	4.97
62103	62103	0.00	11.08

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 2.3-2020-05

Validated substance/substance group **Han Lian Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60540-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Han Lian Cao; Ecliptae prostratae herba

Special notes

When selecting the *Han Lian Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Han Lian Cao	1	0	2

Second-stage model

For differentiation of the substance/substance group *Han Lian Cao* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Han Lian Cao	G095HS141RW1	62679	40	from supplier
PhytoComm	Han Lian Cao	G095HS141RW1	62680	40	from supplier

Validation samples

A total of 30 254 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 *Han Lian Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Han Lian Cao*.
- 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
PhytoComm	Han Lian Cao	G095HS141RW1	62679 [†]	20
PhytoComm	Han Lian Cao	G095HS141RW1	62680 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

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

- 8 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Han Lian Cao*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Han Lian Cao	G095H0770321	1
Phytocomm	Han Lian Cao	G095H0770521	4
Phytocomm	Han Lian Cao	g095h0770321	1
PhytoComm	Han Lian Cao	G095H0770321	2

- 849 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	8	849

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8253 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Han Lian Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Hua She She Cao	6.45	—
Xi Xian Cao	13.31	—
Pu Gong Ying	14.63	—
Jiang Huang	16.21	—
Xia Ku Cao	16.56	—
Huang Lian	16.65	—
Tu Fu Ling	16.97	—
Xin Yi	17.00	—
Hu Zhang	19.21	—
Sang Ye	19.38	—
Shan Yao	21.77	—
Nü Zhen Zi	23.90	—
Zhi Shi	25.48	—
Sha Ren	27.14	—
He Huan Pi	27.23	—
Gui Zhi	29.02	—
Fu Zi	29.48	—
Yi Mu Cao	32.17	—
Rou Cong Rong	33.49	—
Qiang Huo	34.76	—
Du Zhong	35.40	—
Gu Sui Bu	36.11	—
Huang Bo	36.59	—
Sang Ji Shend	40.34	—
Yu Jin	40.60	—
Dan Zhu Ye	40.66	—
Wu Yao	42.00	—
Qing Pi	42.07	—
Gou Teng	42.25	—
Yan Hu Suo	43.48	—
E Zhu	45.44	—
Ji Li	45.48	—
Dan Shen	45.50	—
Cang Er Zi	45.56	—
Chen Pi	45.67	—
Niu Bang Zi	46.27	—
Xiang Fu	46.67	—
Mang Xiao	47.00	—
Hou Po	47.04	—
Wu Mei	48.20	—
Wu Wei Zi	48.50	—
(Bai) Dou Kou	49.13	—
Gua Lou	49.21	—
Ju Hua	49.68	—
Sang Bai Pi	49.85	—
Xu Duan	50.73	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62679	62679	0.00	6.45
62680	62680	0.00	9.78

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

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **He Huan Pi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60175-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

He Huan Pi; Albiziae cortex

Special notes

When selecting the *He Huan Pi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
He Huan Pi	2	0	2

Second-stage model

For differentiation of the substance/substance group *He Huan Pi* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	He Huan Pi	G010H0635822	62402	40	from supplier
PhytoComm	He Huan Pi	G010H0635822	62403	40	from supplier
PhytoComm	He Huan Pi	G010HS114SK1	62645	40	from supplier
PhytoComm	He Huan Pi	G010HS114SK1	62646	40	from supplier

Validation samples

A total of 30 254 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 *He Huan Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *He Huan Pi*.
- 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
PhytoComm	He Huan Pi	G010H0635822	62402 [†]	20
PhytoComm	He Huan Pi	G010H0635822	62403 [†]	20
PhytoComm	He Huan Pi	G010HS114SK1	62645 [†]	20
PhytoComm	He Huan Pi	G010HS114SK1	62646 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *He Huan Pi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	He Huan Pi	g010h0635221	1
Phytocomm	He Huan Pi	G010H0635423	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

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

	False positive	True positive	False negative	True negative
Type A	10	159	1	19 310
Type B	13	80	0	9824
Type C	0	1	1	855

The substance/substance group *He Huan Pi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9262 % (> 99.9077 %)	99.3750 % (> 97.5000 %)
Type B	99.8049 % (> 99.7689 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8302 %)	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.)

[†]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*.

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *He Huan Pi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tao Ren	3.64	—
Ci Wu Jia	4.68	—
Sheng Jiang	5.18	—
Gui Zhi	6.44	—
Di Gu Pi	7.33	—
Bai Zi Ren	7.60	—
Bai Shao Yao	8.47	—
Lian Zi	8.56	—
Huo Ma Ren	8.58	—
Fu Xiao Mai	8.87	—
Tai Zi Shen	10.67	—
Rou Gui	10.94	—
Ling Zhi	11.03	—
Ji Li	11.05	—
Gou Teng	11.05	—
Shen Qu	11.37	—
Zhe Bei Mu	11.85	—
Yi Yi Ren	12.10	—
Zhu Ru	12.46	—
Ban Xia (Jiang)	12.75	—
Bai Xian Pi	12.93	—
Tian Hua Fen	13.17	—
Fu Ling	13.29	—
Ye Jiao Teng	13.87	—
Jiang Huang	15.55	—
Fo Shou	15.78	—
Ji Xue Teng	16.00	—
Gua Lou	16.71	—
Yu Jin	17.06	—
Ma Huang Gen	17.27	—
Ren Dong Teng	17.89	—
Tu Fu Ling	18.83	—
Chen Pi	19.47	—
Tian Men Dong	19.92	—
Chuan Xiong	20.14	—
Pi Pa Ye	20.15	—
Shan Yao	20.29	—
Gu Sui Bu	20.39	—
Yuan Zhi	20.42	—
(Bai) Dou Kou	21.50	—
Xian He Cao	21.69	—
Lian Qiao	21.87	—
Wu Yao	22.26	—
Sha Ren	23.14	—
Long Yan Rou	23.83	—

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Substanz	Distance in main model	Distance in second-stage model
Fu Zi	24.54	—
Dang Shen	24.74	—
Fu Shen	24.81	—
Da Zao	24.82	—
Dan Dou Chi	24.97	—
Sang Bai Pi	26.64	—
Dan Shen	26.66	—
Yan Hu Suo	26.94	—
Mao Dong Qing	28.16	—
Nü Zhen Zi	28.32	—
Qiang Huo	28.36	—
Jiao Gu Lan	29.00	—
Yin Chen Hao	29.18	—
San Qi	29.26	—
Chai Hu	29.70	—
Yu Zhu	30.36	—
Zhi Ke	30.48	—
Huang Bo	31.11	—
Dang Gui Wei	31.17	—
E Zhu	31.34	—
Yin Yang Huo	32.10	—
Jin Yin Hua	32.27	—
Sang Ji Shend	32.56	—
Dang Gui	32.65	—
Hong Jing Tian	32.94	—
Shan Yu Rou	32.97	—
Cang Zhu	33.27	—
Hou Po	33.48	—
He Shou Wu	33.65	—
Ma Huang	33.71	—
Mang Xiao	33.86	—
Yi Mu Cao	33.91	—
Bu Gu Zhi	34.21	—
Xiang Fu	34.36	—
Fang Feng	34.59	—
Che Qian Zi	35.51	—
Wu Wei Zi	36.04	—
Hu Zhang	36.98	—
Zi Su Zi	37.73	—
Wu Zhu Yu	38.35	—
Zhi Mu	38.43	—
Dan Zhu Ye	38.71	—
Huang Qin	39.11	—
Suan Zao Ren	39.19	—
Niu Bang Zi	39.40	—
Xia Ku Cao	39.56	—
Huang Lian	41.98	—
Mu Dan Pi	42.12	—
Xin Yi	43.00	—
Ju Hua	43.73	—
Qing Pi	44.11	—
Gou Qi Zi	44.32	—
Xi Xian Cao	45.62	—
Ge Gen	45.91	—
Du Zhong	46.16	—
Bai Bian Dou	46.95	—
Sang Zhi	46.97	—
Bai Zhu	47.05	—
(Shi) Chang Pu	48.35	—

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Substanz	Distance in main model	Distance in second-stage model
Jie Geng	48.46	–
Cang Er Zi	50.90	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62645	62645	0.00	3.64
62646	62646	0.00	4.68
62402	62402	0.00	13.69
62403	62403	0.00	14.01

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 2.3-2020-05

Validated substance/substance group **He Shou Wu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60101-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

He Shou Wu; Polygoni multiflori radix

Special notes

When selecting the *He Shou Wu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
He Shou Wu	2	0	2

Second-stage model

For differentiation of the substance/substance group *He Shou Wu* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	He Shou Wu	G198H0718821	62301	40	from supplier
PhytoComm	He Shou Wu	G198H0718821	62302	40	from supplier
PhytoComm	He Shou Wu	G198H0718921	62745	40	from supplier
PhytoComm	He Shou Wu	G198H0718921	62746	40	from supplier

Validation samples

A total of 30 254 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 *He Shou Wu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *He Shou Wu*.
- 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
PhytoComm	He Shou Wu	G198H0718821	62301 [†]	20
PhytoComm	He Shou Wu	G198H0718821	62302 [†]	20
PhytoComm	He Shou Wu	G198H0718921	62745 [†]	20
PhytoComm	He Shou Wu	G198H0718921	62746 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

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

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

- 7 spectra from 6 *Apo-Ident* customers from 3 batches from the substance/substance group *He Shou Wu*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	He Shou Wu	G198H0718222	1
Phytocomm	He Shou Wu	g198h0718222	1
Phytocomm	He Shou Wu	G198H0718421	3
PhytoComm	He Shou Wu	G198H0718222	1
PhytoComm	He Shou Wu	G198H0718421	1

- 850 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *He Shou Wu* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *He Shou Wu* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	2	0	7	848

The substance/substance group *He Shou Wu* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.7674 % (> 99.1802 %)	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

[†]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*.

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

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

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

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *He Shou Wu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Xian He Cao	10.63	—
Dan Zhu Ye	12.69	—
Yu Jin	13.31	—
Wu Yao	13.76	—
Sang Ji Shend	13.90	—
Gu Sui Bu	14.09	—
Jing Jie	15.64	—
He Huan Pi	16.07	—
Sang Bai Pi	17.39	—
Chen Pi	20.12	—
Sha Ren	22.25	—
Fang Feng	22.84	—
Nü Zhen Zi	23.78	—
Ge Gen	25.63	—
Yin Chen Hao	25.75	—
Jin Qian Cao	26.22	—
Gui Zhi	26.64	—
Fu Zi	27.48	—
Ji Li	27.54	—
Wu Zhu Yu	28.66	—
Hong Jing Tian	28.72	—
Du Zhong	29.19	—
Jiang Huang	29.25	—
Bu Gu Zhi	29.69	—
Mu Dan Pi	30.95	—
Gou Teng	31.14	—
Qiang Huo	31.82	—
Mang Xiao	32.74	—
Huang Bo	34.27	—
Zhi Shi	34.65	—
(Bai) Dou Kou	35.44	—
Xiang Fu	37.28	—
(Shi) Chang Pu	37.37	—
Shan Yao	37.39	—
E Zhu	37.48	—
Bai Mao Gen	39.51	—
Sang Ye	39.56	—
Ju Hua	39.93	—
Yi Mu Cao	40.02	—
Pu Gong Ying	40.28	—
Du Huo	40.40	—
Xu Duan	40.72	—
Hu Zhang	40.96	—

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Substanz	Distance in main model	Distance in second-stage model
Ba Ji Tian	42.59	—
Wu Jia Pi	43.16	—
Dang Gui	43.54	—
Qing Pi	45.24	—
Huang Qi	45.67	—
Xia Ku Cao	46.83	—
Zhi Ke	48.32	—
Zi Su Zi	48.43	—
Tian Hua Fen	49.46	—
Xie Bai	49.75	—
Ku Shen	50.01	—

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62746	62746	0.00	10.89
62301	62301	0.00	12.69
62302	62302	0.00	13.28
62745	62745	0.00	10.63

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 2.3-2020-05

Validated substance/substance group **Hong Hua**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60206-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hong Hua; Carthami flos

Special notes

When selecting the *Hong Hua* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

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

Validation method

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

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

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hong Hua	1	0	2

Second-stage model

For differentiation of the substance/substance group *Hong Hua* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hong Hua*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Hong Hua	G057HS173SG1	62663	40	from supplier
PhytoComm	Hong Hua	G057HS173SG1	62664	40	from supplier

Validation samples

A total of 30 254 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 *Hong Hua*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Hong Hua*.
- 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
PhytoComm	Hong Hua	G057HS173SG1	62663 [†]	20
PhytoComm	Hong Hua	G057HS173SG1	62664 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Hong Hua*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Hong Hua	G057H0901221	1
Phytocomm	Hong Hua	g057h0901121	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hong Hua* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hong Hua* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	2	855

The substance/substance group *Hong Hua* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hong Hua* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Shan Yao	10.95	—
Shan Yu Rou	12.08	—
Wu Wei Zi	13.22	—
Jiao Gu Lan	15.76	—
Jin Yin Hua	15.84	—
Bai Zhu	16.84	—
Zi Hua Di Ding	17.05	—
Qing Pi	17.24	—
Zhi Ke	18.13	—
Sang Ye	18.41	—
Mao Dong Qing	21.51	—
Cang Zhu	22.98	—
Suan Zao Ren	23.06	—
Chai Hu	23.29	—
Wu Mei	23.61	—
Dan Shen	23.67	—
Hong Jing Tian	24.03	—
Mu Dan Pi	24.55	—
Gua Lou	25.03	—
Huang Bai	25.42	—
Chuan Xiong	25.44	—
Gan Cao	25.64	—
Lian Qiao	27.10	—
Ji Li	27.48	—
Dang Shen	27.54	—
Chen Pi	27.77	—
Chuang Mu Xiang	27.78	—
Du Zhong	27.86	—
Ren Dong Teng	28.63	—
Gou Qi Zi	28.78	—
Cang Er Zi	29.17	—
Qiang Huo	29.20	—
Gui Zhi	31.51	—
Ma Huang	31.66	—
Yan Hu Suo	31.70	—
Pi Pa Ye	31.99	—
Hou Po	32.12	—
Ye Jiao Teng	32.69	—
Chi Shao (Yao)	32.85	—
Zhe Bei Mu	34.00	—
Yuan Zhi	34.10	—
Dan Dou Chi	34.24	—
Pu Gong Ying	34.91	—
Yin Yang Huo	35.06	—
Huang Qin	35.36	—
Bai Shao Yao	36.39	—
He Huan Pi	36.56	—
Huang Lian	36.59	—
Lian Zi	36.76	—
Di Gu Pi	36.82	—
San Qi	37.00	—
Yu Zhu	37.17	—

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Substanz	Distance in main model	Distance in second-stage model
Fu Zi	37.21	—
Tu Fu Ling	37.65	—
Bai Zi Ren	37.68	—
Niu Bang Zi	37.86	—
Long Yan Rou	39.03	—
Dang Gui	39.50	—
Sang Zhi	39.82	—
Tai Zi Shen	39.83	—
Xi Xian Cao	39.85	—
Bai Xian Pi	40.42	—
Che Qian Zi	40.66	—
Bai Mao Gen	41.27	—
Huo Ma Ren	42.49	—
Ling Zhi	42.61	—
Tao Ren	42.84	—
Ku Shen	43.16	—
Ji Xue Teng	43.68	—
Gou Teng	44.67	—
Shen Qu	45.27	—
Wu Yao	45.93	—
Jiang Huang	46.71	—
Yu Jin	47.07	—
Mang Xiao	47.70	—
Dang Gui Wei	48.70	—
Tian Hua Fen	49.44	—
Sheng Jiang	49.45	—
Yi Mu Cao	49.84	—
Xin Yi	50.25	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hong Hua* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62664	62664	0.00	10.95
62663	62663	0.00	11.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Hong Jing Tian**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60031-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hong Jing Tian; Rhodiolae crenulatae radix

Special notes

When selecting the *Hong Jing Tian* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hong Jing Tian	2	0	2

Second-stage model

For differentiation of the substance/substance group *Hong Jing Tian* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hong Jing Tian*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Hong Jing Tian	G237H0906821	62305	40	from supplier
PhytoComm	Hong Jing Tian	G237H0906821	62306	40	from supplier
PhytoComm	Hong Jing Tian	G237HS429SK1	62639	40	from supplier
PhytoComm	Hong Jing Tian	G237HS429SK1	62640	40	from supplier

Validation samples

A total of 30 254 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 *Hong Jing Tian*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Hong Jing Tian*.
- 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
PhytoComm	Hong Jing Tian	G237H0906821	62305 [†]	20
PhytoComm	Hong Jing Tian	G237H0906821	62306 [†]	20
PhytoComm	Hong Jing Tian	G237HS429SK1	62639 [†]	20
PhytoComm	Hong Jing Tian	G237HS429SK1	62640 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 1 *Apo-Ident* customers from 2 batches from the substance/substance group *Hong Jing Tian*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Hong Jing Tian	G237H0906321	1
Phytocomm	Hong Jing Tian	G237H0906221	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hong Jing Tian* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hong Jing Tian* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	78	2	9837
Type C	0	0	2	855

The substance/substance group *Hong Jing Tian* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	97.5000 % (> 93.7500 %)
Type C	100.0000 % (> 98.8302 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hong Jing Tian* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Jin Yin Hua	4.62	—
Mu Dan Pi	8.11	—
Dan Shen	9.37	—
Chuan Xiong	9.37	—
Zi Hua Di Ding	10.49	—
Hou Po	10.88	—
Gua Lou	12.03	—
Gou Qi Zi	12.42	—
Pi Pa Ye	12.89	—
Yuan Zhi	13.24	—
Ren Dong Teng	14.07	—
Ma Huang	14.73	—
Fu Zi	14.76	—
Cang Zhu	14.87	—
Jiao Gu Lan	15.21	—
Shan Yao	15.35	—
Zhi Ke	15.38	—
Yin Yang Huo	15.97	—
Bai Shao Yao	16.12	—
Chai Hu	16.41	—
Qiang Huo	16.66	—
Ye Jiao Teng	16.74	—
Lian Qiao	17.42	—
Yan Hu Suo	17.84	—
Wu Wei Zi	17.94	—
Chen Pi	18.99	—
Shen Qu	19.04	—
Ji Li	19.26	—
Bai Zhu	19.28	—
Dan Dou Chi	19.46	—
Lian Zi	19.56	—
Qing Pi	19.60	—
Mao Dong Qing	19.75	—
Sang Ji Shend	21.06	—
Bai Xian Pi	21.26	—
Shan Yu Rou	21.28	—
Zhe Bei Mu	22.29	—
Chuang Mu Xiang	22.52	—
He Huan Pi	22.56	—
Tu Fu Ling	22.71	—
Di Gu Pi	22.92	—
Ji Xue Teng	23.01	—
Che Qian Zi	23.21	—
Nü Zhen Zi	23.50	—
Gan Cao	23.82	—
Gu Sui Bu	23.96	—
Yin Chen Hao	23.99	—
Yu Jin	24.71	—

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Substanz	Distance in main model	Distance in second-stage model
Long Yan Rou	24.99	—
Tao Ren	25.45	—
Ling Zhi	25.46	—
Gou Teng	25.52	—
San Qi	25.87	—
Yu Zhu	25.97	—
Huang Qin	26.19	—
Tai Zi Shen	26.24	—
Tian Hua Fen	26.25	—
Dang Gui Wei	26.55	—
Dang Gui	27.06	—
Huang Bai	27.07	—
Huang Lian	27.19	—
Dang Shen	27.21	—
Sang Bai Pi	27.49	—
Yi Mu Cao	27.80	—
Ge Gen	28.05	—
Huo Ma Ren	28.57	—
Du Zhong	28.58	—
Bai Zi Ren	28.60	—
Chi Shao (Yao)	28.85	—
Da Zao	29.20	—
Rou Gui	29.49	—
Huang Bo	30.27	—
Xu Duan	30.33	—
Ci Wu Jia	31.06	—
Suan Zao Ren	31.15	—
Sheng Jiang	31.55	—
Cang Er Zi	31.68	—
He Shou Wu	31.71	—
Fu Ling	31.97	—
Gui Zhi	31.99	—
Fang Feng	32.81	—
Sang Zhi	33.05	—
Wu Yao	33.96	—
Zhi Shi	34.09	—
Ma Huang Gen	34.36	—
Xian He Cao	34.62	—
Sha Ren	34.90	—
Wu Zhu Yu	35.39	—
Sang Ye	35.72	—
Hong Hua	36.15	—
Dan Zhu Ye	36.89	—
Ban Xia (Jiang)	37.56	—
Jie Geng	37.66	—
Jing Jie	38.29	—
Hu Zhang	39.13	—
Bai Mao Gen	39.75	—
Fo Shou	40.24	—
Pu Gong Ying	40.55	—
Zhu Ru	40.97	—
Yi Yi Ren	42.01	—
Mang Xiao	42.15	—
Bu Gu Zhi	43.61	—
Zhi Mu	43.94	—
Fu Shen	44.87	—
Ban Zhi Lian	46.09	—
Ju Hua	46.24	—
Xia Ku Cao	46.66	—

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Substanz	Distance in main model	Distance in second-stage model
Tian Men Dong	47.19	—
Chuan Lian Zi	47.31	—
Ku Shen	48.22	—
Huang Qi	49.14	—
Xiang Fu	49.94	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hong Jing Tian* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62306	62306	0.00	16.89
62639	62639	0.00	4.87
62640	62640	0.00	4.62
62305	62305	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 2.3-2020-05

Validated substance/substance group **Hou Po**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50289-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hou Po; Magnoliae officinalis cortex

Special notes

When selecting the *Hou Po* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hou Po	1	0	1

Second-stage model

For differentiation of the substance/substance group *Hou Po* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hou Po*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Hou Po	G154HS184SH1	62613	40	from supplier
PhytoComm	Hou Po	G154HS184SH1	62614	40	from supplier

Validation samples

A total of 30 254 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 *Hou Po*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Hou Po*.
- 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
PhytoComm	Hou Po	G154HS184SH1	62613 [†]	20
PhytoComm	Hou Po	G154HS184SH1	62614 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Hou Po*.
- 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
Phytocomm	Hou Po	G154H0917222	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hou Po* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hou Po* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	1	856

The substance/substance group *Hou Po* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8367 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hou Po* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chai Hu	6.56	—
Dan Dou Chi	7.38	—
Yu Jin	7.47	—
Yan Hu Suo	7.58	—
Ren Dong Teng	8.03	—
Shen Qu	8.13	—
Mao Dong Qing	8.13	—
Yin Yang Huo	8.55	—
Che Qian Zi	8.57	—
Ling Zhi	8.76	—
Shan Yao	8.88	—
Yuan Zhi	9.77	—
Pi Pa Ye	9.90	—
Bai Xian Pi	9.91	—
Qiang Huo	10.24	—
Chuan Xiong	10.51	—
Dan Shen	11.51	—
Ji Li	11.57	—
Tu Fu Ling	12.83	—
Ye Jiao Teng	14.39	—
Hong Jing Tian	14.82	—
Lian Zi	14.94	—
Qing Pi	15.62	—
Fu Zi	15.69	—
Lian Qiao	15.82	—
Du Zhong	16.43	—
Jin Yin Hua	16.46	—
Ma Huang	16.75	—
Jiao Gu Lan	16.83	—
Mu Dan Pi	16.84	—
Zi Hua Di Ding	18.00	—
Ji Xue Teng	18.20	—
Ma Huang Gen	18.69	—
Bai Shao Yao	19.10	—
Gua Lou	19.87	—
He Huan Pi	20.33	—
Gou Teng	21.20	—
Sheng Jiang	21.23	—
Tian Hua Fen	21.57	—
Fu Ling	21.60	—
Chen Pi	21.84	—
Huo Ma Ren	21.95	—
Rou Gui	22.19	—
Wu Wei Zi	22.32	—
Cang Zhu	23.56	—
Gui Zhi	23.64	—
Huang Lian	23.76	—
Bai Zi Ren	24.43	—
Di Gu Pi	25.23	—
Yi Yi Ren	25.34	—
Zhi Ke	25.98	—
Gou Qi Zi	26.53	—

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Substanz	Distance in main model	Distance in second-stage model
Huang Bai	26.88	—
Tai Zi Shen	27.00	—
Zhe Bei Mu	27.03	—
Tao Ren	27.15	—
Suan Zao Ren	28.15	—
Da Zao	30.48	—
Ban Xia (Jiang)	32.31	—
Yu Zhu	33.27	—
San Qi	33.88	—
Fu Xiao Mai	35.08	—
Dang Gui	35.16	—
Huang Qin	35.35	—
Ci Wu Jia	35.47	—
Shan Yu Rou	35.68	—
Zhu Ru	35.73	—
Dang Shen	37.02	—
Long Yan Rou	37.59	—
Sang Zhi	37.63	—
Fu Shen	37.63	—
Chuang Mu Xiang	37.97	—
Fo Shou	38.06	—
Dang Gui Wei	38.39	—
Pu Gong Ying	39.24	—
Chi Shao (Yao)	39.68	—
Mang Xiao	39.79	—
Bai Zhu	40.34	—
Jie Geng	40.45	—
Sang Ye	41.51	—
Cang Er Zi	41.75	—
Tian Men Dong	42.01	—
Gan Cao	44.08	—
Wang Bu Liu Xing	44.87	—
Chuan Lian Zi	45.31	—
Xi Xian Cao	45.60	—
Ban Zhi Lian	46.00	—
Jiang Huang	47.31	—
Zi Su Zi	47.73	—
Bai Mao Gen	48.58	—
Hong Hua	48.61	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hou Po* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62614	62614	0.00	6.56
62613	62613	0.00	7.38

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 2.3-2020-05

Validated substance/substance group **Hu Zhang**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60130-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hu Zhang; Polygoni cuspidati rhizoma et radix

Special notes

When selecting the *Hu Zhang* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hu Zhang	1	0	1

Second-stage model

For differentiation of the substance/substance group *Hu Zhang* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hu Zhang*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Hu Zhang	G197HS373SK1	62565	40	from supplier
PhytoComm	Hu Zhang	G197HS373SK1	62566	40	from supplier

Validation samples

A total of 30 254 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 *Hu Zhang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Hu Zhang*.
- 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
PhytoComm	Hu Zhang	G197HS373SK1	62565 [†]	20
PhytoComm	Hu Zhang	G197HS373SK1	62566 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Hu Zhang*.
- 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
Phytocomm	Hu Zhang	g197h0851321	1
Phytocomm	Hu Zhang	G197H0851321	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hu Zhang* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hu Zhang* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	2	855

The substance/substance group *Hu Zhang* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hu Zhang* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Han Lian Cao	11.60	—
Bai Hua She She Cao	15.67	—
Sang Ye	16.16	—
Huang Lian	21.44	—
Zhi Shi	25.48	—
Xia Ku Cao	25.91	—
Pu Gong Ying	25.94	—
Xi Xian Cao	26.02	—
Sha Ren	26.77	—
Xin Yi	27.77	—
Jiang Huang	28.33	—
Fu Zi	29.50	—
Yi Mu Cao	30.65	—
Shan Yao	31.75	—
Nü Zhen Zi	32.10	—
Sang Ji Shend	33.74	—
Tu Fu Ling	34.07	—
Huang Bo	34.46	—
Gui Zhi	34.73	—
Rou Cong Rong	36.59	—
He Huan Pi	36.88	—
Qiang Huo	37.32	—
Gu Sui Bu	39.62	—
Gou Teng	39.67	—
Dan Zhu Ye	39.96	—
Xu Duan	45.12	—
Wu Yao	45.55	—
Qing Pi	47.41	—
Wu Mei	49.03	—
Ma Huang	49.51	—
Ju Hua	49.68	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hu Zhang* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62566	62566	0.00	11.88
62565	62565	0.00	11.60

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 2.3-2020-05

Validated substance/substance group **Hua Shi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50308-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hua Shi; Talcum

Special notes

When selecting the *Hua Shi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hua Shi	2	0	1

Second-stage model

For differentiation of the substance/substance group *Hua Shi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hua Shi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Hua Shi	G238HS289RM1	62425	40	from supplier
PhytoComm	Hua Shi	G238HS289RM1	62426	40	from supplier
PhytoComm	Hua Shi	G238HS289SK1	62637	40	from supplier
PhytoComm	Hua Shi	G238HS289SK1	62638	40	from supplier

Validation samples

A total of 30 254 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 *Hua Shi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Hua Shi*.
- 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
PhytoComm	Hua Shi	G238HS289RM1	62425 [†]	20
PhytoComm	Hua Shi	G238HS289RM1	62426 [†]	20
PhytoComm	Hua Shi	G238HS289SK1	62637 [†]	20
PhytoComm	Hua Shi	G238HS289SK1	62638 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Hua Shi*.
- 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
Phytocomm	Hua Shi	g238h1332121	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hua Shi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hua Shi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	69	91	19 320
Type B	0	29	51	9837
Type C	0	0	1	856

The substance/substance group *Hua Shi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	43.1250 % (> 41.2500 %)
Type B	100.0000 % (> 99.9282 %)	36.2500 % (> 32.5000 %)
Type C	100.0000 % (> 98.8367 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hua Shi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Mang Xiao	480.52	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hua Shi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62426	62426	0.00	495.73
62637	62637	0.00	570.65
62638	62638	0.00	579.32
62425	62425	0.00	480.52

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Huang Bai**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60949-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Huang Bai; Phellodendri chinensis cortex

Special notes

When selecting the *Huang Bai* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Huang Bai	1	0	0

Second-stage model

For differentiation of the substance/substance group *Huang Bai* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Huang Bai*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Huang Bai	G188HS262SH1	62697	40	from supplier
PhytoComm	Huang Bai	G188HS262SH1	62698	40	from supplier

Validation samples

A total of 30 254 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 *Huang Bai*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Huang Bai*.
- 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
PhytoComm	Huang Bai	G188HS262SH1	62697 [†]	20
PhytoComm	Huang Bai	G188HS262SH1	62698 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Huang Bai*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Huang Bai* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Huang Bai* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

The substance/substance group *Huang Bai* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Huang Bai* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Qing Pi	7.14	—
Jiao Gu Lan	8.84	—
Zhi Ke	9.33	—
Dan Shen	10.27	—
Qiang Huo	11.91	—
Hong Jing Tian	13.92	—
Zi Hua Di Ding	14.17	—
Du Zhong	14.93	—
Chai Hu	15.84	—
Huang Lian	16.30	—
Shan Yao	16.47	—
Jin Yin Hua	17.05	—
Sang Ye	17.15	—
Hou Po	17.30	—
Yin Yang Huo	17.35	—
Wu Wei Zi	17.72	—
Yan Hu Suo	19.15	—
Mao Dong Qing	19.26	—
Ma Huang	20.23	—
Ye Jiao Teng	20.70	—
Mu Dan Pi	21.42	—
Pi Pa Ye	21.43	—
Yu Jin	21.44	—
Bai Xian Pi	21.96	—
Chuan Xiong	22.90	—
Bai Shao Yao	23.58	—
Ren Dong Teng	23.86	—
Shan Yu Rou	25.10	—
Dan Dou Chi	25.91	—
Hong Hua	26.08	—
Pu Gong Ying	26.63	—
Bai Zhu	27.07	—
Gui Zhi	27.07	—
Ji Xue Teng	28.09	—
Gua Lou	28.09	—
Tu Fu Ling	28.29	—
Ji Li	28.32	—
Fu Zi	28.34	—
Lian Zi	28.35	—
Lian Qiao	28.65	—
Di Gu Pi	28.71	—
Wu Mei	28.89	—
Gou Qi Zi	29.45	—
Cang Zhu	29.51	—
Cang Er Zi	30.08	—
Ling Zhi	30.41	—
Che Qian Zi	30.58	—
Xi Xian Cao	31.02	—
He Huan Pi	31.52	—
Huang Qin	33.16	—
Shen Qu	34.11	—
Yuan Zhi	35.55	—
Nü Zhen Zi	37.08	—
Tao Ren	37.19	—
Bai Mao Gen	37.54	—
Chi Shao (Yao)	38.41	—
Gan Cao	39.66	—
Suan Zao Ren	40.25	—
Dang Gui	40.41	—

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Substanz	Distance in main model	Distance in second-stage model
Rou Gui	41.03	—
Zhe Bei Mu	41.13	—
Jiang Huang	41.61	—
Gou Teng	41.70	—
Tian Hua Fen	42.42	—
Ban Zhi Lian	42.45	—
Wu Yao	42.59	—
Chuang Mu Xiang	42.78	—
Dang Shen	43.20	—
Chen Pi	43.33	—
Sheng Jiang	43.75	—
Tai Zi Shen	44.17	—
Bai Zi Ren	44.42	—
Mang Xiao	44.44	—
San Qi	44.78	—
Yu Zhu	45.98	—
Yi Mu Cao	46.06	—
Xin Yi	46.28	—
Huo Ma Ren	46.55	—
Niu Bang Zi	49.71	—
Ma Huang Gen	49.75	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Huang Bai* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62698	62698	0.00	7.14
62697	62697	0.00	8.84

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 2.3-2020-05

Validated substance/substance group **Huang Bo**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60057-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Huang Bo; Phellodendri cortex chinensis

Special notes

When selecting the *Huang Bo* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Huang Bo	1	0	3

Second-stage model

For differentiation of the substance/substance group *Huang Bo* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Huang Bo*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Huang Bo	G188H1203823	62593	40	from supplier
PhytoComm	Huang Bo	G188H1203823	62594	40	from supplier

Validation samples

A total of 30 254 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 *Huang Bo*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Huang Bo*.
- 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
PhytoComm	Huang Bo	G188H1203823	62593 [†]	20
PhytoComm	Huang Bo	G188H1203823	62594 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 5 *Apo-Ident* customers from 3 batches from the substance/substance group *Huang Bo*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Huang Bo	g188h1203123	1
Phytocomm	Huang Bo	h1203022	1
Phytocomm	Huang Bo	G188H1203321	3
PhytoComm	Huang Bo	G188H1203321	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Huang Bo* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Huang Bo* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	2	1	5	849

The substance/substance group *Huang Bo* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.7010 % (> 99.1139 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Huang Bo* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yi Mu Cao	14.98	—
Nü Zhen Zi	18.56	—
Dan Zhu Ye	28.93	—
Xu Duan	31.37	—
Qiang Huo	32.18	—
Rou Cong Rong	32.91	—
Wu Zhu Yu	33.00	—
Gou Teng	34.13	—
Han Lian Cao	39.48	—
Gui Zhi	41.39	—
Yin Chen Hao	42.13	—
Xian He Cao	42.32	—
Wu Yao	42.48	—
Bai Hua She She Cao	42.89	—
Jing Jie	43.32	—
Hu Zhang	43.33	—
Sha Ren	44.46	—
Huang Lian	44.48	—
Xin Yi	44.96	—
Pu Gong Ying	45.30	—
Gu Sui Bu	45.99	—
Zhi Shi	46.52	—
Shen Qu	46.61	—
Cang Er Zi	47.09	—
Fu Zi	47.53	—
Sang Ji Shend	48.33	—
Qing Hao	49.67	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Huang Bo* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62594	62594	0.00	14.98
62593	62593	0.00	15.11

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 2.3-2020-05

Validated substance/substance group **Huang Lian**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60219-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Huang Lian; Coptidis rhizoma

Special notes

When selecting the *Huang Lian* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Huang Lian	2	0	3

Second-stage model

For differentiation of the substance/substance group *Huang Lian* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Huang Lian*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Huang Lian	G079HS261RM1	62287	40	from supplier
PhytoComm	Huang Lian	G079HS261RM1	62288	40	from supplier
PhytoComm	Huang Lian	G079HS261SK1	62707	40	from supplier
PhytoComm	Huang Lian	G079HS261SK1	62708	40	from supplier

Validation samples

A total of 30 254 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 *Huang Lian*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Huang Lian*.
- 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
PhytoComm	Huang Lian	G079HS261RM1	62287 [†]	20
PhytoComm	Huang Lian	G079HS261RM1	62288 [†]	20
PhytoComm	Huang Lian	G079HS261SK1	62707 [†]	20
PhytoComm	Huang Lian	G079HS261SK1	62708 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 5 *Apo-Ident* customers from 4 batches from the substance/substance group *Huang Lian*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Huang Lian	G079H1205321	2
Phytocomm	Huang Lian	g079h1205321	1
Phytocomm	Huang Lian	G079H1205421	1
Phytocomm	Huang Lian	G079H1205521	2
PhytoComm	Huang Lian	G079H1205321	4
PhytoComm	Huang Lian	G079H1205521	2

- 845 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Huang Lian* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Huang Lian* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	12	845

The substance/substance group *Huang Lian* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8248 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Huang Lian* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sang Ye	13.52	—
Hu Zhang	13.80	—
Pu Gong Ying	14.09	—
Ma Huang	20.76	—
Shan Yao	21.73	—
Xin Yi	22.29	—
Han Lian Cao	22.95	—
Bai Hua She She Cao	24.42	—
Nü Zhen Zi	25.35	—
Zhi Ke	25.61	—
Huang Bai	26.95	—
Qiang Huo	27.79	—
Hou Po	28.00	—
Dan Shen	28.10	—
Tu Fu Ling	28.82	—
Qing Pi	29.00	—
Xi Xian Cao	29.14	—
Zhi Shi	29.63	—
Du Zhong	30.21	—
Yin Yang Huo	30.44	—
Gui Zhi	30.51	—
Wu Mei	30.53	—
Ye Jiao Teng	31.41	—
Jiao Gu Lan	31.86	—
Wu Wei Zi	32.01	—
Fu Zi	32.03	—
Yu Jin	32.26	—
Jiang Huang	33.36	—
Xia Ku Cao	34.29	—
Mao Dong Qing	34.31	—
Hong Jing Tian	34.73	—
Yi Mu Cao	35.23	—
Rou Cong Rong	35.42	—
Sha Ren	37.71	—
Zi Hua Di Ding	39.90	—
Jin Yin Hua	40.06	—
Bai Xian Pi	40.20	—
Pi Pa Ye	40.24	—
Chai Hu	41.27	—
Wu Yao	41.78	—
Hong Hua	42.05	—
Huang Qin	42.30	—
Dan Zhu Ye	42.90	—

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Substanz	Distance in main model	Distance in second-stage model
Huang Bo	42.98	—
Che Qian Zi	43.72	—
Gou Teng	44.28	—
Sang Ji Shend	44.68	—
Shan Yu Rou	44.99	—
Bai Shao Yao	45.15	—
Yan Hu Suo	45.18	—
Cang Er Zi	45.78	—
Chuan Xiong	46.04	—
Xu Duan	46.73	—
Bai Mao Gen	47.37	—
Bai Zhu	47.51	—
Gan Cao	48.22	—
Mang Xiao	48.41	—
Xiang Fu	48.49	—
He Huan Pi	48.65	—
Gu Sui Bu	48.91	—
Ren Dong Teng	49.11	—
Lian Zi	49.17	—
Lian Qiao	49.66	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Huang Lian* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62287	62287	0.00	13.52
62707	62707	0.00	13.97
62288	62288	0.00	13.69
62708	62708	0.00	13.80

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Huang Qi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60154-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Huang Qi; Astragali membranacei radix

Special notes

When selecting the *Huang Qi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Huang Qi	2	0	5

Second-stage model

For differentiation of the substance/substance group *Huang Qi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Huang Qi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Huang Qi	G040H1202822	62383	40	from supplier
PhytoComm	Huang Qi	G040H1202822	62384	40	from supplier
PhytoComm	Huang Qi	G040H1202823	62511	40	from supplier
PhytoComm	Huang Qi	G040H1202823	62512	40	from supplier

Validation samples

A total of 30 254 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 *Huang Qi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Huang Qi*.
- 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
PhytoComm	Huang Qi	G040H1202822	62383 [†]	20
PhytoComm	Huang Qi	G040H1202822	62384 [†]	20
PhytoComm	Huang Qi	G040H1202823	62511 [†]	20
PhytoComm	Huang Qi	G040H1202823	62512 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 10 spectra from 5 *Apo-Ident* customers from 6 batches from the substance/substance group *Huang Qi*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Huang Qi	g040h1202222	1
Phytocomm	Huang Qi	g040h1202321	2
Phytocomm	Huang Qi	G040H1202321	1
Phytocomm	Huang Qi	G040H1202423	2
Phytocomm	Huang Qi	G040H1202521	2
PhytoComm	Huang Qi	G040H1202321	1
PhytoComm	Huang Qi	G040H1202621	1

- 847 spectra from 13 *Apo-Ident* customers from a total of 513 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Huang Qi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Huang Qi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	14	4	6	833

The substance/substance group *Huang Qi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	98.8846 % (> 98.2971 %)	n/a (n/a)

[†]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*.

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Huang Qi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Zhu	11.95	—
Chi Shao (Yao)	13.07	—
Jie Geng	15.02	—
(Huai) Niu Xi	19.12	—
Di Gu Pi	19.88	—
Sang Zhi	20.49	—
Yuan Zhi	24.02	—
Bai Mao Gen	24.63	—
Qin Jiao	27.54	—
Mu Dan Pi	29.11	—
Tian Hua Fen	29.46	—
Gua Lou	30.13	—
Xiang Fu	30.38	—
Du Huo	31.57	—
Long Yan Rou	32.04	—
Chen Pi	33.10	—
Da Zao	34.37	—
Gan Cao	34.86	—
Zhi Ke	34.90	—
Mang Xiao	35.64	—
Dang Gui	35.66	—
Ban Zhi Lian	36.25	—
Tu Fu Ling	36.27	—
Shan Yu Rou	36.98	—
Mai Men Dong	38.03	—
Shan Yao	38.25	—
Bai Shao Yao	38.51	—
Qing Pi	38.67	—
Sheng Jiang	38.80	—
Ba Ji Tian	39.47	—
(Shi) Chang Pu	39.54	—
Lai Fu Zi	39.95	—
Tian Men Dong	40.08	—
Lian Zi	40.53	—
Sha Shen (Bei)	40.79	—
San Qi	40.84	—
Bai Xian Pi	41.96	—
Zhe Bei Mu	41.97	—
Gou Qi Zi	41.99	—
Ji Li	42.58	—
E Zhu	43.20	—

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Substanz	Distance in main model	Distance in second-stage model
Huang Qin	43.41	—
Chuan Xiong	43.72	—
Chuan Lian Zi	43.99	—
Fang Feng	44.36	—
Bai He	44.36	—
Rou Gui	45.01	—
Gou Teng	45.63	—
Ye Jiao Teng	45.87	—
Fu Zi	46.15	—
Lian Qiao	46.16	—
Chai Hu	46.27	—
Jin Yin Hua	46.37	—
Dan Shen	46.74	—
Ji Xue Teng	46.79	—
Ku Shen	46.98	—
Wu Yao	47.24	—
Fo Shou	47.43	—
Wu Wei Zi	48.49	—
Cang Er Zi	48.92	—
Huang Lian	49.09	—
Dang Gui Wei	49.09	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Huang Qi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62511	62511	0.00	11.95
62383	62383	0.00	13.54
62384	62384	0.00	13.07
62512	62512	0.00	12.22

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 2.3-2020-05

Validated substance/substance group **Huang Qin**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60012-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Huang Qin; Scutellariae baicalensis radix

Special notes

When selecting the *Huang Qin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Huang Qin	2	0	5

Second-stage model

For differentiation of the substance/substance group *Huang Qin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Huang Qin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Huang Qin	G225HS259RM1	62281	40	from supplier
PhytoComm	Huang Qin	G225HS259RM1	62282	40	from supplier
PhytoComm	Huang Qin	G225HS259SM1	62709	40	from supplier
PhytoComm	Huang Qin	G225HS259SM1	62710	40	from supplier

Validation samples

A total of 30 254 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 *Huang Qin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Huang Qin*.
- 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
PhytoComm	Huang Qin	G225HS259RM1	62281 [†]	20
PhytoComm	Huang Qin	G225HS259RM1	62282 [†]	20
PhytoComm	Huang Qin	G225HS259SM1	62709 [†]	20
PhytoComm	Huang Qin	G225HS259SM1	62710 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Huang Qin*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Herbasin	Huang Qin	g225h120442	1
Phytocomm	Huang Qin	G225H1204221	1
Phytocomm	Huang Qin	g225h1204121	1
Phytocomm	Huang Qin	G225H1204522	3
PhytoComm	Huang Qin	G225H1204221	1
PhytoComm	Huang Qin	G225H1204322	5

- 845 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Huang Qin* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Huang Qin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	12	845

The substance/substance group *Huang Qin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8248 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Huang Qin* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ma Huang	25.44	—
Dang Gui	26.37	—
Yu Zhu	27.22	—
Zhi Ke	29.26	—
Lian Qiao	29.50	—
Jiao Gu Lan	31.04	—
Ye Jiao Teng	31.75	—
Gou Qi Zi	32.21	—
Wu Wei Zi	32.59	—
Gan Cao	32.98	—
Tian Hua Fen	34.24	—
Hou Po	34.38	—
Fu Zi	34.54	—
Yan Hu Suo	35.28	—
Tai Zi Shen	35.65	—
Cang Zhu	36.75	—
Yin Yang Huo	37.20	—
Shan Yu Rou	37.46	—
Bai Shao Yao	37.82	—
Jin Yin Hua	37.87	—
Zi Hua Di Ding	39.12	—
Pi Pa Ye	39.43	—
Dang Gui Wei	41.18	—
He Huan Pi	41.34	—
Long Yan Rou	42.14	—
San Qi	42.63	—
Chuang Mu Xiang	42.79	—
Chi Shao (Yao)	43.39	—
Huang Lian	43.62	—
Hong Hua	44.31	—
Shan Yao	45.21	—
Chen Pi	45.50	—
Hong Jing Tian	45.51	—
Zhe Bei Mu	46.28	—
Dang Shen	46.42	—
Zhi Mu	47.38	—
Tao Ren	48.30	—
Chuan Xiong	48.31	—
Mu Dan Pi	49.08	—
Qiang Huo	49.32	—
Di Gu Pi	49.38	—
Ji Xue Teng	49.54	—
Rou Gui	49.62	—
Hua Shi	58.08	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Huang Qin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62710	62710	0.00	47.93
62282	62282	0.00	25.44
62709	62709	0.00	47.43
62281	62281	0.00	26.10

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Huo Ma Ren**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60234-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Huo Ma Ren; Cannabis semen

Special notes

When selecting the *Huo Ma Ren* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Huo Ma Ren	1	0	1

Second-stage model

For differentiation of the substance/substance group *Huo Ma Ren* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Huo Ma Ren*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Huo Ma Ren	G141HS061SP1	62711	40	from supplier
PhytoComm	Huo Ma Ren	G141HS061SP1	62712	40	from supplier

Validation samples

A total of 30 254 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 *Huo Ma Ren*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Huo Ma Ren*.
- 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
PhytoComm	Huo Ma Ren	G141HS061SP1	62711 [†]	20
PhytoComm	Huo Ma Ren	G141HS061SP1	62712 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 1 batches from the substance/substance group *Huo Ma Ren*.
- 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
Phytocomm	Huo Ma Ren	G141HS061	2

- 855 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Huo Ma Ren* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Huo Ma Ren* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	38	2	9877
Type C	0	0	2	855

The substance/substance group *Huo Ma Ren* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	95.0000 % (> 87.5000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Huo Ma Ren* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
He Huan Pi	5.59	—
Bai Shao Yao	6.88	—
Gou Teng	7.06	—
Shen Qu	7.91	—
Tao Ren	7.93	—
Gui Zhi	8.77	—
Ling Zhi	8.80	—
Sheng Jiang	9.07	—
Lian Zi	9.49	—
Ji Li	9.59	—
Tai Zi Shen	9.84	—
Ji Xue Teng	9.88	—
Rou Gui	9.90	—
Tian Hua Fen	10.13	—
Ci Wu Jia	10.57	—
Zhe Bei Mu	10.62	—
Ren Dong Teng	11.42	—
Bai Xian Pi	11.59	—
Ye Jiao Teng	11.59	—
Fu Ling	12.04	—
Bai Zi Ren	12.22	—
Yi Yi Ren	12.40	—
Ma Huang Gen	12.63	—
Di Gu Pi	13.52	—
Fu Xiao Mai	13.54	—
Ban Xia (Jiang)	14.16	—
Fo Shou	15.26	—
Chen Pi	15.43	—
Chuan Xiong	15.49	—
Yu Jin	15.72	—
Lian Qiao	16.42	—
Tu Fu Ling	16.72	—
Shan Yao	16.76	—
Pi Pa Ye	16.81	—
Dan Dou Chi	17.03	—
Zhu Ru	17.06	—
Gua Lou	17.28	—
Dan Shen	18.74	—
Yan Hu Suo	18.89	—
Fu Zi	19.20	—
Tian Men Dong	21.12	—
Chai Hu	21.28	—
Yin Yang Huo	21.78	—
Da Zao	21.94	—
Mao Dong Qing	21.97	—
Yuan Zhi	22.64	—
Hong Jing Tian	23.71	—
Jiao Gu Lan	23.89	—
Ma Huang	24.15	—
Fu Shen	25.38	—
Hou Po	25.50	—
Long Yan Rou	25.86	—

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Substanz	Distance in main model	Distance in second-stage model
Yu Zhu	26.46	—
Jin Yin Hua	26.53	—
Che Qian Zi	27.47	—
Dang Shen	28.13	—
Dang Gui Wei	28.31	—
Zhi Ke	28.73	—
Cang Zhu	28.93	—
San Qi	29.39	—
Qiang Huo	30.25	—
Wu Wei Zi	30.70	—
Dang Gui	33.14	—
Shan Yu Rou	34.79	—
Huang Qin	35.26	—
Huang Lian	37.35	—
Suan Zao Ren	38.64	—
Gou Qi Zi	38.79	—
Mang Xiao	39.36	—
Sang Zhi	39.77	—
Qing Pi	40.02	—
Du Zhong	40.33	—
Jie Geng	41.97	—
Mu Dan Pi	42.14	—
Zhi Mu	43.83	—
Bai Zhu	43.85	—
Chuan Lian Zi	46.86	—
Gan Cao	47.45	—
Zi Hua Di Ding	48.33	—
Chi Shao (Yao)	49.98	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Huo Ma Ren* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62711	62711	0.00	6.15
62712	62712	0.00	5.59

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 2.3-2020-05

Validated substance/substance group **Ji Li**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60110-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ji Li; Tribuli terrestris fructus

Special notes

When selecting the *Ji Li* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ji Li	3	0	1

Second-stage model

For differentiation of the substance/substance group *Ji Li* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ji Li*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ji Li	G240H1410821	62319	40	from supplier
PhytoComm	Ji Li	G240H1410821	62320	40	from supplier
PhytoComm	Ji Li	G240HS305SK1	62545	40	from supplier
PhytoComm	Ji Li	G240HS305SK1	62546	40	from supplier
PhytoComm	Ji Li	G240HS305SQ1	62721	40	from supplier
PhytoComm	Ji Li	G240HS305SQ1	62722	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Ji Li*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Ji Li*.
- 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
PhytoComm	Ji Li	G240H1410821	62319 [†]	20
PhytoComm	Ji Li	G240H1410821	62320 [†]	20
PhytoComm	Ji Li	G240HS305SK1	62545 [†]	20
PhytoComm	Ji Li	G240HS305SK1	62546 [†]	20
PhytoComm	Ji Li	G240HS305SQ1	62721 [†]	20
PhytoComm	Ji Li	G240HS305SQ1	62722 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Ji Li*.
- 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
PhytoComm	Ji Li	G240H1410421	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ji Li* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ji Li* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	19 240
Type B	2	118	2	9795
Type C	1	0	1	855

The substance/substance group *Ji Li* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.5000 %)
Type B	99.9684 % (> 99.9324 %)	98.3333 % (> 95.8333 %)
Type C	99.9225 % (> 99.3408 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ji Li* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tian Hua Fen	5.35	—
Lian Qiao	5.41	—
Bai Shao Yao	5.81	—
Shen Qu	6.66	—
Tai Zi Shen	7.12	—
Huo Ma Ren	7.13	—
Ling Zhi	7.86	—
Bai Zi Ren	7.93	—
He Huan Pi	7.93	—
Zhe Bei Mu	8.27	—
Lian Zi	8.61	—
Ren Dong Teng	8.90	—
Fu Zi	8.91	—
Pi Pa Ye	9.64	—
Gua Lou	9.70	—
Tao Ren	9.86	—
Ci Wu Jia	10.28	—
Shan Yao	10.46	—
Zhu Ru	10.47	—
Fu Ling	11.35	—
Gui Zhi	11.60	—
Sheng Jiang	12.05	—
Chuan Xiong	12.24	—
Di Gu Pi	12.25	—
Hou Po	12.28	—
Mao Dong Qing	12.81	—
Gou Teng	12.91	—
Yuan Zhi	13.13	—
Ye Jiao Teng	13.15	—
Jiang Huang	13.41	—
Fu Xiao Mai	13.57	—
Chai Hu	13.93	—
Ban Xia (Jiang)	13.96	—
Yu Jin	14.07	—
Chen Pi	14.08	—
Dan Shen	14.68	—
E Zhu	14.99	—
Yi Yi Ren	15.01	—
Che Qian Zi	15.24	—
Jiao Gu Lan	15.67	—
Rou Gui	15.90	—
(Bai) Dou Kou	15.91	—
Ji Xue Teng	16.02	—
Bai Xian Pi	16.27	—

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Substanz	Distance in main model	Distance in second-stage model
Cang Zhu	16.89	—
Tu Fu Ling	17.28	—
Ba Ji Tian	17.37	—
Sha Ren	17.45	—
Dan Dou Chi	17.60	—
Fo Shou	17.73	—
Da Zao	17.94	—
Jin Yin Hua	17.98	—
San Qi	18.07	—
Dang Gui Wei	18.37	—
Yan Hu Suo	18.89	—
Suan Zao Ren	19.60	—
Dang Shen	20.48	—
Ma Huang Gen	20.73	—
Tian Men Dong	20.84	—
Yin Yang Huo	20.86	—
Chuan Lian Zi	21.25	—
Yu Zhu	21.37	—
Wu Wei Zi	21.74	—
Mu Dan Pi	22.43	—
Sha Shen (Bei)	22.49	—
Qiang Huo	23.05	—
Du Huo	23.06	—
Wu Yao	23.50	—
Xian He Cao	23.69	—
Dang Gui	23.73	—
Zi Su Zi	24.07	—
Hong Jing Tian	24.15	—
Ma Huang	25.72	—
Qing Pi	26.10	—
Mang Xiao	26.12	—
Shan Yu Rou	26.19	—
Long Yan Rou	26.23	—
Gou Qi Zi	26.27	—
Zhi Ke	26.59	—
Xiang Fu	26.61	—
(Huai) Niu Xi	26.75	—
Cang Er Zi	27.20	—
Fang Feng	27.44	—
Niu Bang Zi	27.78	—
Sang Zhi	27.81	—
Huang Qin	28.29	—
Du Zhong	28.84	—
(Shi) Chang Pu	29.87	—
Fu Shen	31.12	—
Xie Bai	31.15	—
Lai Fu Zi	31.50	—
Zhi Mu	32.28	—
Bai Bian Dou	32.89	—
Chuang Mu Xiang	33.52	—
Huang Lian	33.76	—
Bai Zhu	35.25	—
Wang Bu Liu Xing	35.32	—
Zi Hua Di Ding	36.20	—
Bai Mao Gen	36.36	—
Zhu Ling	37.57	—
Gan Cao	37.64	—
Huang Qi	37.82	—
Jie Geng	37.93	—

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Substanz	Distance in main model	Distance in second-stage model
Xin Yi	40.28	—
Ju Hua	40.55	—
Sang Ji Shend	40.90	—
Sang Bai Pi	41.27	—
Chi Shao (Yao)	41.58	—
Qin Jiao	43.50	—
Gu Sui Bu	45.05	—
Huang Bai	45.27	—
He Shou Wu	45.69	—
Nü Zhen Zi	46.33	—
Ku Shen	47.08	—
Mai Ya	47.39	—
Xi Xian Cao	47.64	—
Pu Gong Ying	47.67	—
Huang Bo	47.68	—
Long Dan (Cao)	47.95	—
Yin Chen Hao	49.30	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ji Li* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62546	62546	0.00	6.32
62722	62722	0.00	6.10
62545	62545	0.00	5.41
62320	62320	0.00	13.46
62721	62721	0.00	5.35
62319	62319	0.00	13.41

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 2.3-2020-05

Validated substance/substance group **Ji Xue Teng**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60099-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ji Xue Teng; Spatholobi caulis

Special notes

When selecting the *Ji Xue Teng* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ji Xue Teng	2	0	2

Second-stage model

For differentiation of the substance/substance group *Ji Xue Teng* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ji Xue Teng*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ji Xue Teng	G159HS337SK1	62559	40	from supplier
PhytoComm	Ji Xue Teng	G159HS337SK1	62560	40	from supplier
PhytoComm	Ji Xue Teng	G159HS337SQ1	62723	40	from supplier
PhytoComm	Ji Xue Teng	G159HS337SQ1	62724	40	from supplier

Validation samples

A total of 30 254 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 *Ji Xue Teng*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Ji Xue Teng*.
- 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
PhytoComm	Ji Xue Teng	G159HS337SK1	62559 [†]	20
PhytoComm	Ji Xue Teng	G159HS337SK1	62560 [†]	20
PhytoComm	Ji Xue Teng	G159HS337SQ1	62723 [†]	20
PhytoComm	Ji Xue Teng	G159HS337SQ1	62724 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Ji Xue Teng*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ji Xue Teng	G159H2101423	3
Phytocomm	Ji Xue Teng	g159h2101122	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ji Xue Teng* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ji Xue Teng* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	3	158	2	19 317
Type B	1	80	0	9836
Type C	0	0	4	853

The substance/substance group *Ji Xue Teng* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9881 % (> 99.9697 %)	98.7500 % (> 96.8750 %)
Type B	99.9921 % (> 99.9562 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8269 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ji Xue Teng* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ye Jiao Teng	4.48	—
Rou Gui	6.19	—
Ma Huang Gen	6.36	—
Ren Dong Teng	8.24	—
Gou Teng	9.27	—
Fo Shou	10.98	—
Huo Ma Ren	11.11	—
Tai Zi Shen	11.24	—
Bai Shao Yao	11.25	—
Bai Xian Pi	11.91	—
Gui Zhi	13.87	—
He Huan Pi	14.14	—
Dan Dou Chi	14.78	—
Yi Yi Ren	14.82	—
Ling Zhi	15.15	—
Chen Pi	15.41	—
Sheng Jiang	15.94	—
Tu Fu Ling	16.14	—
Shen Qu	16.21	—
Tao Ren	16.75	—
Fu Ling	16.76	—
Fu Shen	16.81	—
Ban Xia (Jiang)	17.01	—
Lian Zi	17.08	—
Dan Shen	17.30	—
Ci Wu Jia	17.59	—
Ma Huang	19.46	—
Yu Jin	19.83	—
Yan Hu Suo	19.83	—
Yin Yang Huo	20.12	—
Zhe Bei Mu	20.19	—
Da Zao	20.63	—
Fu Xiao Mai	20.88	—
Di Gu Pi	21.18	—
Chuan Xiong	21.58	—
Tian Men Dong	21.69	—
Ji Li	21.90	—
Tian Hua Fen	22.24	—
Lian Qiao	23.48	—
Bai Zi Ren	24.39	—
Long Yan Rou	25.05	—
Pi Pa Ye	25.61	—
Hong Jing Tian	25.80	—
Gua Lou	25.87	—
Mao Dong Qing	25.96	—

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Substanz	Distance in main model	Distance in second-stage model
Jin Yin Hua	26.38	—
Yuan Zhi	26.68	—
Shan Yao	27.34	—
Zhu Ru	27.42	—
Chai Hu	27.61	—
Fu Zi	27.83	—
Jiao Gu Lan	28.34	—
Zhi Ke	29.65	—
Hou Po	29.70	—
Yu Zhu	30.18	—
Qiang Huo	31.49	—
Cang Zhu	31.65	—
Dang Shen	34.11	—
Huang Lian	34.63	—
Dang Gui Wei	35.09	—
Wu Wei Zi	35.52	—
Huang Qin	35.72	—
Che Qian Zi	37.41	—
Mang Xiao	37.98	—
Sang Zhi	39.14	—
Jie Geng	39.63	—
Mu Dan Pi	40.07	—
San Qi	40.08	—
Gou Qi Zi	40.23	—
Zi Hua Di Ding	40.36	—
Du Zhong	40.79	—
Shan Yu Rou	40.86	—
Dang Gui	42.88	—
Bai Zhu	43.55	—
Gan Cao	44.52	—
Qing Pi	46.77	—
Chi Shao (Yao)	46.82	—
Ban Zhi Lian	47.77	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ji Xue Teng* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62559	62559	0.00	4.61
62724	62724	0.00	6.19
62560	62560	0.00	4.48
62723	62723	0.00	6.46

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 2.3-2020-05

Validated substance/substance group **Jiang Huang**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60181-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Jiang Huang; Curcumae longae rhizoma

Special notes

When selecting the *Jiang Huang* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Jiang Huang	2	0	2

Second-stage model

For differentiation of the substance/substance group *Jiang Huang* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Jiang Huang*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Jiang Huang	G085H1716721	62373	40	from supplier
PhytoComm	Jiang Huang	G085H1716721	62374	40	from supplier
PhytoComm	Jiang Huang	G085H1716821	62519	40	from supplier
PhytoComm	Jiang Huang	G085H1716821	62520	40	from supplier

Validation samples

A total of 30 254 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 *Jiang Huang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Jiang Huang*.
- 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
PhytoComm	Jiang Huang	G085H1716721	62373 [†]	20
PhytoComm	Jiang Huang	G085H1716721	62374 [†]	20
PhytoComm	Jiang Huang	G085H1716821	62519 [†]	20
PhytoComm	Jiang Huang	G085H1716821	62520 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 2 batches from the substance/substance group *Jiang Huang*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Jiang Huang	G085H1716422	3
PhytoComm	Jiang Huang	G085H1716321	1
PhytoComm	Jiang Huang	G085H1716422	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Jiang Huang* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Jiang Huang* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	2	2	3	850

The substance/substance group *Jiang Huang* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.5349 % (> 98.9480 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Jiang Huang* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Gui Zhi	7.60	—
Sha Ren	13.94	—
Fu Zi	15.74	—
Ji Li	18.74	—
(Bai) Dou Kou	18.93	—
Pu Gong Ying	19.34	—
He Huan Pi	21.34	—
Shan Yao	22.85	—
Wu Yao	23.28	—
E Zhu	23.89	—
Yan Hu Suo	23.96	—
Xi Xian Cao	25.69	—
Qiang Huo	26.62	—
Chen Pi	26.76	—
Wang Bu Liu Xing	26.80	—
Xiang Fu	26.99	—
Wu Mei	27.21	—
Niu Bang Zi	27.70	—
Cang Er Zi	27.84	—
Sang Ye	27.95	—
Qing Pi	28.32	—
Yu Jin	28.51	—
Huang Lian	28.66	—
Xin Yi	29.97	—
Wu Wei Zi	31.04	—
Yi Mu Cao	31.12	—
Hu Zhang	31.41	—
Du Zhong	31.74	—
Zhi Ke	32.06	—
Han Lian Cao	32.54	—
Gua Lou	32.56	—
Tu Fu Ling	33.11	—
Mang Xiao	34.74	—
Zi Su Zi	35.53	—
Xian He Cao	35.70	—
Jiao Gu Lan	36.16	—
Xu Duan	36.27	—
(Shi) Chang Pu	36.83	—
Mao Dong Qing	36.97	—
Huang Bai	37.15	—
Huang Bo	37.29	—
Di Gu Pi	37.84	—
Nü Zhen Zi	38.27	—
Zi Hua Di Ding	38.48	—
Tian Hua Fen	38.88	—

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Substanz	Distance in main model	Distance in second-stage model
Gu Sui Bu	39.68	—
Ku Shen	40.01	—
Sang Ji Shend	40.36	—
Hong Jing Tian	40.39	—
Che Qian Zi	41.03	—
Sha Shen (Bei)	41.05	—
Sang Bai Pi	41.14	—
Ye Jiao Teng	41.59	—
Xie Bai	41.95	—
Bai Hua She She Cao	42.31	—
Hou Po	42.94	—
Mu Dan Pi	43.20	—
Dan Dou Chi	44.13	—
Fang Feng	44.29	—
Ma Huang	45.36	—
Jin Yin Hua	45.47	—
Dan Zhu Ye	45.59	—
Chuan Xiong	46.70	—
He Shou Wu	46.99	—
Du Huo	47.03	—
Ba Ji Tian	47.09	—
Xia Ku Cao	48.12	—
Yin Yang Huo	48.84	—
Bai Bian Dou	48.84	—
Sang Zhi	49.03	—
Dang Gui	49.11	—
Bai Mao Gen	49.36	—
Gan Cao	49.82	—
Lian Qiao	50.08	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Jiang Huang* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62374	62374	0.00	15.78
62520	62520	0.00	7.60
62373	62373	0.00	15.74
62519	62519	0.00	7.80

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical

variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Jiao Gu Lan**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60332-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Jiao Gu Lan; Gynostemma herba

Special notes

When selecting the *Jiao Gu Lan* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Jiao Gu Lan	2	0	1

Second-stage model

For differentiation of the substance/substance group *Jiao Gu Lan* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Jiao Gu Lan*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Jiao Gu Lan	G065HS424RR1	62441	40	from supplier
PhytoComm	Jiao Gu Lan	G065HS424RR1	62442	40	from supplier
PhytoComm	Jiao Gu Lan	G065HS424SG1	62665	40	from supplier
PhytoComm	Jiao Gu Lan	G065HS424SG1	62666	40	from supplier

Validation samples

A total of 30 254 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 *Jiao Gu Lan*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Jiao Gu Lan*.
- 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
PhytoComm	Jiao Gu Lan	G065HS424RR1	62441 [†]	20
PhytoComm	Jiao Gu Lan	G065HS424RR1	62442 [†]	20
PhytoComm	Jiao Gu Lan	G065HS424SG1	62665 [†]	20
PhytoComm	Jiao Gu Lan	G065HS424SG1	62666 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 batches from the substance/substance group *Jiao Gu Lan*.
- 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
Phytocomm	Jiao Gu Lan	G065FB1276421	3

- 854 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Jiao Gu Lan* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Jiao Gu Lan* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	3	854

The substance/substance group *Jiao Gu Lan* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8280 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Jiao Gu Lan* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Jin Yin Hua	7.62	—
Shan Yao	10.44	—
Suan Zao Ren	10.68	—
Cang Zhu	10.78	—
Lian Qiao	11.54	—
Bai Zhu	11.58	—
Hong Jing Tian	11.73	—
Dan Shen	12.19	—
Zi Hua Di Ding	12.25	—
Mu Dan Pi	12.86	—
Shan Yu Rou	13.15	—
Wu Wei Zi	13.28	—
Ji Li	13.60	—
Chai Hu	14.70	—
Qing Pi	14.97	—
Chuan Xiong	15.68	—
Mao Dong Qing	16.03	—
Gou Qi Zi	16.91	—
Zhi Ke	17.16	—
Bai Zi Ren	17.43	—
Gua Lou	18.00	—
Yuan Zhi	18.10	—
Pi Pa Ye	18.72	—
Chen Pi	18.83	—
Dang Shen	18.93	—
Hou Po	19.88	—
Ren Dong Teng	21.19	—
Qiang Huo	21.55	—
Lian Zi	21.62	—
Ling Zhi	22.05	—
Bai Shao Yao	22.30	—
Cang Er Zi	22.49	—
Yan Hu Suo	23.08	—
Huang Bai	23.70	—
Ye Jiao Teng	23.76	—
Fu Zi	23.91	—
Ma Huang	23.98	—
Hong Hua	24.14	—
Yin Yang Huo	24.19	—
Du Zhong	24.46	—
Dan Dou Chi	24.58	—
Shen Qu	25.57	—
Di Gu Pi	25.76	—
Chuang Mu Xiang	26.43	—
Yu Zhu	26.50	—
San Qi	26.54	—
Fu Ling	27.07	—
Zhe Bei Mu	27.33	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Xian Pi	27.62	—
Sang Ye	28.54	—
Huo Ma Ren	28.66	—
He Huan Pi	28.94	—
Tai Zi Shen	29.15	—
Ji Xue Teng	30.17	—
Sheng Jiang	30.77	—
Dang Gui	31.23	—
Chi Shao (Yao)	31.33	—
Huang Lian	31.52	—
Yu Jin	31.90	—
Che Qian Zi	31.96	—
Huang Qin	32.54	—
Gan Cao	32.97	—
Gou Teng	33.37	—
Tao Ren	34.94	—
Dang Gui Wei	35.58	—
Tian Hua Fen	36.33	—
Long Yan Rou	36.38	—
Gui Zhi	36.38	—
Wu Mei	38.03	—
Zhu Ru	38.37	—
Zhi Mu	38.63	—
Tu Fu Ling	38.80	—
Rou Gui	39.10	—
Sang Zhi	39.34	—
Bai Mao Gen	40.32	—
Ci Wu Jia	41.41	—
Yi Yi Ren	42.25	—
Pu Gong Ying	43.24	—
Da Zao	43.39	—
Mang Xiao	44.94	—
Xi Xian Cao	45.11	—
Niu Bang Zi	45.53	—
Ma Huang Gen	46.06	—
Jie Geng	47.61	—
Wu Yao	48.47	—
Ban Xia (Jiang)	48.67	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Jiao Gu Lan* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62665	62665	0.00	10.44
62442	62442	0.00	9.02
62441	62441	0.00	7.62
62666	62666	0.00	10.73

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 2.3-2020-05

Validated substance/substance group **Jie Geng**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60034-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Jie Geng; Platycodi grandiflori radix

Special notes

When selecting the *Jie Geng* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Jie Geng	2	0	2

Second-stage model

For differentiation of the substance/substance group *Jie Geng* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Jie Geng*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Jie Geng	G193H1015721	62247	40	from supplier
PhytoComm	Jie Geng	G193H1015721	62248	40	from supplier
PhytoComm	Jie Geng	G193H1015821	62365	40	from supplier
PhytoComm	Jie Geng	G193H1015821	62366	40	from supplier

Validation samples

A total of 30 254 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 *Jie Geng*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Jie Geng*.
- 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
PhytoComm	Jie Geng	G193H1015721	62247 [†]	20
PhytoComm	Jie Geng	G193H1015721	62248 [†]	20
PhytoComm	Jie Geng	G193H1015821	62365 [†]	20
PhytoComm	Jie Geng	G193H1015821	62366 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 2 batches from the substance/substance group *Jie Geng*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Jie Geng	g193h1015221	1
Phytocomm	Jie Geng	G193H101521	4

- 852 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Jie Geng* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Jie Geng* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	156	4	19 320
Type B	4	72	8	9833
Type C	3	1	4	849

The substance/substance group *Jie Geng* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	97.5000 % (> 95.6250 %)
Type B	99.9789 % (> 99.9430 %)	90.0000 % (> 86.2500 %)
Type C	99.3282 % (> 98.7413 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Jie Geng* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Zhu	3.79	—
Di Gu Pi	9.44	—
Sang Zhi	11.37	—
Huang Qi	16.28	—
Tian Hua Fen	19.33	—
Bai Mao Gen	21.00	—
Chi Shao (Yao)	23.52	—
Du Huo	23.69	—
Sheng Jiang	23.94	—
Gua Lou	25.56	—
Lai Fu Zi	26.11	—
Qing Pi	26.24	—
Qin Jiao	26.38	—
Chuan Lian Zi	27.43	—
Tu Fu Ling	28.06	—
San Qi	28.09	—
Yuan Zhi	28.44	—
Shan Yao	28.48	—
Mu Dan Pi	28.51	—
Xiang Fu	28.55	—
(Huai) Niu Xi	28.80	—
Bai Xian Pi	28.96	—
Long Yan Rou	29.61	—
Lian Zi	29.84	—
Mai Men Dong	29.87	—
Ji Li	30.03	—
Bai He	30.98	—
Ban Zhi Lian	31.54	—
Dang Gui	31.81	—
Tian Men Dong	32.11	—
Bai Shao Yao	32.41	—
Mang Xiao	32.47	—
E Zhu	33.05	—
Chai Hu	33.45	—
Rou Gui	33.53	—
(Shi) Chang Pu	34.59	—
Ba Ji Tian	35.25	—
Ye Jiao Teng	35.90	—
Chen Pi	36.14	—
Zhe Bei Mu	36.29	—
Da Zao	36.62	—
Cang Er Zi	36.74	—
Fu Ling	36.82	—
Sha Shen (Bei)	38.27	—
Zhi Ke	38.38	—

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Substanz	Distance in main model	Distance in second-stage model
Gui Zhi	38.55	—
Fo Shou	38.71	—
Jin Yin Hua	38.87	—
Zi Su Zi	39.11	—
Gou Teng	39.15	—
Chuan Xiong	39.24	—
Xie Bai	40.34	—
Fu Zi	40.74	—
Dang Gui Wei	40.78	—
Ku Shen	40.89	—
Mai Ya	41.15	—
Yi Yi Ren	41.25	—
Shan Yu Rou	41.28	—
Shen Qu	41.96	—
Fang Feng	41.99	—
Wu Wei Zi	42.22	—
Ren Dong Teng	42.38	—
Qiang Huo	43.07	—
Bai Bian Dou	43.12	—
Yu Jin	43.21	—
Ji Xue Teng	43.36	—
Dan Dou Chi	43.81	—
He Huan Pi	43.85	—
Ma Huang Gen	43.96	—
Niu Bang Zi	43.97	—
Gou Qi Zi	44.30	—
Gan Cao	45.30	—
Huang Lian	45.48	—
Dan Shen	45.76	—
Tao Ren	46.30	—
Dang Shen	46.48	—
Wu Yao	46.62	—
Huang Qin	47.02	—
Yin Yang Huo	47.85	—
Jiang Huang	47.94	—
Mao Dong Qing	47.94	—
Zhu Ru	48.35	—
Lian Qiao	48.59	—
Pu Gong Ying	49.10	—
Cang Zhu	49.46	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Jie Geng* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62247	62247	0.00	3.79
62248	62248	0.00	4.62
62366	62366	0.00	9.44
62365	62365	0.00	8.70

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 2.3-2020-05

Validated substance/substance group **Jin Qian Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50293-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Jin Qian Cao; Lysimachiae herba

Special notes

When selecting the *Jin Qian Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Jin Qian Cao	1	0	1

Second-stage model

For differentiation of the substance/substance group *Jin Qian Cao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Jin Qian Cao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Jin Qian Cao	G151H0847821	62465	40	from supplier
PhytoComm	Jin Qian Cao	G151H0847821	62466	40	from supplier

Validation samples

A total of 30 254 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 *Jin Qian Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Jin Qian Cao*.
- 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
PhytoComm	Jin Qian Cao	G151H0847821	62465 [†]	20
PhytoComm	Jin Qian Cao	G151H0847821	62466 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Jin Qian Cao*.
- 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
Phytocomm	Jin Qian Cao	g151h0847122	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Jin Qian Cao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Jin Qian Cao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	1	0	1	855

The substance/substance group *Jin Qian Cao* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.8837 % (> 99.3020 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Jin Qian Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pu Gong Ying	18.29	—
Jing Jie	20.01	—
Wu Jia Pi	22.78	—
Sha Ren	23.72	—
Du Zhong	23.90	—
Dan Zhu Ye	27.64	—
Sang Ji Shend	28.35	—
Gou Teng	28.60	—
Yin Chen Hao	31.90	—
Xuan Shen	32.38	—
Ge Gen	33.29	—
Hong Jing Tian	34.16	—
Yu Xing Cao	34.18	—
Qing Hao	35.08	—
Nü Zhen Zi	35.53	—
Xian He Cao	35.79	—
Sang Bai Pi	37.39	—
Zhi Shi	40.56	—
Qiang Huo	46.08	—
He Shou Wu	46.28	—
Gu Sui Bu	48.42	—
Hua Shi	49.08	—
Huang Bo	50.09	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Jin Qian Cao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62466	62466	0.00	19.14
62465	62465	0.00	18.29

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 2.3-2020-05

Validated substance/substance group **Jin Yin Hua**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60350-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Jin Yin Hua; Lonicerae japonicae flos

Special notes

When selecting the *Jin Yin Hua* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Jin Yin Hua	1	0	0

Second-stage model

For differentiation of the substance/substance group *Jin Yin Hua* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Jin Yin Hua*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Jin Yin Hua	G145HS311SK1	62577	40	from supplier
PhytoComm	Jin Yin Hua	G145HS311SK1	62578	40	from supplier

Validation samples

A total of 30 254 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 *Jin Yin Hua*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Jin Yin Hua*.
- 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
PhytoComm	Jin Yin Hua	G145HS311SK1	62577 [†]	20
PhytoComm	Jin Yin Hua	G145HS311SK1	62578 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Jin Yin Hua*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Jin Yin Hua* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Jin Yin Hua* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	2	40	0	9875
Type C	0	0	0	857

The substance/substance group *Jin Yin Hua* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	99.9842 % (> 99.9484 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Jin Yin Hua* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Jiao Gu Lan	9.37	—
Chuan Xiong	10.39	—
Mu Dan Pi	11.32	—
Fu Zi	11.60	—
Pi Pa Ye	11.60	—
Shan Yu Rou	11.65	—
Lian Qiao	12.08	—
Yan Hu Suo	12.28	—
Hou Po	12.29	—
Gua Lou	12.30	—
Cang Zhu	12.42	—
Gou Qi Zi	13.49	—
Wu Wei Zi	13.74	—
Shan Yao	13.76	—
Ren Dong Teng	14.30	—
Zhi Ke	15.13	—
Yuan Zhi	16.83	—
Ji Li	17.16	—
Qing Pi	17.40	—
Hong Jing Tian	17.73	—
Bai Shao Yao	17.89	—
Dan Shen	18.06	—
Ma Huang	18.10	—
Zi Hua Di Ding	18.15	—
Chen Pi	18.17	—
Chai Hu	18.20	—
Bai Zhu	18.24	—
San Qi	18.30	—
Zhe Bei Mu	19.39	—
Dang Gui	19.52	—
Bai Zi Ren	20.13	—
Dang Shen	20.56	—
Ye Jiao Teng	20.89	—
Chuang Mu Xiang	20.96	—
Suan Zao Ren	21.06	—
Tai Zi Shen	21.44	—
He Huan Pi	21.77	—
Yin Yang Huo	22.01	—
Yu Zhu	22.18	—
Qiang Huo	22.45	—
Lian Zi	22.65	—
Mao Dong Qing	22.71	—
Ji Xue Teng	22.93	—
Huo Ma Ren	23.86	—
Tian Hua Fen	24.05	—
Shen Qu	24.57	—
Gan Cao	25.21	—
Dan Dou Chi	25.86	—
Huang Qin	26.00	—
Tao Ren	26.13	—
Di Gu Pi	26.54	—
Che Qian Zi	26.72	—
Bai Xian Pi	26.95	—
Tu Fu Ling	27.02	—
Dang Gui Wei	27.34	—
Gou Teng	29.34	—
Ling Zhi	29.43	—
Yu Jin	30.00	—
Du Zhong	30.12	—

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Substanz	Distance in main model	Distance in second-stage model
Fu Ling	30.30	—
Huang Lian	30.39	—
Sheng Jiang	31.07	—
Hong Hua	31.59	—
Sang Ye	31.94	—
Chi Shao (Yao)	32.12	—
Huang Bai	32.70	—
Cang Er Zi	32.75	—
Ci Wu Jia	32.98	—
Long Yan Rou	33.53	—
Gui Zhi	34.86	—
Zhi Mu	35.02	—
Ban Xia (Jiang)	35.99	—
Yi Yi Ren	36.08	—
Da Zao	36.37	—
Rou Gui	36.81	—
Sang Zhi	37.53	—
Zhu Ru	37.70	—
Bai Mao Gen	44.18	—
Ma Huang Gen	44.22	—
Mang Xiao	44.68	—
Jie Geng	45.96	—
Fu Xiao Mai	46.16	—
Fo Shou	48.17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Jin Yin Hua* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62577	62577	0.00	9.38
62578	62578	0.00	9.37

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 2.3-2020-05

Validated substance/substance group **Jing Jie**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60088-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Jing Jie; Schizonepetae tenuifoliae herba

Special notes

When selecting the *Jing Jie* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Jing Jie	2	0	1

Second-stage model

For differentiation of the substance/substance group *Jing Jie* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Jing Jie*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Jing Jie	G221H1038822	62497	40	from supplier
PhytoComm	Jing Jie	G221H1038822	62498	40	from supplier
PhytoComm	Jing Jie	G221H1038823	62751	40	from supplier
PhytoComm	Jing Jie	G221H1038823	62752	40	from supplier

Validation samples

A total of 30 254 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 *Jing Jie*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Jing Jie*.
- 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
PhytoComm	Jing Jie	G221H1038822	62497 [†]	20
PhytoComm	Jing Jie	G221H1038822	62498 [†]	20
PhytoComm	Jing Jie	G221H1038823	62751 [†]	20
PhytoComm	Jing Jie	G221H1038823	62752 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Jing Jie*.
- 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
Phytocomm	Jing Jie	g221h1038221	1
Phytocomm	Jing Jie	G221H1038221	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Jing Jie* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Jing Jie* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	2	855

The substance/substance group *Jing Jie* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8302 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Jing Jie* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Du Zhong	7.59	—
Dan Zhu Ye	7.97	—
Sang Bai Pi	14.50	—
Sha Ren	15.55	—
Sang Ji Shend	17.72	—
He Shou Wu	18.24	—
Wu Jia Pi	18.91	—
Jin Qian Cao	19.38	—
Nü Zhen Zi	22.97	—
Xian He Cao	23.07	—
Yin Chen Hao	24.13	—
Bu Gu Zhi	26.11	—
Gu Sui Bu	26.96	—
Pu Gong Ying	28.59	—
Ge Gen	29.72	—
Yu Xing Cao	29.94	—
Gou Teng	31.85	—
Xuan Shen	35.43	—
Wu Zhu Yu	35.80	—
He Huan Pi	35.83	—
Hong Jing Tian	38.63	—
Zhi Shi	39.09	—
Qing Hao	39.10	—
Qiang Huo	40.19	—
Yi Mu Cao	41.60	—
Yu Jin	41.97	—
Huang Bo	42.48	—
Sang Ye	42.69	—
Fang Feng	47.77	—
Hua Shi	49.03	—
Gui Zhi	49.10	—
Chen Pi	49.82	—
Hu Zhang	49.89	—
Fu Zi	50.31	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Jing Jie* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62497	62497	0.00	7.59
62752	62752	0.00	7.97
62498	62498	0.00	7.91
62751	62751	0.00	8.13

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 2.3-2020-05

Validated substance/substance group **Ju Hua**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002256-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ju Hua; Chrysanthemi flos

Special notes

When selecting the *Ju Hua* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ju Hua	1	0	2

Second-stage model

For differentiation of the substance/substance group *Ju Hua* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ju Hua*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ju Hua	G064H1231822	62775	40	from supplier
PhytoComm	Ju Hua	G064H1231822	62776	40	from supplier

Validation samples

A total of 30 254 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 *Ju Hua*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ju Hua*.
- 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
PhytoComm	Ju Hua	G064H1231822	62775 [†]	20
PhytoComm	Ju Hua	G064H1231822	62776 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 4 *Apo-Ident* customers from 2 batches from the substance/substance group *Ju Hua*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ju Hua	G064H1231421	2
PhytoComm	Ju Hua	G064H1231521	1
PhytoComm	Ju Hua	G064H1231421	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ju Hua* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ju Hua* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	2	0	4	851

The substance/substance group *Ju Hua* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.8560 % (> 99.2695 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ju Hua* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fang Feng	16.88	—
Du Huo	19.24	—
(Shi) Chang Pu	20.25	—
Wu Yao	22.13	—
Qing Pi	23.64	—
Xiang Fu	24.56	—
Dang Gui	24.81	—
Chen Pi	25.43	—
Bai Mao Gen	25.83	—
Gua Lou	25.94	—
Gu Sui Bu	27.02	—
Qiang Huo	28.23	—
He Huan Pi	28.79	—
Huang Qi	28.84	—
Gui Zhi	29.24	—
Xie Bai	29.91	—
He Shou Wu	30.26	—
Mu Dan Pi	30.62	—
Sha Ren	31.31	—
Chi Shao (Yao)	32.51	—
Xu Duan	32.66	—
Wu Zhu Yu	33.16	—
Hong Jing Tian	33.55	—
Ku Shen	34.61	—
Huang Bo	35.38	—
Mang Xiao	37.68	—
Xian He Cao	37.83	—
Yi Mu Cao	37.96	—
Ji Li	38.22	—
Shan Yao	38.54	—
Sang Zhi	38.95	—
Jiang Huang	38.99	—
Yin Chen Hao	39.43	—
Cang Er Zi	39.55	—
Sang Ji Shend	39.90	—
Yu Jin	40.17	—
Ge Gen	40.64	—
(Huai) Niu Xi	40.80	—
Tian Hua Fen	41.00	—
Zhi Ke	42.71	—
Fu Zi	42.75	—
Di Gu Pi	43.24	—
Pu Gong Ying	43.27	—
Yuan Zhi	43.65	—
Ba Ji Tian	43.69	—
E Zhu	43.76	—
Nü Zhen Zi	43.99	—
Niu Bang Zi	44.88	—
Wu Wei Zi	44.91	—
Xin Yi	45.16	—
Gan Cao	46.14	—
(Bai) Dou Kou	46.29	—

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Substanz	Distance in main model	Distance in second-stage model
Sang Bai Pi	46.98	—
Jie Geng	47.24	—
Zhi Shi	47.64	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ju Hua* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62775	62775	0.00	16.88
62776	62776	0.00	17.52

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Jue Ming Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002262-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Jue Ming Zi; Cassiae torae semen

Special notes

When selecting the *Jue Ming Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Jue Ming Zi	1	0	1

Second-stage model

For differentiation of the substance/substance group *Jue Ming Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Jue Ming Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Jue Ming Zi	G059H1097921	62773	40	from supplier

Validation samples

A total of 30 254 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 *Jue Ming Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 440 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 79 spectra of 2 reference samples from the substance/substance group *Jue Ming Zi*.
- 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
PhytoComm	Jue Ming Zi	G059H1097921	62773 [†]	20
PhytoComm	Jue Ming Zi	G059H1097921	62774	59

- 9838 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 1 batches from the substance/substance group *Jue Ming Zi*.
- 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
Phytocomm	Jue Ming Zi	G059H1097221	1
PhytoComm	Jue Ming Zi	G059H1097221	3

- 853 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Jue Ming Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Jue Ming Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	19 440
Type B	0	79	0	9838
Type C	0	0	4	853

The substance/substance group *Jue Ming Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9636 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.4051 %)
Type C	100.0000 % (> 98.8269 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Jue Ming Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Shu Di (Huang)	14.08	—
Ai Ye	21.48	—
(Sheng) Di Huang	26.19	—
Yu Xing Cao	30.14	—
Guang Huo Xiang	31.93	—
Hua Shi	43.00	—
Pu Gong Ying	45.27	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Jue Ming Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62773	62773	0.00	14.08

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 2.3-2020-05

Validated substance/substance group **Ku Shen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60112-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ku Shen; Sophorae flavescentis radix

Special notes

When selecting the *Ku Shen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ku Shen	1	0	2

Second-stage model

For differentiation of the substance/substance group *Ku Shen* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ku Shen*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ku Shen	G233H0908822	62499	40	from supplier
PhytoComm	Ku Shen	G233H0908822	62500	40	from supplier

Validation samples

A total of 30 254 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 *Ku Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ku Shen*.
- 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
PhytoComm	Ku Shen	G233H0908822	62499 [†]	20
PhytoComm	Ku Shen	G233H0908822	62500 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Ku Shen*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ku Shen	G233H0908121	1
Phytocomm	Ku Shen	h0908121	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ku Shen* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ku Shen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	1	0	2	854

The substance/substance group *Ku Shen* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.8450 % (> 99.2600 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ku Shen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Niu Bang Zi	17.56	—
Cang Er Zi	20.21	—
Yi Mu Cao	21.87	—
Xiang Fu	24.23	—
(Huai) Niu Xi	24.25	—
Shan Yao	26.07	—
Gua Lou	26.76	—
Zhi Zi	27.99	—
Qing Pi	28.05	—
Lian Qiao	28.67	—
Gan Cao	29.36	—
Di Gu Pi	29.68	—
Dong Gua Zi	31.29	—
Tian Hua Fen	31.95	—
Shen Qu	32.06	—
Jiang Huang	32.34	—
Huang Bo	32.67	—
Sang Zhi	33.12	—
Wu Wei Zi	33.80	—
Gui Zhi	34.30	—
Nü Zhen Zi	34.42	—
Yuan Zhi	35.13	—
Huang Qi	35.65	—
Zhi Ke	36.00	—
Jin Yin Hua	36.75	—
Wu Mei	37.13	—
Wu Yao	37.17	—
Chi Shao (Yao)	37.41	—
Qiang Huo	38.46	—
(Bai) Dou Kou	39.16	—
Xie Bai	39.80	—
Shan Yu Rou	40.09	—
Xu Duan	40.09	—
Mu Dan Pi	40.52	—
Bai Mao Gen	41.13	—
Mang Xiao	41.16	—
(Shi) Chang Pu	41.29	—
Pu Gong Ying	41.41	—
Fu Zi	42.10	—
Jie Geng	43.33	—
Chuan Xiong	43.82	—
Zi Su Zi	45.37	—
Sha Ren	45.81	—
Huang Bai	48.17	—
Du Huo	48.38	—
Suan Zao Ren	49.03	—
Hou Po	49.52	—
Yan Hu Suo	49.57	—
Xi Xian Cao	49.84	—
Jiao Gu Lan	50.02	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ku Shen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62499	62499	0.00	18.49
62500	62500	0.00	17.56

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 2.3-2020-05

Validated substance/substance group **Lai Fu Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60067-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lai Fu Zi; Raphani sativi semen

Special notes

When selecting the *Lai Fu Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Lai Fu Zi	1	0	2

Second-stage model

For differentiation of the substance/substance group *Lai Fu Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lai Fu Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Lai Fu Zi	G209H1220821	62491	40	from supplier
PhytoComm	Lai Fu Zi	G209H1220821	62492	40	from supplier

Validation samples

A total of 30 254 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 *Lai Fu Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Lai Fu Zi*.
- 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
PhytoComm	Lai Fu Zi	G209H1220821	62491 [†]	20
PhytoComm	Lai Fu Zi	G209H1220821	62492 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 3 batches from the substance/substance group *Lai Fu Zi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Herbasin	Lai Fu Zi	g209h1220321	1
Phytocomm	Lai Fu Zi	G209H1220221	1
Phytocomm	Lai Fu Zi	G209H1220321	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lai Fu Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lai Fu Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	3	854

The substance/substance group *Lai Fu Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8280 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lai Fu Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
San Qi	19.29	—
Sheng Jiang	20.82	—
Jie Geng	20.99	—
Di Gu Pi	23.43	—
Bai Bian Dou	25.38	—
Bai Zhu	25.75	—
Bai He	26.76	—
Tian Hua Fen	26.77	—
Chuan Lian Zi	27.05	—
Mang Xiao	29.10	—
Qing Pi	29.71	—
Sang Zhi	30.28	—
Shan Yao	32.68	—
Mai Men Dong	34.02	—
Cang Er Zi	34.52	—
Zi Su Zi	34.92	—
E Zhu	35.31	—
Bai Xian Pi	38.37	—
Mai Ya	38.42	—
Xie Bai	38.86	—
Ji Li	38.89	—
Du Huo	38.91	—
Mu Dan Pi	40.47	—
Qiang Huo	41.18	—
Lian Zi	41.23	—
Fu Ling	41.82	—
Tu Fu Ling	41.85	—
Huang Qi	41.96	—
Jiang Huang	42.15	—
Dang Gui	42.53	—
Ba Ji Tian	43.57	—
Gui Zhi	43.86	—
Rou Gui	44.03	—
Yi Yi Ren	44.79	—
Tian Men Dong	45.66	—
Da Zao	45.85	—
Chai Hu	46.18	—
Gua Lou	46.81	—
Qin Jiao	47.01	—
Ku Shen	47.39	—
Yan Hu Suo	47.43	—
Bai Shao Yao	47.87	—
Long Dan (Cao)	48.83	—
Ren Dong Teng	48.94	—
Fang Feng	49.05	—
Yuan Zhi	49.32	—
Ye Jiao Teng	49.91	—
Wu Wei Zi	49.99	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lai Fu Zi* is separated from critical neighbours in a second-stage model, all

the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62491	62491	0.00	19.74
62492	62492	0.00	19.29

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 2.3-2020-05

Validated substance/substance group **Lian Qiao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60146-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lian Qiao; Forsythiae fructus

Special notes

When selecting the *Lian Qiao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Lian Qiao	2	0	3

Second-stage model

For differentiation of the substance/substance group *Lian Qiao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lian Qiao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Lian Qiao	G105H1132821	62337	40	from supplier
PhytoComm	Lian Qiao	G105H1132821	62338	40	from supplier
PhytoComm	Lian Qiao	G105HS252RW1	62685	40	from supplier
PhytoComm	Lian Qiao	G105HS252RW1	62686	40	from supplier

Validation samples

A total of 30 254 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 *Lian Qiao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Lian Qiao*.
- 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
PhytoComm	Lian Qiao	G105H1132821	62337 [†]	20
PhytoComm	Lian Qiao	G105H1132821	62338 [†]	20
PhytoComm	Lian Qiao	G105HS252RW1	62685 [†]	20
PhytoComm	Lian Qiao	G105HS252RW1	62686 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Lian Qiao*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Lian Qiao	G105H1132221	1
Phytocomm	Lian Qiao	G105H1132521	1
PhytoComm	Lian Qiao	G105H1132321	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lian Qiao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lian Qiao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	1	80	0	9836
Type C	0	0	3	854

The substance/substance group *Lian Qiao* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	99.9947 % (> 99.9588 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8280 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lian Qiao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ji Li	5.43	—
Yuan Zhi	6.04	—
Shan Yao	6.70	—
Bai Zi Ren	9.09	—
Lian Zi	10.48	—
Suan Zao Ren	11.02	—
Pi Pa Ye	11.18	—
Jiao Gu Lan	11.31	—
Chuan Xiong	12.08	—
Shen Qu	12.31	—
Ling Zhi	12.66	—
Cang Zhu	13.18	—
Fu Zi	13.33	—
Mao Dong Qing	13.44	—
Hou Po	13.63	—
San Qi	15.02	—
Jin Yin Hua	15.19	—
Ren Dong Teng	15.78	—
Huo Ma Ren	15.89	—
Fu Ling	15.98	—
Gua Lou	16.52	—
Dan Shen	16.62	—
Bai Shao Yao	16.86	—
Chen Pi	17.20	—
Chai Hu	17.58	—
Niu Bang Zi	18.08	—
Wu Wei Zi	18.59	—
Zhe Bei Mu	18.61	—
Tai Zi Shen	18.62	—
Sheng Jiang	19.03	—
Tu Fu Ling	19.47	—
Mu Dan Pi	19.76	—
Dang Shen	20.29	—
He Huan Pi	20.61	—
Tian Hua Fen	20.64	—
Shan Yu Rou	20.68	—
Yu Jin	20.73	—
Dan Dou Chi	21.26	—
Yu Zhu	21.42	—
Di Gu Pi	21.59	—
Yan Hu Suo	22.15	—
Bai Xian Pi	22.29	—
Gou Qi Zi	22.33	—
Gui Zhi	22.65	—
Dang Gui	23.35	—

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Substanz	Distance in main model	Distance in second-stage model
Gan Cao	23.59	—
Zhu Ru	23.92	—
Ye Jiao Teng	24.45	—
Che Qian Zi	24.56	—
Gou Teng	24.67	—
Ji Xue Teng	25.14	—
Chuang Mu Xiang	25.29	—
Qing Pi	25.52	—
Yin Yang Huo	25.54	—
Zhi Ke	25.81	—
Qiang Huo	26.01	—
Hong Jing Tian	26.36	—
Dang Gui Wei	26.48	—
Tao Ren	27.46	—
Ku Shen	27.47	—
Du Zhong	28.59	—
Yi Yi Ren	28.82	—
Chi Shao (Yao)	29.04	—
Zhi Mu	29.86	—
Xiang Fu	30.47	—
Ci Wu Jia	30.71	—
Rou Gui	31.41	—
Ban Xia (Jiang)	31.99	—
Ma Huang	32.04	—
Fu Xiao Mai	32.22	—
Zi Hua Di Ding	32.35	—
Ma Huang Gen	32.65	—
Huang Qin	33.76	—
Bai Zhu	34.15	—
Da Zao	34.53	—
Cang Er Zi	35.46	—
Huang Lian	36.20	—
(Huai) Niu Xi	36.31	—
Tian Men Dong	39.65	—
Sang Zhi	39.93	—
Long Yan Rou	40.67	—
Fo Shou	41.48	—
Huang Bai	41.98	—
Wu Yao	42.57	—
Mang Xiao	43.73	—
Wu Mei	45.01	—
Chuan Lian Zi	45.02	—
Sang Ye	45.29	—
Huang Bo	45.58	—
Dong Gua Zi	45.69	—
Yi Mu Cao	45.99	—
Fu Shen	47.12	—
Zhi Zi	47.95	—
Jie Geng	49.09	—
Bai Mao Gen	49.86	—
Zi Su Zi	50.06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lian Qiao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62338	62338	0.00	18.08
62685	62685	0.00	6.22
62337	62337	0.00	18.13
62686	62686	0.00	5.43

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 2.3-2020-05

Validated substance/substance group **Lian Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60248-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lian Zi; Nelumbinis semen

Special notes

When selecting the *Lian Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Lian Zi	1	0	0

Second-stage model

For differentiation of the substance/substance group *Lian Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lian Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Lian Zi	G171HS312SK1	62567	40	from supplier
PhytoComm	Lian Zi	G171HS312SK1	62568	40	from supplier

Validation samples

A total of 30 254 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 *Lian Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Lian Zi*.
- 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
PhytoComm	Lian Zi	G171HS312SK1	62567 [†]	20
PhytoComm	Lian Zi	G171HS312SK1	62568 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Lian Zi*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lian Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lian Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

The substance/substance group *Lian Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lian Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Ji Li	7.68	—
Ling Zhi	8.70	—
Shen Qu	10.58	—
Tu Fu Ling	11.11	—
Huo Ma Ren	11.27	—
Ren Dong Teng	11.60	—
Bai Shao Yao	12.13	—
He Huan Pi	12.18	—
Bai Xian Pi	12.38	—
Fu Ling	12.86	—
Bai Zi Ren	13.07	—
Sheng Jiang	13.48	—
Tao Ren	13.97	—
Yuan Zhi	13.98	—
Zhe Bei Mu	13.99	—
Gui Zhi	14.62	—
Lian Qiao	15.14	—
Tai Zi Shen	15.17	—
Chai Hu	15.32	—
Shan Yao	15.52	—
Gua Lou	15.54	—
Ye Jiao Teng	15.76	—
Pi Pa Ye	16.08	—
Chen Pi	16.23	—
Chuan Xiong	16.58	—
Mao Dong Qing	16.69	—
Ci Wu Jia	17.03	—
Rou Gui	17.33	—
Dan Dou Chi	17.37	—
Yu Jin	17.46	—
Tian Hua Fen	17.88	—
Gou Teng	18.32	—
Fu Zi	18.66	—
Di Gu Pi	18.69	—
Zhu Ru	19.29	—
Dan Shen	19.78	—
Yi Yi Ren	19.87	—
Jiao Gu Lan	20.07	—
San Qi	20.76	—
Hou Po	21.43	—
Yu Zhu	22.19	—
Cang Zhu	22.29	—
Fu Xiao Mai	22.41	—
Tian Men Dong	22.49	—
Ma Huang Gen	22.92	—
Ji Xue Teng	23.24	—
Hong Jing Tian	23.34	—
Fo Shou	24.27	—
Dang Gui Wei	24.30	—
Dang Shen	24.56	—
Yin Yang Huo	24.62	—
Che Qian Zi	25.18	—
Ban Xia (Jiang)	25.82	—
Suan Zao Ren	26.23	—
Qiang Huo	28.26	—
Jin Yin Hua	28.29	—
Da Zao	28.39	—
Zhi Ke	28.39	—
Ma Huang	28.70	—

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Substanz	Distance in main model	Distance in second-stage model
Yan Hu Suo	29.07	—
Long Yan Rou	29.45	—
Gou Qi Zi	30.97	—
Wu Wei Zi	31.47	—
Dang Gui	31.47	—
Shan Yu Rou	32.74	—
Fu Shen	35.27	—
Mu Dan Pi	35.60	—
Qing Pi	36.01	—
Du Zhong	37.87	—
Sang Zhi	38.98	—
Chuan Lian Zi	39.05	—
Huang Qin	39.16	—
Chuang Mu Xiang	39.62	—
Huang Lian	39.73	—
Bai Zhu	39.85	—
Mang Xiao	40.08	—
Zhi Mu	40.29	—
Jie Geng	42.77	—
Zi Hua Di Ding	45.95	—
Chi Shao (Yao)	47.49	—
Bai Bian Dou	49.53	—
Zi Su Zi	49.81	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lian Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62567	62567	0.00	9.14
62568	62568	0.00	7.68

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 2.3-2020-05

Validated substance/substance group **Ling Zhi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60187-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ling Zhi; Ganoderma

Special notes

When selecting the *Ling Zhi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ling Zhi	1	0	2

Second-stage model

For differentiation of the substance/substance group *Ling Zhi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ling Zhi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ling Zhi	G109HS355RP1	62453	40	from supplier
PhytoComm	Ling Zhi	G109HS355RP1	62454	40	from supplier

Validation samples

A total of 30 254 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 *Ling Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ling Zhi*.
- 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
PhytoComm	Ling Zhi	G109HS355RP1	62453 [†]	20
PhytoComm	Ling Zhi	G109HS355RP1	62454 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Ling Zhi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ling Zhi	g109fb2405321	1
PhytoComm	Ling Zhi	G109F-B2405221	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ling Zhi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ling Zhi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	2	855

The substance/substance group *Ling Zhi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ling Zhi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ren Dong Teng	5.32	—
Bai Xian Pi	7.19	—
Yu Jin	7.25	—
Dan Dou Chi	7.36	—
Chai Hu	8.32	—
Hou Po	8.70	—
Shen Qu	8.79	—
Lian Zi	9.27	—
Mao Dong Qing	10.12	—
Yuan Zhi	10.33	—
Ji Li	10.94	—
Lian Qiao	11.46	—
Tu Fu Ling	11.89	—
Ye Jiao Teng	12.85	—
Che Qian Zi	13.15	—
Yin Yang Huo	13.74	—
Shan Yao	14.76	—
He Huan Pi	15.03	—
Sheng Jiang	15.94	—
Dan Shen	16.41	—
Yan Hu Suo	16.46	—
Jiao Gu Lan	16.47	—
Pi Pa Ye	16.58	—
Chuan Xiong	16.91	—
Gou Teng	17.02	—
Rou Gui	17.36	—
Huo Ma Ren	17.49	—
Qiang Huo	17.86	—
Fu Ling	17.88	—
Fu Zi	18.11	—
Ji Xue Teng	18.37	—
Gui Zhi	18.92	—
Tian Hua Fen	19.83	—
Ma Huang Gen	20.18	—
Yi Yi Ren	20.45	—
Bai Shao Yao	20.77	—
Hong Jing Tian	21.80	—
Jin Yin Hua	21.88	—
Du Zhong	22.15	—
Tao Ren	22.34	—
Gua Lou	22.50	—
Bai Zi Ren	22.67	—
Tai Zi Shen	22.99	—
Qing Pi	23.12	—
Zhe Bei Mu	23.12	—
Suan Zao Ren	23.86	—
Wu Wei Zi	23.86	—
Chen Pi	24.33	—
Di Gu Pi	24.68	—
Ma Huang	25.20	—
Mu Dan Pi	25.56	—
Cang Zhu	26.15	—

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Substanz	Distance in main model	Distance in second-stage model
Zhi Ke	26.17	—
Ci Wu Jia	29.47	—
Fu Xiao Mai	30.50	—
Ban Xia (Jiang)	31.26	—
Huang Lian	31.37	—
Yu Zhu	31.37	—
Zhu Ru	31.67	—
Zi Hua Di Ding	31.93	—
San Qi	32.23	—
Gou Qi Zi	33.63	—
Dang Shen	35.64	—
Fu Shen	35.76	—
Dang Gui	35.88	—
Da Zao	36.11	—
Fo Shou	36.77	—
Dang Gui Wei	37.26	—
Tian Men Dong	37.45	—
Long Yan Rou	37.50	—
Huang Bai	38.27	—
Chuang Mu Xiang	39.23	—
Shan Yu Rou	39.74	—
Mang Xiao	40.52	—
Huang Qin	41.09	—
Sang Zhi	41.82	—
Wang Bu Liu Xing	45.65	—
Bai Zhu	45.76	—
Chuan Lian Zi	46.32	—
Cang Er Zi	46.96	—
Chi Shao (Yao)	46.99	—
Jie Geng	47.56	—
Zi Su Zi	48.44	—
Bai Bian Dou	48.52	—
Ban Zhi Lian	49.68	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ling Zhi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62453	62453	0.00	7.25
62454	62454	0.00	5.32

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 2.3-2020-05

Validated substance/substance group **Long Dan (Cao)**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60227-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Long Dan (Cao); Gentianae scabrae radix

Special notes

When selecting the *Long Dan (Cao)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Long Dan (Cao)	1	0	2

Second-stage model

For differentiation of the substance/substance group *Long Dan (Cao)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Long Dan (Cao)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Long Dan (Cao)	G112H1705821	62531	40	from supplier
PhytoComm	Long Dan (Cao)	G112H1705821	62532	40	from supplier

Validation samples

A total of 30 254 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 *Long Dan (Cao)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Long Dan (Cao)*.
- 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
PhytoComm	Long Dan (Cao)	G112H1705821	62531 [†]	20
PhytoComm	Long Dan (Cao)	G112H1705821	62532 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 4 *Apo-Ident* customers from 2 batches from the substance/substance group *Long Dan (Cao)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
PhytoComm	Long Dan (Cao)	g112h1705022	1
PhytoComm	Long Dan (Cao)	G112H1705321	3

- 853 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Long Dan (Cao)* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Long Dan (Cao)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	4	853

The substance/substance group *Long Dan (Cao)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8269 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Long Dan (Cao)* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Jie Geng	16.70	—
Di Gu Pi	16.92	—
Chuan Lian Zi	17.37	—
Da Zao	17.43	—
Mai Ya	17.92	—
Dang Gui	19.30	—
Mang Xiao	22.04	—
San Qi	22.46	—
Lai Fu Zi	23.30	—
Du Huo	23.78	—
Sang Zhi	23.90	—
Sha Shen (Bei)	23.91	—
E Zhu	23.95	—
Bai Bian Dou	26.49	—
Ji Li	27.09	—
Mai Men Dong	28.02	—
Bai He	28.98	—
Ba Ji Tian	30.29	—
Sheng Jiang	31.13	—
(Huai) Niu Xi	31.20	—
Bai Zhu	32.23	—
Qin Jiao	32.34	—
Mu Dan Pi	33.45	—
Zhu Ling	33.89	—
Huang Qi	33.91	—
Fang Feng	33.95	—
Jiang Huang	36.47	—
Yan Hu Suo	36.85	—
He Huan Pi	37.51	—
Xian He Cao	38.35	—
Chen Pi	38.53	—
Tian Hua Fen	38.59	—
Sha Ren	39.09	—
Yu Jin	39.86	—
Bai Mao Gen	40.54	—
Gui Zhi	40.72	—
Zi Su Zi	40.90	—
Cang Er Zi	41.77	—
Shan Yao	41.88	—
Ban Zhi Lian	45.16	—
Xie Bai	45.23	—
Qing Pi	47.68	—
(Shi) Chang Pu	49.55	—
(Bai) Dou Kou	50.04	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Long Dan (Cao)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62531	62531	0.00	16.90
62532	62532	0.00	16.70

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 2.3-2020-05

Validated substance/substance group **Long Yan Rou**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60463-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Long Yan Rou; Euphoriae longanae arillus

Special notes

When selecting the *Long Yan Rou* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Long Yan Rou	2	0	1

Second-stage model

For differentiation of the substance/substance group *Long Yan Rou* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Long Yan Rou*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Long Yan Rou	G144HS324RN1	62267	40	from supplier
PhytoComm	Long Yan Rou	G144HS324RN1	62268	40	from supplier
PhytoComm	Long Yan Rou	G144HS324SQ1	62727	40	from supplier
PhytoComm	Long Yan Rou	G144HS324SQ1	62728	40	from supplier

Validation samples

A total of 30 254 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 *Long Yan Rou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Long Yan Rou*.
- 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
PhytoComm	Long Yan Rou	G144HS324RN1	62267 [†]	20
PhytoComm	Long Yan Rou	G144HS324RN1	62268 [†]	20
PhytoComm	Long Yan Rou	G144HS324SQ1	62727 [†]	20
PhytoComm	Long Yan Rou	G144HS324SQ1	62728 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Long Yan Rou*.
- 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
PhytoComm	Long Yan Rou	G144H1708221	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Long Yan Rou* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Long Yan Rou* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	1	856

The substance/substance group *Long Yan Rou* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8367 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Long Yan Rou* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chen Pi	6.03	—
Da Zao	10.24	—
Yu Zhu	11.67	—
Gou Qi Zi	12.44	—
Gua Lou	12.65	—
Dang Shen	14.96	—
Fo Shou	15.25	—
Dang Gui Wei	16.27	—
Ye Jiao Teng	16.84	—
Tian Men Dong	17.01	—
Di Gu Pi	17.72	—
Bai Shao Yao	17.84	—
Chuan Xiong	18.49	—
Zhe Bei Mu	18.69	—
Ma Huang	18.89	—
Jie Geng	19.08	—
Cang Zhu	19.32	—
Tao Ren	19.61	—
Yuan Zhi	20.38	—
Bai Zhu	20.54	—
Gou Teng	21.06	—
San Qi	21.48	—
Tai Zi Shen	21.68	—
Chuang Mu Xiang	22.25	—
Hong Jing Tian	22.27	—
Shen Qu	22.60	—
Zhi Ke	23.29	—
Dang Gui	23.52	—
Rou Gui	23.64	—
He Huan Pi	23.65	—
Gui Zhi	23.73	—
Ban Xia (Jiang)	23.73	—
Tu Fu Ling	24.27	—
Ji Xue Teng	24.56	—
Pi Pa Ye	24.64	—
Fu Shen	24.79	—
Ren Dong Teng	25.11	—
Ci Wu Jia	25.48	—
Lian Zi	25.87	—
Lian Qiao	26.04	—
Huang Qin	26.05	—
Dan Shen	26.26	—
Shan Yu Rou	27.01	—
Yin Yang Huo	27.36	—
Bai Xian Pi	27.48	—
Shan Yao	27.54	—
Gan Cao	28.14	—
Sheng Jiang	28.78	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Zi Ren	28.80	—
Jin Yin Hua	28.82	—
Ma Huang Gen	28.90	—
Fu Xiao Mai	29.11	—
Ji Li	29.19	—
Jiao Gu Lan	29.61	—
Fu Zi	30.73	—
Huo Ma Ren	30.78	—
Hou Po	31.02	—
Sang Zhi	31.03	—
Fu Ling	31.83	—
Dan Dou Chi	33.13	—
Mai Men Dong	33.77	—
Chi Shao (Yao)	33.84	—
Wu Wei Zi	33.85	—
Ling Zhi	33.89	—
Yi Yi Ren	34.15	—
Yan Hu Suo	34.62	—
Zi Hua Di Ding	34.69	—
Chai Hu	35.32	—
Huang Qi	36.63	—
Tian Hua Fen	36.67	—
Mao Dong Qing	36.72	—
Mu Dan Pi	37.12	—
Yu Jin	37.38	—
Zhu Ru	38.10	—
Zhi Mu	40.48	—
Qiang Huo	40.82	—
Mang Xiao	41.13	—
Che Qian Zi	41.35	—
Suan Zao Ren	44.56	—
Huang Lian	45.16	—
Chuan Lian Zi	49.82	—
Du Huo	50.02	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Long Yan Rou* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62267	62267	0.00	13.82
62268	62268	0.00	12.96
62728	62728	0.00	6.03
62727	62727	0.00	6.33

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 2.3-2020-05

Validated substance/substance group **Ma Huang**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50283-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ma Huang; Ephedrae herba

Special notes

When selecting the *Ma Huang* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ma Huang	2	0	2

Second-stage model

For differentiation of the substance/substance group *Ma Huang* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ma Huang*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ma Huang	G097HS255RT1	62681	40	from supplier
PhytoComm	Ma Huang	G097HS255RT1	62682	40	from supplier
PhytoComm	Ma Huang	G097HS255SL1	62693	40	from supplier
PhytoComm	Ma Huang	G097HS255SL1	62694	40	from supplier

Validation samples

A total of 30 254 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 *Ma Huang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Ma Huang*.
- 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
PhytoComm	Ma Huang	G097HS255RT1	62681 [†]	20
PhytoComm	Ma Huang	G097HS255RT1	62682 [†]	20
PhytoComm	Ma Huang	G097HS255SL1	62693 [†]	20
PhytoComm	Ma Huang	G097HS255SL1	62694 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Ma Huang*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ma Huang	G097H1101522	2
PhytoComm	Ma Huang	G097H1101623	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ma Huang* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ma Huang* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	3	854

The substance/substance group *Ma Huang* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8280 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ma Huang* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zhi Ke	11.62	—
Bai Shao Yao	11.81	—
Ye Jiao Teng	12.41	—
Jin Yin Hua	14.75	—
Hou Po	15.75	—
Ji Xue Teng	16.29	—
Fu Zi	16.71	—
Pi Pa Ye	17.07	—
Chuan Xiong	17.18	—
Dan Shen	17.41	—
Yan Hu Suo	17.43	—
Zi Hua Di Ding	17.98	—
Yu Zhu	18.10	—
Ren Dong Teng	18.12	—
Tai Zi Shen	18.68	—
Yin Yang Huo	18.73	—
Tao Ren	18.78	—
Lian Qiao	18.90	—
Gua Lou	18.91	—
Huang Lian	19.10	—
He Huan Pi	19.16	—
Tian Hua Fen	19.38	—
Hong Jing Tian	19.45	—
Huang Bai	19.58	—
Cang Zhu	19.81	—
Huang Qin	20.34	—
Gou Qi Zi	20.59	—
Rou Gui	20.99	—
Chen Pi	21.55	—
Jiao Gu Lan	21.94	—
Zhe Bei Mu	21.94	—
Dang Gui	22.44	—
Huo Ma Ren	23.25	—
Shan Yao	23.59	—
Bai Xian Pi	23.65	—
Shen Qu	23.93	—
Lian Zi	23.95	—
Dan Dou Chi	24.42	—
Dang Gui Wei	24.46	—
Yuan Zhi	25.24	—
Ci Wu Jia	25.45	—
Gou Teng	25.74	—
Di Gu Pi	25.86	—
Tu Fu Ling	26.22	—
Da Zao	26.24	—
Qiang Huo	26.27	—
Gan Cao	26.38	—
Dang Shen	26.46	—

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Substanz	Distance in main model	Distance in second-stage model
Gui Zhi	26.51	—
Ji Li	26.56	—
Mu Dan Pi	26.75	—
Long Yan Rou	26.83	—
Wu Wei Zi	26.87	—
Ling Zhi	27.69	—
Shan Yu Rou	28.04	—
Sheng Jiang	28.08	—
Yu Jin	28.25	—
San Qi	28.43	—
Bai Zi Ren	29.30	—
Fo Shou	29.98	—
Chai Hu	30.20	—
Che Qian Zi	30.20	—
Ban Xia (Jiang)	30.58	—
Qing Pi	31.78	—
Ma Huang Gen	31.85	—
Du Zhong	32.31	—
Mao Dong Qing	32.75	—
Fu Shen	32.96	—
Chi Shao (Yao)	33.39	—
Chuang Mu Xiang	33.71	—
Fu Ling	34.11	—
Sang Ye	34.26	—
Pu Gong Ying	34.44	—
Ban Zhi Lian	35.30	—
Bai Zhu	35.53	—
Yi Yi Ren	37.70	—
Sang Zhi	39.08	—
Tian Men Dong	39.99	—
Wu Yao	40.06	—
Zhu Ru	40.50	—
Fu Xiao Mai	40.83	—
Jie Geng	40.95	—
Bai Mao Gen	41.27	—
Zhi Mu	41.80	—
Mang Xiao	42.75	—
Cang Er Zi	43.54	—
Hong Hua	46.47	—
Suan Zao Ren	46.55	—
Jiang Huang	49.68	—
(Shi) Chang Pu	49.74	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ma Huang* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62693	62693	0.00	11.89
62694	62694	0.00	11.81
62682	62682	0.00	11.84
62681	62681	0.00	11.62

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 2.3-2020-05

Validated substance/substance group **Ma Huang Gen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60063-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ma Huang Gen; Ephedrae radix

Special notes

When selecting the *Ma Huang Gen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ma Huang Gen	1	0	0

Second-stage model

For differentiation of the substance/substance group *Ma Huang Gen* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ma Huang Gen*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ma Huang Gen	G278HS393RN1	62261	40	from supplier
PhytoComm	Ma Huang Gen	G278HS393RN1	62262	40	from supplier

Validation samples

A total of 30 254 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 *Ma Huang Gen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ma Huang Gen*.
- 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
PhytoComm	Ma Huang Gen	G278HS393RN1	62261 [†]	20
PhytoComm	Ma Huang Gen	G278HS393RN1	62262 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Ma Huang Gen*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ma Huang Gen* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ma Huang Gen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	1	78	2	19 399
Type B	4	35	5	9873
Type C	1	0	0	856

The substance/substance group *Ma Huang Gen* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9960 % (> 99.9777 %)	97.5000 % (> 93.7500 %)
Type B	99.9684 % (> 99.9326 %)	87.5000 % (> 80.0000 %)
Type C	99.8843 % (> 99.3015 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ma Huang Gen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Rou Gui	3.16	—
Gou Teng	6.10	—
Fu Shen	8.57	—
Yi Yi Ren	10.86	—
Ji Xue Teng	12.00	—
Gui Zhi	12.89	—
Fu Ling	13.48	—
Sheng Jiang	14.04	—
Ban Xia (Jiang)	16.87	—
Fo Shou	18.37	—
Fu Xiao Mai	19.44	—
Bai Xian Pi	19.45	—
Ye Jiao Teng	20.06	—
Di Gu Pi	20.38	—
He Huan Pi	20.83	—
Huo Ma Ren	21.15	—
Ling Zhi	22.28	—
Bai Shao Yao	22.36	—
Lian Zi	23.15	—
Tai Zi Shen	24.03	—
Tian Men Dong	24.11	—
Ci Wu Jia	24.34	—
Tao Ren	24.67	—
Ren Dong Teng	24.97	—
Zhu Ru	26.34	—
Da Zao	27.05	—
Zhe Bei Mu	27.05	—
Bai Zi Ren	27.39	—
Shen Qu	27.54	—
Tu Fu Ling	27.58	—
Long Yan Rou	28.15	—
Chen Pi	28.24	—
Dan Dou Chi	29.10	—
Ji Li	29.56	—
Yu Jin	32.18	—
Dan Shen	32.66	—
Tian Hua Fen	32.86	—
Yan Hu Suo	34.15	—
Chuan Xiong	34.57	—
Lian Qiao	34.73	—
Pi Pa Ye	36.62	—
Gua Lou	37.28	—
Yuan Zhi	37.85	—
Mang Xiao	38.86	—
Jiao Gu Lan	39.34	—
Zhi Ke	39.52	—
Shan Yao	39.57	—
Yin Yang Huo	39.97	—
Dang Shen	40.85	—
Chai Hu	41.80	—
Mao Dong Qing	42.08	—
Hong Jing Tian	42.13	—
Yu Zhu	42.88	—
Jin Yin Hua	44.26	—
Ma Huang	44.28	—
Shan Yu Rou	44.95	—
Huang Qin	45.64	—
Wu Wei Zi	46.74	—
Fu Zi	46.79	—

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Substanz	Distance in main model	Distance in second-stage model
Cang Zhu	48.28	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ma Huang Gen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62261	62261	0.00	3.16
62262	62262	0.00	6.04

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Mai Men Dong**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60024-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mai Men Dong; Ophiopogonis radix

Special notes

When selecting the *Mai Men Dong* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mai Men Dong	2	0	2

Second-stage model

For differentiation of the substance/substance group *Mai Men Dong* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mai Men Dong*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Mai Men Dong	G176H1118622	62113	40	from supplier
PhytoComm	Mai Men Dong	G176H1118622	62114	40	from supplier
PhytoComm	Mai Men Dong	G176HS236SH1	62611	40	from supplier
PhytoComm	Mai Men Dong	G176HS236SH1	62612	40	from supplier

Validation samples

A total of 30 254 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 *Mai Men Dong*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Mai Men Dong*.
- 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
PhytoComm	Mai Men Dong	G176H1118622	62113 [†]	20
PhytoComm	Mai Men Dong	G176H1118622	62114 [†]	20
PhytoComm	Mai Men Dong	G176HS236SH1	62611 [†]	20
PhytoComm	Mai Men Dong	G176HS236SH1	62612 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Mai Men Dong*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Mai Men Dong	g176h1118221	1
Phytocomm	Mai Men Dong	G176H1118521	3

- 853 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mai Men Dong* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mai Men Dong* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	2	2	853

The substance/substance group *Mai Men Dong* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8269 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mai Men Dong* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Da Zao	10.63	—
Chen Pi	13.88	—
Tian Men Dong	14.99	—
Dang Shen	15.35	—
Bai Zhu	19.81	—
Gua Lou	21.65	—
Fo Shou	21.67	—
Jie Geng	21.87	—
Di Gu Pi	23.11	—
Ye Jiao Teng	24.11	—
Rou Gui	26.28	—
Mang Xiao	27.03	—
Fu Xiao Mai	27.88	—
Yuan Zhi	28.46	—
Bai Shao Yao	28.55	—
Chuan Xiong	28.59	—
Chuan Lian Zi	29.98	—
Long Yan Rou	30.84	—
He Huan Pi	31.79	—
Shan Yu Rou	32.13	—
Pi Pa Ye	33.31	—
Mu Dan Pi	33.32	—
Ji Li	33.80	—
Bai He	33.87	—
Yu Zhu	34.27	—
Tai Zi Shen	34.33	—
Shen Qu	34.58	—
Dang Gui	34.72	—
Lai Fu Zi	35.19	—
Huang Qi	35.29	—
Fu Ling	35.76	—
Gou Teng	35.87	—
Tian Hua Fen	36.41	—
Zhi Mu	36.50	—
Lian Zi	36.83	—
Fu Shen	37.02	—
Cang Zhu	37.40	—
Bai Xian Pi	37.42	—
Sheng Jiang	37.55	—
Ban Xia (Jiang)	37.73	—
Du Huo	37.87	—
Chuang Mu Xiang	38.02	—
San Qi	38.29	—
Tao Ren	38.58	—
Sang Zhi	38.62	—
Huang Qin	39.23	—
Gui Zhi	39.55	—
Mai Ya	39.79	—

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Substanz	Distance in main model	Distance in second-stage model
Qin Jiao	39.99	—
Shan Yao	40.04	—
Ma Huang Gen	40.50	—
Dang Gui Wei	41.06	—
Ma Huang	41.31	—
Yi Yi Ren	42.42	—
Gou Qi Zi	42.52	—
Zhi Ke	42.80	—
Ci Wu Jia	43.35	—
Bai Bian Dou	43.85	—
Ren Dong Teng	44.12	—
Ji Xue Teng	44.33	—
Lian Qiao	44.79	—
Tu Fu Ling	45.03	—
Jiao Gu Lan	45.58	—
Bai Zi Ren	45.72	—
Ba Ji Tian	46.92	—
Ling Zhi	48.48	—
Zhe Bei Mu	49.22	—
Long Dan (Cao)	49.61	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mai Men Dong* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62612	62612	0.00	10.63
62611	62611	0.00	11.53
62113	62113	0.00	21.45
62114	62114	0.00	19.81

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 2.3-2020-05

Validated substance/substance group **Mai Ya**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60210-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mai Ya; Hordei vulgaris fructus germinatus

Special notes

When selecting the *Mai Ya* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mai Ya	1	0	2

Second-stage model

For differentiation of the substance/substance group *Mai Ya* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mai Ya*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Mai Ya	G123H1119821	62535	40	from supplier
PhytoComm	Mai Ya	G123H1119821	62536	40	from supplier

Validation samples

A total of 30 254 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 *Mai Ya*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Mai Ya*.
- 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
PhytoComm	Mai Ya	G123H1119821	62535 [†]	20
PhytoComm	Mai Ya	G123H1119821	62536 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Mai Ya*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Mai Ya	G123H1119521	1
Phytocomm	Mai Ya	g123h1119022	1
PhytoComm	Mai Ya	G123H1119821	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mai Ya* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mai Ya* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	1	2	854

The substance/substance group *Mai Ya* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8280 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mai Ya* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai He	15.34	—
Di Gu Pi	15.72	—
Chuan Lian Zi	17.74	—
Long Dan (Cao)	18.40	—
Sheng Jiang	18.92	—
Jie Geng	20.20	—
San Qi	21.57	—
Zhu Ling	22.22	—
Mang Xiao	22.53	—
Ban Zhi Lian	23.69	—
Dang Gui	23.77	—
Sang Zhi	24.82	—
E Zhu	26.34	—
Da Zao	26.40	—
Mai Men Dong	27.70	—
Du Huo	28.27	—
Ji Li	30.69	—
Mu Dan Pi	31.02	—
Yan Hu Suo	31.02	—
Bai Bian Dou	31.36	—
Tian Hua Fen	32.42	—
Lai Fu Zi	33.67	—
Qin Jiao	33.83	—
Jiang Huang	36.38	—
(Huai) Niu Xi	36.61	—
Sha Shen (Bei)	38.60	—
Bai Zhu	38.84	—
Cang Er Zi	38.96	—
Rou Gui	39.38	—
Sha Ren	39.72	—
Ba Ji Tian	39.84	—
Huang Qi	40.27	—
Gui Zhi	40.45	—
Shan Yao	40.46	—
Chen Pi	41.75	—
He Huan Pi	42.05	—
Fu Ling	42.19	—
Zi Su Zi	43.13	—
Yi Yi Ren	43.49	—
Yu Jin	44.43	—
(Bai) Dou Kou	45.01	—
Fang Feng	45.37	—
Xian He Cao	46.34	—
Xie Bai	46.82	—
Wang Bu Liu Xing	47.04	—
Lian Zi	47.44	—
Bai Xian Pi	47.91	—
(Shi) Chang Pu	49.07	—
Qing Pi	49.44	—
Tian Men Dong	50.40	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mai Ya* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62535	62535	0.00	15.34
62536	62536	0.00	15.92

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 2.3-2020-05

Validated substance/substance group **Man Jing Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60025-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Man Jing Zi; Vitis fructus

Special notes

When selecting the *Man Jing Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Man Jing Zi	1	0	1

Second-stage model

For differentiation of the substance/substance group *Man Jing Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Man Jing Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Man Jing Zi	G250H1505822	62501	40	from supplier
PhytoComm	Man Jing Zi	G250H1505822	62502	40	from supplier

Validation samples

A total of 30 254 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 *Man Jing Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Man Jing Zi*.
- 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
PhytoComm	Man Jing Zi	G250H1505822	62501 [†]	20
PhytoComm	Man Jing Zi	G250H1505822	62502 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Man Jing Zi*.
- 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
PhytoComm	Man Jing Zi	G250H1505122	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Man Jing Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Man Jing Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	1	856

The substance/substance group *Man Jing Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8367 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Man Jing Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hua Shi	30.66	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Man Jing Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62501	62501	0.00	30.70
62502	62502	0.00	30.66

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 2.3-2020-05

Validated substance/substance group **Mang Xiao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50387-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mang Xiao; Mirabilitum

Special notes

When selecting the *Mang Xiao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mang Xiao	1	0	0

Second-stage model

For differentiation of the substance/substance group *Mang Xiao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mang Xiao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Mang Xiao	G160H0627821	62469	40	from supplier
PhytoComm	Mang Xiao	G160H0627821	62470	40	from supplier

Validation samples

A total of 30 254 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 *Mang Xiao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Mang Xiao*.
- 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
PhytoComm	Mang Xiao	G160H0627821	62469 [†]	20
PhytoComm	Mang Xiao	G160H0627821	62470 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Mang Xiao*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mang Xiao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mang Xiao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

The substance/substance group *Mang Xiao* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mang Xiao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Hua Shi	44.78	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mang Xiao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62470	62470	0.00	45.03
62469	62469	0.00	44.78

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Mao Dong Qing**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60028-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mao Dong Qing; Ilicis pubescendis radix

Special notes

When selecting the *Mao Dong Qing* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mao Dong Qing	2	0	0

Second-stage model

For differentiation of the substance/substance group *Mao Dong Qing* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mao Dong Qing*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Mao Dong Qing	G319HS063RN1	62417	40	from supplier
PhytoComm	Mao Dong Qing	G319HS063RN1	62418	40	from supplier
PhytoComm	Mao Dong Qing	G319HS063SK1	62619	40	from supplier
PhytoComm	Mao Dong Qing	G319HS063SK1	62620	40	from supplier

Validation samples

A total of 30 254 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 *Mao Dong Qing*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Mao Dong Qing*.
- 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
PhytoComm	Mao Dong Qing	G319HS063RN1	62417 [†]	20
PhytoComm	Mao Dong Qing	G319HS063RN1	62418 [†]	20
PhytoComm	Mao Dong Qing	G319HS063SK1	62619 [†]	20
PhytoComm	Mao Dong Qing	G319HS063SK1	62620 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Mao Dong Qing*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mao Dong Qing* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mao Dong Qing* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	4	79	1	9833
Type C	0	0	0	857

The substance/substance group *Mao Dong Qing* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	99.9631 % (> 99.9272 %)	98.7500 % (> 95.0000 %)
Type C	100.0000 % (> 98.8345 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mao Dong Qing* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Xian Pi	6.92	—
Du Zhong	6.98	—
Yin Yang Huo	7.95	—
Ling Zhi	8.15	—
Yu Jin	9.71	—
Ye Jiao Teng	9.73	—
Che Qian Zi	10.00	—
Hou Po	11.13	—
Qiang Huo	12.40	—
Dan Dou Chi	13.44	—
Jiao Gu Lan	15.29	—
Xi Xian Cao	15.84	—
Shen Qu	16.78	—
Ren Dong Teng	16.81	—
Yuan Zhi	16.91	—
Zi Hua Di Ding	17.47	—
Qing Pi	17.82	—
Yan Hu Suo	18.01	—
Mu Dan Pi	18.43	—
Lian Zi	18.80	—
Ji Li	19.10	—
Huang Bai	19.44	—
Tu Fu Ling	19.82	—
Ji Xue Teng	20.02	—
Shan Yao	20.06	—
Rou Gui	20.95	—
Pi Pa Ye	22.19	—
Nü Zhen Zi	23.14	—
Dan Shen	23.22	—
Zhi Ke	23.31	—
Chai Hu	23.80	—
Ma Huang	24.01	—
Pu Gong Ying	24.05	—
Huang Lian	24.10	—
Hong Jing Tian	24.20	—
Wu Mei	24.20	—
He Huan Pi	24.32	—
Wang Bu Liu Xing	24.39	—
Ma Huang Gen	25.36	—
Gou Teng	25.45	—
Chuan Xiong	25.98	—
Lian Qiao	27.18	—
Jin Yin Hua	27.97	—
Di Gu Pi	28.51	—
Chen Pi	28.68	—
Wu Wei Zi	28.68	—
Sang Ye	29.28	—
Sheng Jiang	30.55	—
Yi Yi Ren	30.79	—
Gui Zhi	30.81	—
Ban Zhi Lian	31.07	—
Bai Shao Yao	31.32	—

continued on the next page

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Substanz	Distance in main model	Distance in second-stage model
Huo Ma Ren	32.92	—
Gua Lou	34.00	—
Xin Yi	34.32	—
Fu Zi	34.51	—
Cang Zhu	35.77	—
E Zhu	36.78	—
Mang Xiao	36.94	—
Jiang Huang	37.19	—
Cang Er Zi	37.28	—
Gou Qi Zi	37.30	—
Tian Hua Fen	37.54	—
Fu Shen	37.71	—
Fu Ling	38.29	—
Tao Ren	39.10	—
Tai Zi Shen	39.24	—
Hong Hua	39.86	—
Zhe Bei Mu	41.01	—
Bai Bian Dou	42.12	—
Zi Su Zi	43.67	—
Da Zao	44.18	—
Shan Yu Rou	44.28	—
Sang Zhi	44.97	—
Fo Shou	45.49	—
Ban Xia (Jiang)	45.66	—
Ci Wu Jia	46.33	—
Chi Shao (Yao)	46.40	—
Chuan Lian Zi	46.83	—
Fu Xiao Mai	47.15	—
Yi Mu Cao	47.18	—
Long Yan Rou	47.68	—
Suan Zao Ren	47.78	—
Jie Geng	48.22	—
Bai Zi Ren	48.70	—
Huang Qin	49.42	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mao Dong Qing* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62620	62620	0.00	9.89
62417	62417	0.00	6.98
62619	62619	0.00	9.94
62418	62418	0.00	6.92

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 2.3-2020-05

Validated substance/substance group **Mu Dan Pi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60113-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mu Dan Pi; Moutan cortex radicis

Special notes

When selecting the *Mu Dan Pi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mu Dan Pi	2	0	5

Second-stage model

For differentiation of the substance/substance group *Mu Dan Pi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mu Dan Pi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Mu Dan Pi	G166HS129RT1	62433	40	from supplier
PhytoComm	Mu Dan Pi	G166HS129RT1	62434	40	from supplier
PhytoComm	Mu Dan Pi	G166H0741821	62475	40	from supplier
PhytoComm	Mu Dan Pi	G166H0741821	62476	40	from supplier

Validation samples

A total of 30 254 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 *Mu Dan Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Mu Dan Pi*.
- 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
PhytoComm	Mu Dan Pi	G166HS129RT1	62433 [†]	20
PhytoComm	Mu Dan Pi	G166HS129RT1	62434 [†]	20
PhytoComm	Mu Dan Pi	G166H0741821	62475 [†]	20
PhytoComm	Mu Dan Pi	G166H0741821	62476 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 5 batches from the substance/substance group *Mu Dan Pi*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Mu Dan Pi	G166H0741121	1
Phytocomm	Mu Dan Pi	G166H0741122	2
Phytocomm	Mu Dan Pi	g166j074122	1
Phytocomm	Mu Dan Pi	G166H0741321	2
Phytocomm	Mu Dan Pi	G166H0741421	4
PhytoComm	Mu Dan Pi	G166H0741321	1

- 846 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mu Dan Pi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mu Dan Pi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	77	3	9837
Type C	0	0	11	846

The substance/substance group *Mu Dan Pi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	96.2500 % (> 92.5000 %)
Type C	100.0000 % (> 98.8249 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mu Dan Pi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dan Shen	5.72	—
Zi Hua Di Ding	7.99	—
Du Huo	10.48	—
Dang Gui	10.93	—
Jin Yin Hua	11.25	—
Hou Po	11.93	—
Qiang Huo	13.22	—
Jiao Gu Lan	13.99	—
Yin Yang Huo	14.62	—
Zhi Ke	15.37	—
Chai Hu	15.37	—
Huang Bai	15.71	—
Ye Jiao Teng	15.77	—
Chuan Xiong	15.80	—
Hong Jing Tian	15.89	—
Shan Yao	16.39	—
Dan Dou Chi	16.76	—
Mao Dong Qing	16.85	—
Yu Jin	17.24	—
Bai Xian Pi	17.35	—
Yuan Zhi	18.04	—
Bai Mao Gen	18.39	—
Wu Wei Zi	18.63	—
Du Zhong	18.71	—
Pi Pa Ye	18.83	—
Qing Pi	18.88	—
Huang Lian	19.31	—
Ren Dong Teng	19.37	—
Ma Huang	19.50	—
Di Gu Pi	19.74	—
Sang Zhi	19.83	—
Ji Xue Teng	20.22	—
Gua Lou	20.31	—
Bai Shao Yao	20.52	—
Lian Zi	20.71	—
Ba Ji Tian	21.12	—
Che Qian Zi	21.17	—
Fu Zi	21.29	—
Shen Qu	21.40	—
Gou Qi Zi	21.61	—
Fang Feng	22.52	—
Yan Hu Suo	22.83	—
Ji Li	23.69	—

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Substanz	Distance in main model	Distance in second-stage model
Pu Gong Ying	24.06	—
Huang Qi	24.35	—
(Shi) Chang Pu	25.31	—
Cang Zhu	25.33	—
Chi Shao (Yao)	25.49	—
Lian Qiao	25.83	—
Ling Zhi	25.91	—
Tu Fu Ling	26.07	—
He Huan Pi	26.20	—
Chen Pi	26.47	—
Jie Geng	27.29	—
Gou Teng	27.63	—
Shan Yu Rou	28.29	—
E Zhu	28.49	—
Tian Hua Fen	28.76	—
Wu Yao	29.45	—
(Huai) Niu Xi	29.78	—
Cang Er Zi	29.83	—
Sang Ye	29.88	—
Mang Xiao	29.99	—
Rou Gui	30.59	—
Da Zao	30.76	—
Xian He Cao	31.12	—
Bai Zhu	31.79	—
Sha Shen (Bei)	32.28	—
Zhe Bei Mu	32.46	—
Huo Ma Ren	32.64	—
Tao Ren	32.67	—
Qin Jiao	32.87	—
Huang Qin	32.91	—
Gan Cao	33.36	—
Ma Huang Gen	33.75	—
Gui Zhi	33.95	—
Ju Hua	34.28	—
Long Yan Rou	34.45	—
Ban Zhi Lian	34.99	—
Hong Hua	36.10	—
Chuang Mu Xiang	36.47	—
Xie Bai	36.65	—
Long Dan (Cao)	36.68	—
Jiang Huang	36.73	—
Xiang Fu	36.76	—
Chuan Lian Zi	36.98	—
Sheng Jiang	37.56	—
San Qi	37.65	—
Sha Ren	38.49	—
Ci Wu Jia	39.70	—
Tai Zi Shen	40.35	—
Dang Gui Wei	40.65	—
Xi Xian Cao	41.47	—
Dang Shen	41.97	—
Yu Zhu	42.54	—
Ban Xia (Jiang)	42.82	—
Fu Ling	42.83	—
Suan Zao Ren	42.95	—
Zi Su Zi	43.02	—
Mai Ya	43.06	—
Bai Zi Ren	43.24	—
Sang Ji Shend	43.40	—

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Substanz	Distance in main model	Distance in second-stage model
Niu Bang Zi	43.51	—
Lai Fu Zi	43.63	—
(Bai) Dou Kou	43.91	—
Fo Shou	44.16	—
Yi Yi Ren	45.37	—
Yi Mu Cao	45.74	—
Gu Sui Bu	46.28	—
Fu Shen	46.67	—
Zhu Ru	48.27	—
He Shou Wu	48.67	—
Ku Shen	48.72	—
Wu Mei	48.92	—
Mai Men Dong	49.04	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mu Dan Pi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62475	62475	0.00	10.58
62434	62434	0.00	5.72
62476	62476	0.00	10.48
62433	62433	0.00	5.94

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Niu Bang Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002261-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Niu Bang Zi; Arctii fructus

Special notes

When selecting the *Niu Bang Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Niu Bang Zi	1	0	2

Second-stage model

For differentiation of the substance/substance group *Niu Bang Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Niu Bang Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Niu Bang Zi	G026H0433822	62765	40	from supplier
PhytoComm	Niu Bang Zi	G026H0433822	62766	40	from supplier

Validation samples

A total of 30 254 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 *Niu Bang Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Niu Bang Zi*.
- 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
PhytoComm	Niu Bang Zi	G026H0433822	62765 [†]	20
PhytoComm	Niu Bang Zi	G026H0433822	62766 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 8 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Niu Bang Zi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
phytocomm	Niu Bang Zi	g026h0433321	2
Phytocomm	Niu Bang Zi	G026H0433321	1
Phytocomm	Niu Bang Zi	G026H0433521	3
PhytoComm	Niu Bang Zi	G026H0433321	2

- 849 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Niu Bang Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Niu Bang Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	8	849

The substance/substance group *Niu Bang Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8253 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Niu Bang Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Gua Lou	12.91	—
Qing Pi	14.16	—
Ku Shen	16.55	—
Shan Yao	24.95	—
Di Gu Pi	25.13	—
Sang Zhi	25.24	—
Yi Mu Cao	25.93	—
Cang Er Zi	27.97	—
(Huai) Niu Xi	28.19	—
Gui Zhi	28.28	—
Xiang Fu	29.02	—
Xie Bai	29.23	—
Jiang Huang	30.26	—
Tian Hua Fen	32.14	—
Zhi Ke	32.19	—
Du Huo	33.07	—
Dong Gua Zi	35.19	—
Yan Hu Suo	35.49	—
Wu Yao	36.02	—
Chi Shao (Yao)	36.84	—
Wu Wei Zi	37.30	—
(Bai) Dou Kou	37.36	—
Jie Geng	37.51	—
(Shi) Chang Pu	38.23	—
Mu Dan Pi	38.32	—
Mang Xiao	38.59	—
Sha Ren	38.68	—
Huang Bo	39.19	—
Pu Gong Ying	39.58	—
Gan Cao	39.60	—
Zi Su Zi	39.67	—
Qiang Huo	39.73	—
Huang Qi	39.87	—
Bai Mao Gen	40.16	—
Fang Feng	40.43	—
E Zhu	41.27	—
Lian Qiao	41.31	—
Ji Li	41.41	—
Nü Zhen Zi	41.60	—
Jin Yin Hua	42.33	—
Fu Zi	42.38	—
Chen Pi	43.10	—
Yuan Zhi	43.60	—
Zhi Zi	44.06	—
Ju Hua	44.06	—
Shen Qu	44.27	—
Wu Mei	45.36	—
Sha Shen (Bei)	46.32	—
Sheng Jiang	46.42	—
Xian He Cao	46.61	—
Xin Yi	48.82	—
Dang Gui	48.88	—

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Substanz	Distance in main model	Distance in second-stage model
Jiao Gu Lan	48.97	—
Chuan Xiong	49.18	—
Sang Ye	49.32	—
Huang Bai	50.11	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Niu Bang Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62765	62765	0.00	13.16
62766	62766	0.00	12.91

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 2.3-2020-05

Validated substance/substance group **Nü Zhen Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60065-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Nü Zhen Zi; Ligustri lucidi fructus

Special notes

When selecting the *Nü Zhen Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Nü Zhen Zi	3	0	2

Second-stage model

For differentiation of the substance/substance group *Nü Zhen Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Nü Zhen Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Nü Zhen Zi	G138H0345721	62213	40	from supplier
PhytoComm	Nü Zhen Zi	G138H0345721	62214	40	from supplier
PhytoComm	Nü Zhen Zi	G138H0345821	62343	40	from supplier
PhytoComm	Nü Zhen Zi	G138H0345821	62344	40	from supplier
PhytoComm	Nü Zhen Zi	G138HS010SK1	62569	40	from supplier
PhytoComm	Nü Zhen Zi	G138HS010SK1	62570	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Nü Zhen Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Nü Zhen Zi*.
- 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
PhytoComm	Nü Zhen Zi	G138H0345721	62213 [†]	20
PhytoComm	Nü Zhen Zi	G138H0345721	62214 [†]	20
PhytoComm	Nü Zhen Zi	G138H0345821	62343 [†]	20
PhytoComm	Nü Zhen Zi	G138H0345821	62344 [†]	20
PhytoComm	Nü Zhen Zi	G138HS010SK1	62569 [†]	20
PhytoComm	Nü Zhen Zi	G138HS010SK1	62570 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Nü Zhen Zi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Nü Zhen Zi	G138H0345421	1
Phytocomm	Nü Zhen Zi	420319901	1
PhytoComm	Nü Zhen Zi	G138H0345421	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Nü Zhen Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Nü Zhen Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	19 240
Type B	0	120	0	9797
Type C	0	0	3	854

The substance/substance group *Nü Zhen Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9281 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8280 %)	n/a (n/a)

[†]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*.

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Nü Zhen Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yin Chen Hao	8.94	—
Qiang Huo	11.56	—
Dan Zhu Ye	16.43	—
Sang Ye	16.61	—
Xi Xian Cao	17.24	—
Shan Yao	17.44	—
Gou Teng	18.49	—
Yi Mu Cao	18.97	—
Xin Yi	19.01	—
Du Zhong	19.61	—
Huang Bo	20.66	—
Jing Jie	22.93	—
Pu Gong Ying	22.98	—
Qing Pi	23.67	—
Hong Jing Tian	23.68	—
Mao Dong Qing	23.74	—
Wu Mei	24.14	—
Sha Ren	24.24	—
Wu Zhu Yu	24.38	—
Huang Lian	26.82	—
Jiang Huang	27.13	—
Yu Jin	27.22	—
Dan Shen	27.23	—
Tu Fu Ling	27.42	—
Xu Duan	27.77	—
Gui Zhi	27.96	—
Wu Wei Zi	29.68	—
Zhi Ke	29.85	—
Sang Ji Shend	29.86	—
Hou Po	30.10	—
Hu Zhang	30.20	—
He Huan Pi	30.50	—
Jiao Gu Lan	31.44	—
Gu Sui Bu	32.01	—
Sang Bai Pi	32.14	—
Ling Zhi	32.25	—
Xian He Cao	32.28	—
Fu Zi	32.49	—
Hong Hua	33.29	—
Yin Yang Huo	33.46	—
Ye Jiao Teng	34.15	—

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Substanz	Distance in main model	Distance in second-stage model
Han Lian Cao	34.74	—
Bai Xian Pi	34.75	—
Wang Bu Liu Xing	34.96	—
Huang Bai	35.37	—
Jin Yin Hua	35.59	—
Zhi Shi	35.68	—
Di Gu Pi	35.91	—
Ma Huang	35.95	—
Cang Er Zi	36.45	—
Bai Hua She She Cao	37.05	—
He Shou Wu	37.13	—
Dan Dou Chi	37.27	—
Zi Hua Di Ding	37.29	—
Bu Gu Zhi	37.32	—
Wu Yao	39.59	—
Chai Hu	41.10	—
Pi Pa Ye	41.29	—
Ge Gen	41.29	—
Shan Yu Rou	41.71	—
Ku Shen	41.81	—
Chuan Xiong	41.82	—
Fang Feng	41.90	—
Wu Jia Pi	42.06	—
Yan Hu Suo	42.12	—
Xia Ku Cao	42.79	—
Lian Qiao	42.83	—
Qing Hao	43.53	—
Chen Pi	43.55	—
Bai Shao Yao	44.56	—
Rou Cong Rong	45.25	—
Jin Qian Cao	45.46	—
Ren Dong Teng	45.67	—
Gua Lou	46.07	—
Mang Xiao	46.08	—
Ji Li	46.97	—
Lian Zi	47.68	—
E Zhu	47.80	—
Zhi Zi	48.76	—
Che Qian Zi	49.49	—
Cang Zhu	49.69	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Nü Zhen Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62214	62214	0.00	8.94
62570	62570	0.00	16.62
62213	62213	0.00	9.14
62569	62569	0.00	16.61
62343	62343	0.00	11.56
62344	62344	0.00	12.02

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 2.3-2020-05

Validated substance/substance group **Pi Pa Ye**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60201-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pi Pa Ye; Eriobotryae japonicae folium

Special notes

When selecting the *Pi Pa Ye* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Pi Pa Ye	1	0	1

Second-stage model

For differentiation of the substance/substance group *Pi Pa Ye* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pi Pa Ye*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Pi Pa Ye	G099HS166RP1	62451	40	from supplier
PhytoComm	Pi Pa Ye	G099HS166RP1	62452	40	from supplier

Validation samples

A total of 30 254 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 *Pi Pa Ye*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Pi Pa Ye*.
- 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
PhytoComm	Pi Pa Ye	G099HS166RP1	62451 [†]	20
PhytoComm	Pi Pa Ye	G099HS166RP1	62452 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Pi Pa Ye*.
- 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
Phytocomm	Pi Pa Ye	G099H0832221	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pi Pa Ye* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pi Pa Ye* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	2	79	1	19 398
Type B	3	32	8	9874
Type C	0	0	1	856

The substance/substance group *Pi Pa Ye* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9921 % (> 99.9737 %)	98.7500 % (> 95.0000 %)
Type B	99.9763 % (> 99.9405 %)	80.0000 % (> 72.5000 %)
Type C	100.0000 % (> 98.8367 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pi Pa Ye* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Shan Yao	4.21	—
Lian Qiao	5.90	—
Fu Zi	6.73	—
Ren Dong Teng	7.41	—
Ji Li	8.13	—
Gua Lou	8.73	—
Chuan Xiong	8.90	—
Bai Zi Ren	9.47	—
Shen Qu	9.56	—
Tian Hua Fen	9.86	—
Huo Ma Ren	9.90	—
Cang Zhu	10.32	—
Chen Pi	10.72	—
Bai Shao Yao	11.35	—
Jin Yin Hua	12.02	—
San Qi	12.05	—
Zhe Bei Mu	12.55	—
Yuan Zhi	12.71	—
Hou Po	13.15	—
Tai Zi Shen	13.48	—
Jiao Gu Lan	13.70	—
Lian Zi	13.96	—
He Huan Pi	15.01	—
Fu Ling	15.30	—
Dan Shen	15.89	—
Ling Zhi	16.43	—
Ye Jiao Teng	16.98	—
Mao Dong Qing	17.28	—
Yu Zhu	17.29	—
Gou Qi Zi	17.41	—
Ji Xue Teng	17.68	—
Tao Ren	17.80	—
Dang Shen	17.83	—
Dang Gui Wei	17.93	—
Hong Jing Tian	18.24	—
Di Gu Pi	18.27	—
Dang Gui	18.30	—
Chai Hu	18.37	—
Che Qian Zi	18.37	—
Gou Teng	18.47	—
Ci Wu Jia	18.59	—
Zhu Ru	18.62	—
Tu Fu Ling	18.65	—
Yan Hu Suo	19.70	—
Wu Wei Zi	19.76	—
Sheng Jiang	20.12	—
Shan Yu Rou	20.63	—
Gui Zhi	20.71	—
Yin Yang Huo	20.91	—
Dan Dou Chi	21.00	—
Yu Jin	21.40	—
Da Zao	22.21	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Xian Pi	22.22	—
Ma Huang	22.35	—
Mu Dan Pi	22.80	—
Ban Xia (Jiang)	23.03	—
Yi Yi Ren	23.10	—
Qiang Huo	23.85	—
Suan Zao Ren	24.05	—
Zhi Ke	24.24	—
Fo Shou	24.24	—
Rou Gui	24.63	—
Fu Xiao Mai	25.74	—
Qing Pi	25.79	—
Chuang Mu Xiang	26.03	—
Ma Huang Gen	26.85	—
Huang Qin	27.14	—
Long Yan Rou	27.54	—
Zhi Mu	29.28	—
Gan Cao	29.67	—
Tian Men Dong	29.82	—
Zi Hua Di Ding	31.69	—
Bai Zhu	31.86	—
Sang Zhi	33.04	—
Huang Lian	33.54	—
Du Zhong	34.31	—
Chi Shao (Yao)	36.19	—
Cang Er Zi	39.41	—
Fu Shen	39.58	—
Jie Geng	39.93	—
Mang Xiao	41.64	—
Chuan Lian Zi	43.33	—
Huang Bai	44.98	—
Sang Ye	46.81	—
Hong Hua	48.37	—
Bai Mao Gen	49.67	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pi Pa Ye* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62452	62452	0.00	4.21
62451	62451	0.00	4.31

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 2.3-2020-05

Validated substance/substance group **Pu Gong Ying**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50358-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pu Gong Ying; Taraxaci mongolici herba cum radice

Special notes

When selecting the *Pu Gong Ying* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Pu Gong Ying	3	0	1

Second-stage model

For differentiation of the substance/substance group *Pu Gong Ying* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pu Gong Ying*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Pu Gong Ying	G239H1315623	62119	40	from supplier
PhytoComm	Pu Gong Ying	G239H1315623	62120	40	from supplier
PhytoComm	Pu Gong Ying	G239H1315623	62163	40	from supplier
PhytoComm	Pu Gong Ying	G239H1315623	62164	40	from supplier
PhytoComm	Pu Gong Ying	G239HS308RN1	62263	40	from supplier
PhytoComm	Pu Gong Ying	G239HS308RN1	62264	40	from supplier
PhytoComm	Pu Gong Ying	G239HS308SH1	62635	40	from supplier
PhytoComm	Pu Gong Ying	G239HS308SH1	62636	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 8 reference samples from the substance/substance group *Pu Gong Ying*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 160 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 8 reference samples from the substance/substance group *Pu Gong Ying*.
- 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
PhytoComm	Pu Gong Ying	G239H1315623	62119 [†]	20
PhytoComm	Pu Gong Ying	G239H1315623	62120 [†]	20
PhytoComm	Pu Gong Ying	G239H1315623	62163 [†]	20
PhytoComm	Pu Gong Ying	G239H1315623	62164 [†]	20

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Supplier	Substance	Batch	Sample ID	Spectra
PhytoComm	Pu Gong Ying	G239HS308RN1	62263 [†]	20
PhytoComm	Pu Gong Ying	G239HS308RN1	62264 [†]	20
PhytoComm	Pu Gong Ying	G239HS308SH1	62635 [†]	20
PhytoComm	Pu Gong Ying	G239HS308SH1	62636 [†]	20

- 9757 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 4 *Apo-Ident* customers from 1 batches from the substance/substance group *Pu Gong Ying*.
- 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
Phytocomm	Pu Gong Ying	G239H1315321	5
PhytoComm	Pu Gong Ying	G239H1315321	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pu Gong Ying* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pu Gong Ying* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 160
Type B	0	159	1	9757
Type C	3	0	6	848

The substance/substance group *Pu Gong Ying* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

[†]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*.

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9280 %)	99.3750 % (> 97.5000 %)
Type C	99.7121 % (> 99.1250 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pu Gong Ying* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Huang Lian	7.46	—
Sang Ye	7.69	—
Xin Yi	8.80	—
Tu Fu Ling	9.24	—
Xi Xian Cao	11.44	—
Nü Zhen Zi	14.75	—
Shan Yao	14.75	—
Jin Qian Cao	17.56	—
Gui Zhi	18.39	—
Dan Shen	18.78	—
Yin Chen Hao	18.94	—
Hu Zhang	20.11	—
Fu Zi	20.37	—
Han Lian Cao	20.64	—
Jiang Huang	21.01	—
Zhi Ke	21.69	—
Gou Teng	21.94	—
Du Zhong	22.52	—
Qiang Huo	25.09	—
Jing Jie	25.41	—
Mao Dong Qing	25.49	—
Jiao Gu Lan	25.59	—
Sha Ren	26.26	—
Yu Jin	26.45	—
Xuan Shen	27.19	—
Dan Zhu Ye	27.78	—
Wu Jia Pi	27.90	—
Qing Hao	28.08	—
Bai Hua She She Cao	28.24	—
Wu Mei	29.14	—
Hong Jing Tian	29.41	—
Ma Huang	30.02	—
Hou Po	30.49	—
Qing Pi	30.74	—
Wu Yao	30.80	—
Ye Jiao Teng	31.54	—

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Substanz	Distance in main model	Distance in second-stage model
Wu Wei Zi	31.60	—
Xiang Fu	31.65	—
Yi Mu Cao	31.94	—
Sang Ji Shend	31.95	—
Yin Yang Huo	32.38	—
Yu Xing Cao	32.64	—
Huang Bai	32.96	—
Zhi Shi	33.53	—
Guang Huo Xiang	33.85	—
Cang Er Zi	35.42	—
Yan Hu Suo	36.06	—
Bai Xian Pi	37.38	—
Jin Yin Hua	37.54	—
(Shi) Chang Pu	37.63	—
Che Qian Zi	37.90	—
Gua Lou	38.67	—
Zi Hua Di Ding	38.77	—
Bai Mao Gen	39.03	—
Mu Dan Pi	39.24	—
Di Gu Pi	39.35	—
Huang Bo	39.41	—
Chai Hu	39.74	—
Dan Dou Chi	39.88	—
He Huan Pi	40.08	—
Xu Duan	40.87	—
Wang Bu Liu Xing	40.95	—
Ge Gen	41.21	—
Xian He Cao	42.19	—
Chi Shao (Yao)	42.21	—
Xia Ku Cao	42.23	—
E Zhu	42.33	—
Pi Pa Ye	42.43	—
Niu Bang Zi	43.08	—
Mang Xiao	43.21	—
Hong Hua	43.63	—
Chuan Xiong	43.79	—
Gu Sui Bu	43.93	—
Lian Zi	45.01	—
(Sheng) Di Huang	45.06	—
Bai Shao Yao	45.51	—
Gan Cao	45.88	—
Shan Yu Rou	46.22	—
Ji Li	46.32	—
Wu Zhu Yu	46.40	—
Ren Dong Teng	47.18	—
Du Huo	47.55	—
Lian Qiao	47.58	—
Shu Di (Huang)	47.83	—
Huang Qin	47.88	—
Ai Ye	47.97	—
Gou Qi Zi	48.00	—
Hua Shi	48.12	—
(Bai) Dou Kou	48.41	—
Sang Bai Pi	48.52	—
Ling Zhi	49.64	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pu Gong Ying* is separated from critical neighbours in a second-stage model,

all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62164	62164	0.00	17.56
62263	62263	0.00	7.97
62119	62119	0.00	18.82
62163	62163	0.00	17.61
62120	62120	0.00	18.94
62636	62636	0.00	7.77
62635	62635	0.00	7.69
62264	62264	0.00	7.46

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 2.3-2020-05

Validated substance/substance group **Qiang Huo**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60109-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Qiang Huo; Notopterygii rhizoma et radix

Special notes

When selecting the *Qiang Huo* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Qiang Huo	2	0	2

Second-stage model

For differentiation of the substance/substance group *Qiang Huo* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Qiang Huo*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Qiang Huo	G172H0840721	62361	40	from supplier
PhytoComm	Qiang Huo	G172H0840721	62362	40	from supplier
PhytoComm	Qiang Huo	G172HS154SL1	62719	40	from supplier
PhytoComm	Qiang Huo	G172HS154SL1	62720	40	from supplier

Validation samples

A total of 30 254 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 *Qiang Huo*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Qiang Huo*.
- 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
PhytoComm	Qiang Huo	G172H0840721	62361 [†]	20
PhytoComm	Qiang Huo	G172H0840721	62362 [†]	20
PhytoComm	Qiang Huo	G172HS154SL1	62719 [†]	20
PhytoComm	Qiang Huo	G172HS154SL1	62720 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Qiang Huo*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Qiang Huo	G172H0840321	1
Phytocomm	Qiang Huo	g172h0841321	1
PhytoComm	Qiang Huo	G172H0840321	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Qiang Huo* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Qiang Huo* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	78	2	9837
Type C	2	1	2	852

The substance/substance group *Qiang Huo* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	97.5000 % (> 93.7500 %)
Type C	99.8450 % (> 99.2590 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Qiang Huo* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Mao Dong Qing	6.22	—
Yu Jin	7.74	—
Ling Zhi	7.78	—
Hou Po	7.94	—
Du Zhong	8.90	—
Bai Xian Pi	9.53	—
Dan Dou Chi	10.26	—
Yin Yang Huo	10.29	—
Qing Pi	11.75	—
Nü Zhen Zi	12.21	—
Yi Mu Cao	13.35	—
Ye Jiao Teng	13.49	—
Zi Hua Di Ding	13.66	—
Chai Hu	13.68	—
Huang Bo	14.60	—
Shen Qu	15.26	—
Lian Zi	15.75	—
Jiao Gu Lan	15.79	—
Dan Shen	16.02	—
Mu Dan Pi	16.31	—
Ji Li	16.40	—
Shan Yao	16.97	—
Pi Pa Ye	17.66	—
Hong Jing Tian	17.73	—
Che Qian Zi	17.75	—
Yuan Zhi	17.77	—
Yin Chen Hao	18.08	—
Yan Hu Suo	18.36	—
Ren Dong Teng	18.60	—
Gui Zhi	19.40	—
He Huan Pi	19.46	—
Lian Qiao	20.05	—
Huang Bai	20.65	—
Chuan Xiong	20.69	—
Jin Yin Hua	21.48	—
Xu Duan	22.65	—
Ji Xue Teng	22.69	—
Zhi Ke	22.87	—
Gu Sui Bu	23.11	—
Ma Huang	23.20	—
Huang Lian	23.39	—
Wu Zhu Yu	23.52	—
Di Gu Pi	23.58	—
Wu Wei Zi	23.86	—
Bai Shao Yao	24.53	—

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Substanz	Distance in main model	Distance in second-stage model
Fu Zi	25.06	—
Sha Ren	25.75	—
Gou Teng	26.17	—
Gua Lou	26.26	—
Sang Ji Shend	26.32	—
Wu Yao	26.32	—
Tu Fu Ling	26.61	—
Dan Zhu Ye	27.26	—
Sheng Jiang	27.85	—
Chen Pi	27.96	—
Cang Zhu	28.05	—
Rou Gui	28.14	—
Ma Huang Gen	28.79	—
Gou Qi Zi	30.11	—
Pu Gong Ying	30.15	—
Sang Bai Pi	30.22	—
Fang Feng	31.24	—
Hu Zhang	31.24	—
Xian He Cao	31.46	—
Jiang Huang	32.37	—
Ju Hua	32.48	—
Huo Ma Ren	32.48	—
Wang Bu Liu Xing	33.73	—
Xi Xian Cao	33.98	—
Sang Ye	34.24	—
Zhe Bei Mu	35.61	—
Yi Yi Ren	36.09	—
Fu Ling	36.11	—
Xiang Fu	36.17	—
Tao Ren	36.40	—
Bu Gu Zhi	36.62	—
Jing Jie	36.63	—
Xia Ku Cao	36.94	—
Cang Er Zi	37.01	—
Tian Hua Fen	37.02	—
Ku Shen	37.37	—
Ban Zhi Lian	37.78	—
Suan Zao Ren	38.38	—
Sang Zhi	38.78	—
Chi Shao (Yao)	39.18	—
Mang Xiao	39.40	—
Shan Yu Rou	39.91	—
Tai Zi Shen	39.97	—
Ge Gen	39.99	—
Bai Zi Ren	40.31	—
Wu Mei	41.46	—
He Shou Wu	41.53	—
Bai Zhu	41.55	—
Zi Su Zi	41.84	—
Chuan Lian Zi	41.84	—
Bai Hua She She Cao	41.91	—
Jie Geng	42.21	—
Da Zao	42.28	—
E Zhu	42.78	—
San Qi	43.30	—
Huang Qin	43.40	—
(Bai) Dou Kou	43.41	—
Rou Cong Rong	43.63	—
Chuang Mu Xiang	43.65	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Bian Dou	43.81	—
Ci Wu Jia	43.83	—
Yu Zhu	44.38	—
Zhi Shi	44.53	—
(Shi) Chang Pu	44.59	—
Hong Hua	44.71	—
Xin Yi	44.76	—
Bai Mao Gen	45.27	—
Dang Shen	45.37	—
Ban Xia (Jiang)	45.52	—
Dang Gui	45.79	—
Zhu Ru	45.79	—
Han Lian Cao	46.23	—
Fu Shen	46.50	—
Long Yan Rou	47.15	—
Xie Bai	48.97	—
Dang Gui Wei	49.29	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Qiang Huo* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62361	62361	0.00	12.21
62719	62719	0.00	6.95
62362	62362	0.00	12.97
62720	62720	0.00	6.22

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 2.3-2020-05

Validated substance/substance group **Qin Jiao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60222-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Qin Jiao; Gentianae macrophyllae radix

Special notes

When selecting the *Qin Jiao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Qin Jiao	1	0	2

Second-stage model

For differentiation of the substance/substance group *Qin Jiao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Qin Jiao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Qin Jiao	G113H1059921	62735	40	from supplier
PhytoComm	Qin Jiao	G113H1059921	62736	40	from supplier

Validation samples

A total of 30 254 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 *Qin Jiao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Qin Jiao*.
- 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
PhytoComm	Qin Jiao	G113H1059921	62735 [†]	20
PhytoComm	Qin Jiao	G113H1059921	62736 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Qin Jiao*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
PhytoComm	Qin Jiao	G113H1059121	1
PhytoComm	Qin Jiao	G113H1059521	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Qin Jiao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Qin Jiao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	2	0	2	853

The substance/substance group *Qin Jiao* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.8450 % (> 99.2600 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Qin Jiao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Zhu	12.40	—
Huang Qi	12.84	—
Jie Geng	15.03	—
Sang Zhi	18.28	—
Di Gu Pi	18.92	—
Bai Mao Gen	21.19	—
(Huai) Niu Xi	21.29	—
Mu Dan Pi	21.56	—
Dang Gui	24.21	—
Tian Hua Fen	24.39	—
Ba Ji Tian	25.21	—
Chi Shao (Yao)	25.53	—
Du Huo	25.95	—
Yuan Zhi	27.26	—
Qing Pi	29.27	—
Lai Fu Zi	29.43	—
Mai Men Dong	29.76	—
Gua Lou	30.30	—
Sha Shen (Bei)	30.85	—
Mang Xiao	31.45	—
Sheng Jiang	32.36	—
San Qi	32.70	—
Bai He	32.89	—
Fang Feng	33.35	—
(Shi) Chang Pu	33.52	—
Chuan Lian Zi	35.84	—
Da Zao	36.02	—
E Zhu	36.31	—
Shan Yao	37.00	—
Xiang Fu	37.06	—
Mai Ya	37.21	—
Ji Li	37.64	—
Ban Zhi Lian	39.50	—
Chen Pi	40.14	—
Cang Er Zi	40.52	—
Xie Bai	42.58	—
Tu Fu Ling	43.10	—
Zi Su Zi	43.19	—
Ku Shen	43.82	—
Long Dan (Cao)	43.98	—
Lian Zi	44.88	—
Zhi Ke	45.01	—
Bai Shao Yao	45.19	—
Gui Zhi	46.91	—
Yan Hu Suo	47.04	—
Niu Bang Zi	47.98	—
Bai Bian Dou	48.04	—
Tian Men Dong	48.33	—
Chai Hu	48.48	—
Bai Xian Pi	48.96	—
Xian He Cao	49.01	—
Jiang Huang	49.25	—

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Substanz	Distance in main model	Distance in second-stage model
Gan Cao	49.87	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Qin Jiao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62735	62735	0.00	13.34
62736	62736	0.00	12.40

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 2.3-2020-05

Validated substance/substance group **Qing Hao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60198-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Qing Hao; Artemisiae apiacae herba

Special notes

When selecting the *Qing Hao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Qing Hao	1	0	0

Second-stage model

For differentiation of the substance/substance group *Qing Hao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Qing Hao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Qing Hao	G031H0810821	62769	40	from supplier
PhytoComm	Qing Hao	G031H0810821	62770	40	from supplier

Validation samples

A total of 30 254 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 *Qing Hao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Qing Hao*.
- 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
PhytoComm	Qing Hao	G031H0810821	62769 [†]	20
PhytoComm	Qing Hao	G031H0810821	62770 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Qing Hao*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Qing Hao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Qing Hao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

The substance/substance group *Qing Hao* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Qing Hao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Gou Teng	11.86	—
Pu Gong Ying	19.67	—
Sha Ren	27.02	—
Nü Zhen Zi	36.86	—
Xuan Shen	37.18	—
Jing Jie	37.63	—
Yin Chen Hao	38.11	—
Huang Bo	39.61	—
Dan Zhu Ye	42.36	—
Yi Mu Cao	42.87	—
Wu Jia Pi	44.00	—
Zhi Shi	45.21	—
Jin Qian Cao	47.14	—
Xin Yi	47.44	—
Sang Ji Shend	48.91	—
Hua Shi	50.36	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Qing Hao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62770	62770	0.00	12.02
62769	62769	0.00	11.86

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 2.3-2020-05

Validated substance/substance group **Qing Pi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50371-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Qing Pi; Citri reticulatae viride pericarpium

Special notes

When selecting the *Qing Pi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Qing Pi	2	0	2

Second-stage model

For differentiation of the substance/substance group *Qing Pi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Qing Pi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Qing Pi	G074H0809821	62379	40	from supplier
PhytoComm	Qing Pi	G074H0809821	62380	40	from supplier
PhytoComm	Qing Pi	G074HS361SK1	62671	40	from supplier
PhytoComm	Qing Pi	G074HS361SK1	62672	40	from supplier

Validation samples

A total of 30 254 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 *Qing Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Qing Pi*.
- 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
PhytoComm	Qing Pi	G074H0809821	62379 [†]	20
PhytoComm	Qing Pi	G074H0809821	62380 [†]	20
PhytoComm	Qing Pi	G074HS361SK1	62671 [†]	20
PhytoComm	Qing Pi	G074HS361SK1	62672 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Qing Pi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Qing Pi	g074h100713	1
PhytoComm	Qing Pi	G074H0809621	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Qing Pi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Qing Pi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	2	855

The substance/substance group *Qing Pi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8302 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Qing Pi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Huang Bai	9.07	—
Wu Wei Zi	10.84	—
Zhi Ke	12.12	—
Gua Lou	12.51	—
Niu Bang Zi	13.98	—
Sang Zhi	14.08	—
Sang Ye	14.51	—
Shan Yao	14.96	—
Di Gu Pi	15.84	—
Jiao Gu Lan	15.92	—
Zi Hua Di Ding	16.00	—
Qiang Huo	16.29	—
Du Zhong	16.90	—
Mao Dong Qing	17.96	—
Chai Hu	18.11	—
Jin Yin Hua	19.44	—
Xiang Fu	20.26	—
Hou Po	20.98	—
Dan Shen	20.98	—
(Huai) Niu Xi	21.31	—
Ma Huang	21.45	—
Hong Hua	21.73	—
Huang Lian	21.87	—
Hong Jing Tian	22.14	—
Shan Yu Rou	22.19	—
Yan Hu Suo	22.75	—
Yin Yang Huo	23.52	—
Wu Mei	23.56	—
Jie Geng	23.69	—
Du Huo	23.83	—
Ku Shen	24.29	—
Bai Mao Gen	24.51	—
Tian Hua Fen	24.71	—
Cang Er Zi	24.91	—
Ye Jiao Teng	24.94	—
(Shi) Chang Pu	25.28	—
Gui Zhi	25.31	—
Bai Zhu	25.34	—
Pi Pa Ye	25.65	—
Chuan Xiong	26.72	—
Lian Qiao	27.60	—
Cang Zhu	27.83	—
Mu Dan Pi	27.97	—
Ren Dong Teng	27.98	—
Chi Shao (Yao)	28.28	—
Huang Qi	29.03	—
Bai Shao Yao	29.12	—
Gou Qi Zi	29.44	—

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Substanz	Distance in main model	Distance in second-stage model
Xi Xian Cao	29.54	—
Pu Gong Ying	30.36	—
Ji Li	30.50	—
Sha Shen (Bei)	30.64	—
Yi Mu Cao	30.96	—
Dan Dou Chi	31.16	—
Bai Xian Pi	31.36	—
Jiang Huang	31.71	—
Che Qian Zi	31.75	—
He Huan Pi	31.97	—
Yu Jin	32.30	—
Fu Zi	32.38	—
Wu Yao	32.41	—
Xie Bai	33.03	—
E Zhu	33.12	—
Tu Fu Ling	33.15	—
Ling Zhi	34.53	—
Lian Zi	35.52	—
(Bai) Dou Kou	35.53	—
Sheng Jiang	35.56	—
Mang Xiao	35.77	—
Huang Qin	35.95	—
Qin Jiao	36.09	—
Fang Feng	36.58	—
Yuan Zhi	36.66	—
Suan Zao Ren	36.88	—
Zi Su Zi	36.96	—
Dang Gui	37.42	—
Gan Cao	37.67	—
Nü Zhen Zi	37.72	—
Tao Ren	38.41	—
Sha Ren	38.74	—
Ji Xue Teng	39.66	—
Dong Gua Zi	39.74	—
San Qi	39.95	—
Lai Fu Zi	40.23	—
Chen Pi	40.27	—
Dang Shen	40.79	—
Zhe Bei Mu	41.44	—
Tai Zi Shen	41.93	—
Huo Ma Ren	42.41	—
Bai Zi Ren	42.60	—
Shen Qu	42.72	—
Gou Teng	43.36	—
Ban Zhi Lian	43.86	—
Xin Yi	44.37	—
Chuan Lian Zi	44.84	—
Huang Bo	44.89	—
Yu Zhu	44.98	—
Xian He Cao	46.06	—
Ju Hua	47.03	—
Chuang Mu Xiang	47.36	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Qing Pi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62380	62380	0.00	13.11
62671	62671	0.00	9.07
62672	62672	0.00	10.57
62379	62379	0.00	12.51

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 2.3-2020-05

Validated substance/substance group **Ren Dong Teng**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60104-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ren Dong Teng; Lonicerae japonicae caulis

Special notes

When selecting the *Ren Dong Teng* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ren Dong Teng	1	0	0

Second-stage model

For differentiation of the substance/substance group *Ren Dong Teng* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ren Dong Teng*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ren Dong Teng	G297HS144SK1	62695	40	from supplier
PhytoComm	Ren Dong Teng	G297HS144SK1	62696	40	from supplier

Validation samples

A total of 30 254 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 *Ren Dong Teng*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Ren Dong Teng*.
- 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
PhytoComm	Ren Dong Teng	G297HS144SK1	62695 [†]	20
PhytoComm	Ren Dong Teng	G297HS144SK1	62696 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Ren Dong Teng*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ren Dong Teng* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ren Dong Teng* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

The substance/substance group *Ren Dong Teng* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ren Dong Teng* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Ling Zhi	5.00	—
Shen Qu	6.05	—
Bai Xian Pi	7.04	—
Ye Jiao Teng	8.41	—
Dan Dou Chi	8.91	—
Ji Li	9.13	—
Ji Xue Teng	9.24	—
Yu Jin	9.40	—
Lian Zi	9.59	—
Chai Hu	9.75	—
Rou Gui	10.01	—
Yuan Zhi	10.13	—
Huo Ma Ren	10.17	—
Gou Teng	10.94	—
Ma Huang Gen	11.11	—
Chuan Xiong	11.34	—
Hou Po	11.62	—
Shan Yao	11.79	—
Mao Dong Qing	11.81	—
Lian Qiao	12.30	—
Che Qian Zi	12.41	—
Pi Pa Ye	12.44	—
Bai Shao Yao	12.81	—
Tu Fu Ling	12.83	—
He Huan Pi	12.89	—
Yin Yang Huo	13.41	—
Dan Shen	13.51	—
Fu Ling	13.63	—
Yan Hu Suo	14.07	—
Fu Zi	14.08	—
Tian Hua Fen	14.19	—
Sheng Jiang	14.60	—
Chen Pi	15.31	—
Gui Zhi	15.80	—
Yi Yi Ren	17.65	—
Tai Zi Shen	17.85	—
Jiao Gu Lan	17.90	—
Tao Ren	18.19	—
Gua Lou	18.26	—
Fo Shou	18.44	—
Zhe Bei Mu	18.50	—
Qiang Huo	18.64	—
Bai Zi Ren	18.75	—
Hong Jing Tian	19.27	—
Jin Yin Hua	19.60	—
Ma Huang	20.37	—
Ci Wu Jia	21.48	—
Di Gu Pi	22.24	—
Ban Xia (Jiang)	23.24	—
Cang Zhu	23.73	—
Fu Xiao Mai	23.80	—
Fu Shen	24.34	—
Wu Wei Zi	25.33	—
Da Zao	25.84	—
Zhu Ru	25.87	—
Qing Pi	26.00	—
Du Zhong	26.53	—
Tian Men Dong	26.65	—
Yu Zhu	27.65	—

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Substanz	Distance in main model	Distance in second-stage model
Suan Zao Ren	27.68	—
Zhi Ke	27.80	—
Long Yan Rou	28.17	—
Mu Dan Pi	28.54	—
San Qi	29.06	—
Huang Lian	30.57	—
Dang Gui Wei	30.93	—
Gou Qi Zi	31.23	—
Dang Shen	32.67	—
Zi Hua Di Ding	33.31	—
Dang Gui	33.71	—
Huang Qin	36.39	—
Sang Zhi	37.54	—
Shan Yu Rou	37.68	—
Mang Xiao	38.12	—
Chuang Mu Xiang	40.46	—
Jie Geng	40.46	—
Huang Bai	42.55	—
Chi Shao (Yao)	43.60	—
Chuan Lian Zi	43.62	—
Bai Zhu	45.21	—
Gan Cao	46.75	—
Ban Zhi Lian	46.77	—
Cang Er Zi	48.87	—
Zhi Mu	49.08	—
Zi Su Zi	49.10	—
Wang Bu Liu Xing	50.33	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ren Dong Teng* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62695	62695	0.00	7.04
62696	62696	0.00	5.00

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group	Rou Cong Rong
Substance class	TCM - Granulated herbal extracts (PhytoComm)
Report date	25/11/2020
Report number	60182-2020-11-25
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Rou Cong Rong; Cistanchis herba

Special notes

When selecting the *Rou Cong Rong* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Rou Cong Rong	1	0	0

Second-stage model

For differentiation of the substance/substance group *Rou Cong Rong* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Rou Cong Rong*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Rou Cong Rong	G072HS108SG1	62667	40	from supplier
PhytoComm	Rou Cong Rong	G072HS108SG1	62668	40	from supplier

Validation samples

A total of 30 254 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 *Rou Cong Rong*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Rou Cong Rong*.
- 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
PhytoComm	Rou Cong Rong	G072HS108SG1	62667 [†]	20
PhytoComm	Rou Cong Rong	G072HS108SG1	62668 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Rou Cong Rong*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Rou Cong Rong* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Rou Cong Rong* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

The substance/substance group *Rou Cong Rong* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Rou Cong Rong* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Bai Hua She She Cao	16.94	—
Hu Zhang	17.03	—
Han Lian Cao	20.24	—
Zhi Shi	20.39	—
Xin Yi	21.18	—
Pu Gong Ying	24.18	—
Sha Ren	24.63	—
Huang Lian	24.66	—
Dan Zhu Ye	24.82	—
Sang Ye	25.33	—
Fu Zi	25.75	—
Huang Bo	27.84	—
Yi Mu Cao	28.40	—
Gou Teng	28.59	—
Gu Sui Bu	29.40	—
Xi Xian Cao	29.49	—
Xia Ku Cao	30.54	—
Gui Zhi	31.66	—
Xu Duan	32.37	—
Nü Zhen Zi	32.48	—
Sang Ji Shend	32.61	—
Jiang Huang	33.10	—
Tu Fu Ling	33.31	—
Qiang Huo	34.32	—
Shan Yao	35.12	—
Wu Zhu Yu	37.07	—
Ju Hua	37.74	—
Wu Yao	40.91	—
He Huan Pi	41.33	—
Wu Wei Zi	42.23	—
Cang Er Zi	45.08	—
Xian He Cao	45.31	—
Jing Jie	45.92	—
Qing Pi	46.78	—
Gan Cao	48.31	—
Wu Mei	48.82	—
Ma Huang	49.80	—
Yu Jin	50.82	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Rou Cong Rong* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62667	62667	0.00	16.94
62668	62668	0.00	17.49

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 2.3-2020-05

Validated substance/substance group **Rou Gui**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60169-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Rou Gui; Cinnamomi cassiae cortex

Special notes

When selecting the *Rou Gui* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Rou Gui	2	0	3

Second-stage model

For differentiation of the substance/substance group *Rou Gui* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Rou Gui*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Rou Gui	G069HS204RN1	62271	40	from supplier
PhytoComm	Rou Gui	G069HS204RN1	62272	40	from supplier
PhytoComm	Rou Gui	G069HS204RM1	62443	40	from supplier
PhytoComm	Rou Gui	G069HS204RM1	62444	40	from supplier

Validation samples

A total of 30 254 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 *Rou Gui*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Rou Gui*.
- 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
PhytoComm	Rou Gui	G069HS204RN1	62271 [†]	20
PhytoComm	Rou Gui	G069HS204RN1	62272 [†]	20
PhytoComm	Rou Gui	G069HS204RM1	62443 [†]	20
PhytoComm	Rou Gui	G069HS204RM1	62444 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 5 *Apo-Ident* customers from 4 batches from the substance/substance group *Rou Gui*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Rou Gui	H0617022	1
Phytocomm	Rou Gui	G069H0617323	1
Phytocomm	Rou Gui	g069h0617123	1
PhytoComm	Rou Gui	G069H0617123	2
PhytoComm	Rou Gui	G069H0617323	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Rou Gui* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Rou Gui* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	2	159	1	19 318
Type B	7	76	4	9830
Type C	1	0	6	850

The substance/substance group *Rou Gui* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9842 % (> 99.9658 %)	99.3750 % (> 97.5000 %)
Type B	99.9051 % (> 99.8692 %)	95.0000 % (> 91.2500 %)
Type C	99.7674 % (> 99.1804 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Rou Gui* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ma Huang Gen	6.88	—
Gui Zhi	6.90	—
Sheng Jiang	7.56	—
Yi Yi Ren	8.35	—
Gou Teng	8.86	—
Ban Xia (Jiang)	9.08	—
Ji Xue Teng	10.82	—
Fu Shen	10.87	—
Fu Xiao Mai	11.33	—
Di Gu Pi	11.39	—
Fu Ling	11.92	—
He Huan Pi	13.00	—
Fo Shou	13.43	—
Tao Ren	14.00	—
Bai Xian Pi	15.14	—
Ye Jiao Teng	15.68	—
Ci Wu Jia	15.89	—
Tai Zi Shen	15.99	—
Huo Ma Ren	16.70	—
Bai Shao Yao	16.91	—
Zhu Ru	17.10	—
Lian Zi	17.48	—
Ling Zhi	17.72	—
Shen Qu	18.49	—
Bai Zi Ren	18.70	—
Tian Men Dong	18.87	—
Ji Li	19.84	—
Zhe Bei Mu	20.68	—
Long Yan Rou	20.77	—
Da Zao	21.80	—
Chen Pi	22.44	—
Tu Fu Ling	24.10	—
Ren Dong Teng	24.70	—
Gua Lou	24.72	—
Tian Hua Fen	26.42	—
Pi Pa Ye	27.64	—
Chuan Xiong	27.85	—
Yuan Zhi	28.35	—
Yu Jin	29.08	—
Dan Dou Chi	29.20	—
Lian Qiao	30.11	—
Dan Shen	30.84	—
Dang Shen	30.99	—

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Substanz	Distance in main model	Distance in second-stage model
Yan Hu Suo	31.70	—
Shan Yao	32.73	—
Yu Zhu	34.84	—
Zhi Ke	34.90	—
Jiao Gu Lan	35.29	—
Yin Yang Huo	36.90	—
Shan Yu Rou	37.00	—
Ma Huang	37.81	—
Hong Jing Tian	37.83	—
Chai Hu	38.28	—
Fu Zi	38.66	—
Mao Dong Qing	38.67	—
Huang Qin	39.58	—
Mang Xiao	39.60	—
Jin Yin Hua	39.94	—
Cang Zhu	40.53	—
Dang Gui Wei	41.03	—
San Qi	41.40	—
Dang Gui	43.19	—
Wu Wei Zi	43.84	—
Hou Po	46.68	—
Jie Geng	46.79	—
Bai Zhu	47.02	—
Sang Zhi	47.69	—
Qiang Huo	48.58	—
Zhi Mu	49.02	—
Huang Lian	50.33	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Rou Gui* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62272	62272	0.00	6.97
62443	62443	0.00	6.90
62444	62444	0.00	6.88
62271	62271	0.00	7.19

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **San Qi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60415-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

San Qi; Notoginseng radix

Special notes

When selecting the *San Qi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
San Qi	2	0	1

Second-stage model

For differentiation of the substance/substance group *San Qi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *San Qi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	San Qi	G203H0312721	62245	40	from supplier
PhytoComm	San Qi	G203H0312721	62246	40	from supplier
PhytoComm	San Qi	G203HS030SL1	62701	40	from supplier
PhytoComm	San Qi	G203HS030SL1	62702	40	from supplier

Validation samples

A total of 30 254 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 *San Qi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *San Qi*.
- 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
PhytoComm	San Qi	G203H0312721	62245 [†]	20
PhytoComm	San Qi	G203H0312721	62246 [†]	20
PhytoComm	San Qi	G203HS030SL1	62701 [†]	20
PhytoComm	San Qi	G203HS030SL1	62702 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *San Qi*.
- 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
PhytoComm	San Qi	g203h0312021	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *San Qi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *San Qi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	2	0	1	854

The substance/substance group *San Qi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.6512 % (> 99.0695 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *San Qi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chuan Xiong	7.71	—
Lian Qiao	8.88	—
Shan Yao	9.00	—
Yuan Zhi	9.15	—
Dang Shen	10.05	—
Pi Pa Ye	10.10	—
Bai Shao Yao	10.62	—
Shan Yu Rou	11.33	—
Cang Zhu	11.65	—
Bai Zi Ren	11.77	—
Sheng Jiang	12.20	—
Ji Li	12.51	—
Suan Zao Ren	14.73	—
Huo Ma Ren	15.25	—
Jiao Gu Lan	15.26	—
Lai Fu Zi	15.40	—
Zhi Mu	16.06	—
Gua Lou	16.13	—
Jin Yin Hua	16.19	—
Dang Gui	16.35	—
Zhe Bei Mu	16.41	—
Dang Gui Wei	17.19	—
Tian Hua Fen	17.65	—
Lian Zi	17.69	—
Ren Dong Teng	17.89	—
Di Gu Pi	18.21	—
Gou Qi Zi	18.27	—
Shen Qu	18.59	—
Tai Zi Shen	19.20	—
Yu Zhu	19.29	—
Chen Pi	19.50	—
Zi Su Zi	19.72	—
He Huan Pi	19.95	—
Fu Zi	20.31	—
Hou Po	20.37	—
Wu Wei Zi	20.48	—
Mu Dan Pi	20.64	—
Qing Pi	21.20	—
Ye Jiao Teng	21.36	—
Mao Dong Qing	21.36	—
Fu Ling	21.42	—
Zhu Ru	21.67	—
Chuang Mu Xiang	22.04	—
E Zhu	22.84	—
Ling Zhi	22.98	—
Cang Er Zi	23.45	—
Sang Zhi	23.98	—
Chuan Lian Zi	24.10	—

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Substanz	Distance in main model	Distance in second-stage model
Zhi Ke	24.22	—
Gui Zhi	24.38	—
Jie Geng	24.48	—
Ci Wu Jia	24.66	—
Bai Bian Dou	25.91	—
Bai Zhu	25.92	—
Yi Yi Ren	26.52	—
Tao Ren	26.66	—
Dan Shen	26.82	—
Gou Teng	26.87	—
Ji Xue Teng	27.28	—
Tu Fu Ling	27.29	—
Fu Xiao Mai	27.50	—
Ban Xia (Jiang)	29.18	—
Xiang Fu	29.51	—
Mang Xiao	29.51	—
Da Zao	29.57	—
Rou Gui	29.86	—
Che Qian Zi	29.87	—
Yan Hu Suo	29.97	—
Huang Qin	30.29	—
Fo Shou	30.77	—
Mai Ya	30.98	—
Bai He	31.47	—
Qiang Huo	31.57	—
Chai Hu	31.71	—
Bai Xian Pi	31.80	—
Tian Men Dong	32.00	—
Gan Cao	32.26	—
Yu Jin	32.73	—
Ku Shen	32.84	—
Dan Dou Chi	33.12	—
Yin Yang Huo	33.50	—
Long Yan Rou	34.10	—
(Shi) Chang Pu	34.25	—
Hong Jing Tian	34.29	—
Huang Qi	35.38	—
Ma Huang	36.31	—
Jiang Huang	36.85	—
Qin Jiao	37.06	—
Niu Bang Zi	37.37	—
Xie Bai	39.16	—
Ba Ji Tian	39.18	—
Bai Mao Gen	40.39	—
Ma Huang Gen	40.50	—
Mai Men Dong	41.04	—
Du Zhong	41.73	—
Chi Shao (Yao)	42.54	—
Du Huo	42.73	—
Dong Gua Zi	42.77	—
Zi Hua Di Ding	43.08	—
Sha Shen (Bei)	43.54	—
Long Dan (Cao)	43.60	—
Wang Bu Liu Xing	43.63	—
Huang Lian	44.27	—
Fang Feng	46.17	—
(Huai) Niu Xi	46.36	—
Pu Gong Ying	47.33	—
Fu Shen	47.35	—

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Substanz	Distance in main model	Distance in second-stage model
(Bai) Dou Kou	48.85	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *San Qi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62245	62245	0.00	12.21
62246	62246	0.00	12.20
62701	62701	0.00	8.55
62702	62702	0.00	7.71

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 2.3-2020-05

Validated substance/substance group **Sang Bai Pi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50287-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sang Bai Pi; Mori cortex

Special notes

When selecting the *Sang Bai Pi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sang Bai Pi	1	0	2

Second-stage model

For differentiation of the substance/substance group *Sang Bai Pi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sang Bai Pi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Sang Bai Pi	G161H1042822	62471	40	from supplier
PhytoComm	Sang Bai Pi	G161H1042822	62472	40	from supplier

Validation samples

A total of 30 254 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 *Sang Bai Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Sang Bai Pi*.
- 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
PhytoComm	Sang Bai Pi	G161H1042822	62471 [†]	20
PhytoComm	Sang Bai Pi	G161H1042822	62472 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Sang Bai Pi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
PhytoComm	Sang Bai Pi	G161H1042321	1
PhytoComm	Sang Bai Pi	G161H1042321	2
PhytoComm	Sang Bai Pi	G161H1042322	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sang Bai Pi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sang Bai Pi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	1	0	4	852

The substance/substance group *Sang Bai Pi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.7674 % (> 99.1809 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sang Bai Pi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dan Zhu Ye	12.95	—
Sang Ji Shend	16.00	—
Nü Zhen Zi	16.68	—
Jing Jie	17.48	—
Bu Gu Zhi	20.50	—
He Shou Wu	21.94	—
Gu Sui Bu	23.08	—
Jin Qian Cao	26.09	—
Du Zhong	26.53	—
He Huan Pi	26.64	—
Xian He Cao	27.12	—
Ge Gen	29.80	—
Wu Jia Pi	34.78	—
Yin Chen Hao	35.41	—
Yi Mu Cao	35.98	—
Gui Zhi	37.46	—
Yu Jin	38.21	—
Gou Teng	38.72	—
Chen Pi	39.19	—
Sha Ren	39.70	—
Qiang Huo	40.41	—
Wu Zhu Yu	40.45	—
Huang Bo	40.76	—
Fang Feng	40.87	—
Fu Zi	41.40	—
Hong Jing Tian	41.48	—
Pu Gong Ying	42.23	—
Hu Zhang	43.17	—
Mang Xiao	45.15	—
Wu Yao	46.12	—
Jiang Huang	46.75	—
Zhi Shi	49.40	—
Hua Shi	49.97	—
Sang Ye	51.06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sang Bai Pi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62471	62471	0.00	14.64
62472	62472	0.00	12.95

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 2.3-2020-05

Validated substance/substance group **Sang Ji Shend**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60142-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sang Ji Shend; Taxilli herba

Special notes

When selecting the *Sang Ji Shend* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sang Ji Shend	2	0	3

Second-stage model

For differentiation of the substance/substance group *Sang Ji Shend* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sang Ji Shend*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Sang Ji Shend	G146H1045821	62345	40	from supplier
PhytoComm	Sang Ji Shend	G146H1045821	62346	40	from supplier
PhytoComm	Sang Ji Shend	G146H1045822	62543	40	from supplier
PhytoComm	Sang Ji Shend	G146H1045822	62544	40	from supplier

Validation samples

A total of 30 254 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 *Sang Ji Shend*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Sang Ji Shend*.
- 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
PhytoComm	Sang Ji Shend	G146H1045821	62345 [†]	20
PhytoComm	Sang Ji Shend	G146H1045821	62346 [†]	20
PhytoComm	Sang Ji Shend	G146H1045822	62543 [†]	20
PhytoComm	Sang Ji Shend	G146H1045822	62544 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 5 *Apo-Ident* customers from 3 batches from the substance/substance group *Sang Ji Shend*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Sang Ji Shend	g146h1045222	1
Phytocomm	Sang Ji Shend	G146H1045522	4
PhytoComm	Sang Ji Shend	G146H1045322	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sang Ji Shend* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sang Ji Shend* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	2	4	851

The substance/substance group *Sang Ji Shend* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8258 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sang Ji Shend* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sang Bai Pi	13.77	—
Gu Sui Bu	16.19	—
Ge Gen	23.98	—
Xian He Cao	24.45	—
He Shou Wu	24.96	—
Wu Zhu Yu	31.40	—
Zhi Shi	31.64	—
Nü Zhen Zi	31.91	—
He Huan Pi	31.97	—
Hong Jing Tian	32.67	—
Yu Jin	33.92	—
Dan Zhu Ye	34.69	—
Bu Gu Zhi	36.19	—
Yin Chen Hao	37.25	—
Jing Jie	37.55	—
Chen Pi	37.60	—
Qiang Huo	39.86	—
Mang Xiao	40.97	—
Fang Feng	41.80	—
Gui Zhi	42.69	—
Sha Ren	42.84	—
Fu Zi	43.61	—
Wu Yao	44.31	—
Huang Bo	46.53	—
Xu Duan	49.05	—
Jin Qian Cao	49.51	—
Hua Shi	50.00	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sang Ji Shend* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62543	62543	0.00	13.77
62346	62346	0.00	15.69
62345	62345	0.00	15.57
62544	62544	0.00	13.82

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Sang Ye**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60079-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sang Ye; Mori albi folium

Special notes

When selecting the *Sang Ye* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sang Ye	1	0	2

Second-stage model

For differentiation of the substance/substance group *Sang Ye* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sang Ye*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Sang Ye	G162HS206RQ1	62461	40	from supplier
PhytoComm	Sang Ye	G162HS206RQ1	62462	40	from supplier

Validation samples

A total of 30 254 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 *Sang Ye*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Sang Ye*.
- 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
PhytoComm	Sang Ye	G162HS206RQ1	62461 [†]	20
PhytoComm	Sang Ye	G162HS206RQ1	62462 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 2 batches from the substance/substance group *Sang Ye*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Sang Ye	G162H1043121	1
Phytocomm	Sang Ye	G162H1043421	4

- 852 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sang Ye* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sang Ye* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	1	40	0	9876
Type C	0	0	5	852

The substance/substance group *Sang Ye* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	99.9960 % (> 99.9603 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sang Ye* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pu Gong Ying	12.64	—
Huang Lian	12.81	—
Shan Yao	13.35	—
Nü Zhen Zi	17.19	—
Wu Mei	18.13	—
Tu Fu Ling	18.37	—
Xin Yi	18.39	—
Gui Zhi	18.91	—
Xi Xian Cao	18.94	—
Qiang Huo	20.31	—
Wu Wei Zi	21.10	—
Qing Pi	21.46	—
Fu Zi	21.87	—
Du Zhong	22.32	—
Dan Shen	22.54	—
Huang Bai	24.70	—
Zhi Ke	24.93	—
Mao Dong Qing	25.17	—
Hong Jing Tian	26.01	—
Jiang Huang	27.14	—
Ma Huang	27.91	—
Hong Hua	29.11	—
Hou Po	29.30	—
Yin Yang Huo	30.46	—
Hu Zhang	30.65	—
Han Lian Cao	31.21	—
Yu Jin	31.63	—
Ye Jiao Teng	31.91	—
Jiao Gu Lan	31.99	—
Cang Er Zi	33.29	—
Chai Hu	34.02	—
Yi Mu Cao	34.49	—
Wu Yao	35.37	—
Jin Yin Hua	36.95	—
Zi Hua Di Ding	37.92	—
Shan Yu Rou	38.08	—
Xiang Fu	39.85	—
Bai Xian Pi	40.24	—
Wang Bu Liu Xing	40.73	—
Gan Cao	40.85	—
Bai Hua She She Cao	40.90	—
Bai Mao Gen	41.16	—
Pi Pa Ye	42.21	—
Chuan Xiong	42.40	—
Di Gu Pi	42.63	—
Che Qian Zi	42.73	—
Bai Zhu	42.88	—
Sha Ren	42.93	—
He Huan Pi	42.96	—
Xu Duan	43.54	—
Yan Hu Suo	43.83	—
Dan Dou Chi	44.22	—

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Substanz	Distance in main model	Distance in second-stage model
Lian Qiao	44.58	—
Gua Lou	44.76	—
Bai Shao Yao	45.11	—
Chi Shao (Yao)	45.86	—
Ren Dong Teng	46.21	—
Huang Qin	46.47	—
(Shi) Chang Pu	47.00	—
Mang Xiao	47.24	—
Gou Qi Zi	48.10	—
Mu Dan Pi	48.26	—
Lian Zi	48.85	—
Niu Bang Zi	49.03	—
E Zhu	49.22	—
Cang Zhu	49.51	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sang Ye* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62462	62462	0.00	12.64
62461	62461	0.00	13.35

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 2.3-2020-05

Validated substance/substance group **Sang Zhi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60091-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sang Zhi; Mori albae ramulus

Special notes

When selecting the *Sang Zhi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sang Zhi	2	0	0

Second-stage model

For differentiation of the substance/substance group *Sang Zhi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sang Zhi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Sang Zhi	G164H1044721	62359	40	from supplier
PhytoComm	Sang Zhi	G164H1044721	62360	40	from supplier
PhytoComm	Sang Zhi	G164H1044821	62473	40	from supplier
PhytoComm	Sang Zhi	G164H1044821	62474	40	from supplier

Validation samples

A total of 30 254 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 *Sang Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Sang Zhi*.
- 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
PhytoComm	Sang Zhi	G164H1044721	62359 [†]	20
PhytoComm	Sang Zhi	G164H1044721	62360 [†]	20
PhytoComm	Sang Zhi	G164H1044821	62473 [†]	20
PhytoComm	Sang Zhi	G164H1044821	62474 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Sang Zhi*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sang Zhi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sang Zhi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	7	0	0	850

The substance/substance group *Sang Zhi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.1204 % (> 98.5376 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sang Zhi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Di Gu Pi	5.00	—
Tian Hua Fen	8.66	—
Jie Geng	11.18	—
Xiang Fu	11.38	—
Qing Pi	13.23	—
Gua Lou	15.32	—
Bai Mao Gen	16.07	—
(Shi) Chang Pu	16.67	—
Sha Shen (Bei)	17.34	—
Sheng Jiang	18.26	—
Bai Zhu	18.26	—
Du Huo	18.31	—
Cang Er Zi	18.34	—
Chuan Lian Zi	19.49	—
Huang Qi	19.82	—
Qin Jiao	20.67	—
Shan Yao	20.67	—
(Huai) Niu Xi	20.74	—
Mu Dan Pi	21.12	—
Dang Gui	22.37	—
Niu Bang Zi	23.76	—
E Zhu	24.05	—
Ban Zhi Lian	24.24	—
Ji Li	24.95	—
Lai Fu Zi	25.41	—
Pu Gong Ying	26.84	—
San Qi	26.89	—
Zi Su Zi	27.57	—
Yuan Zhi	27.68	—
Chi Shao (Yao)	28.61	—
Bai He	28.69	—
Ku Shen	28.93	—
Ba Ji Tian	29.11	—
Tu Fu Ling	29.85	—
Mai Ya	30.45	—
Mang Xiao	30.74	—
Jiang Huang	30.79	—
Gui Zhi	31.15	—
(Bai) Dou Kou	31.35	—
Yan Hu Suo	31.78	—
Wu Wei Zi	31.92	—
Lian Zi	32.10	—
Fang Feng	32.67	—
Bai Xian Pi	32.70	—
Mai Men Dong	32.90	—
Jin Yin Hua	33.71	—
Xie Bai	34.28	—
Qiang Huo	34.81	—
Wu Yao	35.32	—
Zhi Ke	35.87	—
Bai Shao Yao	36.25	—
Fu Ling	36.30	—

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Substanz	Distance in main model	Distance in second-stage model
Huang Lian	36.36	—
Chai Hu	36.51	—
Yi Mu Cao	36.67	—
Tian Men Dong	37.09	—
Long Dan (Cao)	38.01	—
Gou Teng	38.49	—
Chuan Xiong	38.58	—
Chen Pi	38.88	—
Ren Dong Teng	38.88	—
Rou Gui	39.21	—
He Huan Pi	39.36	—
Da Zao	40.26	—
Sha Ren	40.43	—
Ji Xue Teng	40.55	—
Ye Jiao Teng	40.56	—
Fo Shou	40.60	—
Yu Jin	40.88	—
Shen Qu	41.13	—
Gan Cao	41.31	—
Fu Zi	41.73	—
Zhu Ling	41.80	—
Shan Yu Rou	42.32	—
Zhe Bei Mu	42.55	—
Dan Dou Chi	42.80	—
Che Qian Zi	42.90	—
Dong Gua Zi	42.97	—
Bai Bian Dou	43.54	—
Lian Qiao	43.79	—
Du Zhong	44.06	—
Yi Yi Ren	44.96	—
Xian He Cao	45.59	—
Gou Qi Zi	45.92	—
Zi Hua Di Ding	45.93	—
Sang Ye	46.47	—
Yin Yang Huo	46.99	—
Cang Zhu	47.25	—
Dan Shen	47.26	—
Mao Dong Qing	47.46	—
Xin Yi	47.72	—
Zhu Ru	47.92	—
Jiao Gu Lan	48.67	—
Hou Po	48.74	—
Pi Pa Ye	48.90	—
Ju Hua	49.35	—
Ling Zhi	49.85	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sang Zhi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62473	62473	0.00	5.05
62474	62474	0.00	5.00
62360	62360	0.00	8.66
62359	62359	0.00	9.22

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 2.3-2020-05

Validated substance/substance group **Sha Ren**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60184-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sha Ren; Amomi villosi fructus

Special notes

When selecting the *Sha Ren* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sha Ren	3	0	4

Second-stage model

For differentiation of the substance/substance group *Sha Ren* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sha Ren*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Sha Ren	G018H0939622	62095	40	from supplier
PhytoComm	Sha Ren	G018H0939622	62096	40	from supplier
PhytoComm	Sha Ren	G018H0939821	62401	40	from supplier
PhytoComm	Sha Ren	G018H0939821	62404	40	from supplier
PhytoComm	Sha Ren	G018H0939922	62763	40	from supplier
PhytoComm	Sha Ren	G018H0939922	62764	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Sha Ren*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Sha Ren*.
- 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
PhytoComm	Sha Ren	G018H0939622	62095 [†]	20
PhytoComm	Sha Ren	G018H0939622	62096 [†]	20
PhytoComm	Sha Ren	G018H0939821	62401 [†]	20
PhytoComm	Sha Ren	G018H0939821	62404 [†]	20
PhytoComm	Sha Ren	G018H0939922	62763 [†]	20
PhytoComm	Sha Ren	G018H0939922	62764 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 5 *Apo-Ident* customers from 5 batches from the substance/substance group *Sha Ren*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Sha Ren	H0939022	1
Phytocomm	Sha Ren	g018h0939321	1
Phytocomm	Sha Ren	G018H0939321	1
Phytocomm	Sha Ren	G018H0939522	1
PhytoComm	Sha Ren	G018H0939523	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sha Ren* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sha Ren* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	19 240
Type B	0	120	0	9797
Type C	1	0	5	851

The substance/substance group *Sha Ren* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9281 %)	100.0000 % (> 95.0000 %)
Type C	99.8837 % (> 99.2969 %)	n/a (n/a)

[†]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*.

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sha Ren* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Jing Jie	9.38	—
Dan Zhu Ye	11.97	—
Wu Jia Pi	13.72	—
Du Zhong	14.17	—
Gu Sui Bu	14.86	—
Fu Zi	15.47	—
Gui Zhi	16.41	—
He Shou Wu	17.58	—
Yu Jin	17.65	—
Wu Yao	18.31	—
Chen Pi	18.59	—
Sang Bai Pi	18.60	—
Jiang Huang	19.29	—
Wu Zhu Yu	20.27	—
Bu Gu Zhi	20.36	—
Sang Ji Shend	21.63	—
(Bai) Dou Kou	21.92	—
Yu Xing Cao	22.39	—
Xian He Cao	23.17	—
Jin Qian Cao	25.90	—
He Huan Pi	26.62	—
Ji Li	27.01	—
Yin Chen Hao	27.40	—
Xiang Fu	29.59	—
Pu Gong Ying	29.99	—
Xuan Shen	31.01	—
Shan Yao	31.33	—
Sang Ye	31.35	—
Fang Feng	31.76	—
Yan Hu Suo	32.18	—
(Shi) Chang Pu	32.32	—
Qiang Huo	32.45	—
Mang Xiao	34.46	—
Nü Zhen Zi	35.36	—
Huang Bo	36.11	—
E Zhu	37.31	—
Ge Gen	37.74	—
Hong Jing Tian	37.86	—
Mu Dan Pi	37.98	—
Qing Hao	38.81	—
Zhi Shi	39.19	—

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Substanz	Distance in main model	Distance in second-stage model
Hu Zhang	39.20	—
Gou Teng	39.48	—
Qing Pi	40.14	—
Tian Hua Fen	41.48	—
Zhi Ke	42.66	—
Xie Bai	42.66	—
Guang Huo Xiang	43.29	—
Wang Bu Liu Xing	43.29	—
Xin Yi	44.33	—
Sha Shen (Bei)	44.59	—
Niu Bang Zi	45.00	—
Bai Hua She She Cao	45.26	—
Xu Duan	45.30	—
Gua Lou	45.59	—
Cang Er Zi	45.65	—
Di Gu Pi	46.24	—
Xi Xian Cao	46.34	—
Yi Mu Cao	46.60	—
(Sheng) Di Huang	46.62	—
Ku Shen	46.73	—
Zi Su Zi	46.78	—
Hua Shi	47.95	—
Dang Gui	47.97	—
Han Lian Cao	48.89	—
Huang Lian	48.97	—
Tu Si Zi	49.43	—
Shu Di (Huang)	50.61	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sha Ren* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62095	62095	0.00	9.97
62763	62763	0.00	12.37
62404	62404	0.00	15.66
62096	62096	0.00	9.38
62401	62401	0.00	15.47
62764	62764	0.00	11.97

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 2.3-2020-05

Validated substance/substance group **Sha Shen (Bei)**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60200-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sha Shen (Bei); Glehniae radix

Special notes

When selecting the *Sha Shen (Bei)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sha Shen (Bei)	1	0	1

Second-stage model

For differentiation of the substance/substance group *Sha Shen (Bei)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sha Shen (Bei)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Sha Shen (Bei)	G117H0754821	62587	40	from supplier

Validation samples

A total of 30 254 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 *Sha Shen (Bei)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 440 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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.

- 79 spectra of 2 reference samples from the substance/substance group *Sha Shen (Bei)*.
- 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
PhytoComm	Sha Shen (Bei)	G117H0754821	62587 [†]	20
PhytoComm	Sha Shen (Bei)	G117H0754821	62588	59

- 9838 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 1 batches from the substance/substance group *Sha Shen (Bei)*.
- 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
Phytocomm	Sha Shen (Bei)	G117H0754322	4

- 853 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sha Shen (Bei)* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sha Shen (Bei)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	40	0	19 440
Type B	0	79	0	9838
Type C	1	0	4	852

The substance/substance group *Sha Shen (Bei)* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9636 %)	100.0000 % (> 85.0000 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.4051 %)
Type C	99.8450 % (> 99.2584 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sha Shen (Bei)* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
E Zhu	9.89	—
Ji Li	10.17	—
Yan Hu Suo	13.54	—
Chuan Lian Zi	16.04	—
Jiang Huang	16.88	—
Di Gu Pi	16.90	—
Sheng Jiang	17.78	—
(Bai) Dou Kou	17.78	—
Cang Er Zi	19.16	—
Ba Ji Tian	19.23	—
Sang Zhi	21.05	—
San Qi	23.16	—
Sha Ren	23.24	—
(Huai) Niu Xi	23.38	—
Wang Bu Liu Xing	24.02	—
Zi Su Zi	24.20	—
Dang Gui	24.36	—
Mu Dan Pi	24.45	—
Lai Fu Zi	24.82	—
Mang Xiao	25.05	—
Gui Zhi	25.05	—
Du Huo	25.58	—
Niu Bang Zi	26.00	—
Xiang Fu	26.36	—
He Huan Pi	26.90	—
Shan Yao	27.19	—
Zhu Ling	27.83	—
Mai Ya	28.18	—
Bai Bian Dou	28.31	—
Tian Hua Fen	28.83	—
(Shi) Chang Pu	29.22	—
Chen Pi	29.83	—
Long Dan (Cao)	31.65	—
Wu Yao	32.32	—
Fang Feng	32.36	—
Yuan Zhi	32.72	—
Jie Geng	33.80	—
Xie Bai	33.98	—
Qing Pi	34.49	—
Xian He Cao	35.38	—
Huang Lian	35.60	—
Fu Ling	35.70	—
Yu Jin	35.97	—
Qin Jiao	36.77	—
Ban Zhi Lian	36.88	—
Rou Gui	38.03	—
Huang Qi	38.50	—
Fu Zi	38.71	—
Bai Xian Pi	40.05	—
Bai Mao Gen	40.17	—
Da Zao	40.66	—
Lian Zi	40.84	—

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Substanz	Distance in main model	Distance in second-stage model
Pu Gong Ying	42.90	—
Xin Yi	43.23	—
Bai Zhu	43.43	—
Zhi Ke	43.82	—
Du Zhong	43.88	—
Gua Lou	44.33	—
Tu Fu Ling	44.55	—
Wu Wei Zi	44.65	—
Qiang Huo	44.73	—
Mai Men Dong	44.74	—
Bai He	45.34	—
Ji Xue Teng	45.71	—
Gou Teng	46.71	—
Ku Shen	47.61	—
Ye Jiao Teng	48.14	—
Xi Xian Cao	48.25	—
Hong Jing Tian	48.33	—
Jin Yin Hua	48.59	—
Dan Dou Chi	48.61	—
Sang Ji Shend	48.89	—
Yi Yi Ren	49.29	—
Tian Men Dong	49.39	—
Mao Dong Qing	49.42	—
Bai Shao Yao	50.14	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sha Shen (Bei)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62587	62587	0.00	9.89

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 2.3-2020-05

Validated substance/substance group **Shan Yao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60207-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Shan Yao; Dioscoreae oppositae rhizoma

Special notes

When selecting the *Shan Yao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Shan Yao	3	0	1

Second-stage model

For differentiation of the substance/substance group *Shan Yao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Shan Yao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Shan Yao	G091H0330821	62331	40	from supplier
PhytoComm	Shan Yao	G091H0330821	62332	40	from supplier
PhytoComm	Shan Yao	G091HS024RQ1	62447	40	from supplier
PhytoComm	Shan Yao	G091HS024RQ1	62448	40	from supplier
PhytoComm	Shan Yao	G091H0330822	62523	40	from supplier
PhytoComm	Shan Yao	G091H0330822	62524	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Shan Yao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Shan Yao*.
- 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
PhytoComm	Shan Yao	G091H0330821	62331 [†]	20
PhytoComm	Shan Yao	G091H0330821	62332 [†]	20
PhytoComm	Shan Yao	G091HS024RQ1	62447 [†]	20
PhytoComm	Shan Yao	G091HS024RQ1	62448 [†]	20
PhytoComm	Shan Yao	G091H0330822	62523 [†]	20
PhytoComm	Shan Yao	G091H0330822	62524 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 1 batches from the substance/substance group *Shan Yao*.
- 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
Phytocomm	Shan Yao	G091H0330521	2
PhytoComm	Shan Yao	G091H0330521	2

- 853 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Shan Yao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Shan Yao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	2	240	0	19 238
Type B	10	119	1	9787
Type C	3	4	0	850

The substance/substance group *Shan Yao* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9881 % (> 99.9697 %)	100.0000 % (> 97.5000 %)
Type B	99.8655 % (> 99.8296 %)	99.1667 % (> 96.6667 %)
Type C	99.6512 % (> 99.0646 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Shan Yao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pi Pa Ye	3.84	—
Fu Zi	4.62	—
Lian Qiao	5.09	—
Ren Dong Teng	7.46	—
Ji Li	8.05	—
Shen Qu	9.76	—
Wu Wei Zi	9.93	—
Yuan Zhi	9.97	—
Bai Zi Ren	10.06	—
Huo Ma Ren	10.18	—
Gua Lou	10.46	—
Chuan Xiong	10.57	—
Lian Zi	12.06	—
Jiao Gu Lan	12.14	—
Hou Po	12.38	—
Bai Shao Yao	12.39	—
Tian Hua Fen	12.64	—
Jin Yin Hua	13.23	—
Tai Zi Shen	13.77	—
Zhe Bei Mu	14.03	—
He Huan Pi	14.30	—
Cang Zhu	14.92	—
Ling Zhi	15.07	—
Tu Fu Ling	15.32	—
Chen Pi	15.98	—
San Qi	16.17	—
Ji Xue Teng	16.17	—
Dan Shen	16.39	—
Fu Ling	16.47	—
Chai Hu	16.66	—
Yan Hu Suo	16.79	—
Che Qian Zi	17.31	—
Tao Ren	17.75	—
Mao Dong Qing	18.22	—
Yu Jin	18.38	—
Di Gu Pi	18.64	—
Shan Yu Rou	19.04	—
Ye Jiao Teng	19.05	—
Sheng Jiang	19.18	—
Cang Er Zi	19.32	—
Gou Teng	19.42	—
Bai Xian Pi	19.66	—
Yin Yang Huo	19.68	—

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Substanz	Distance in main model	Distance in second-stage model
Dan Dou Chi	19.93	—
Mu Dan Pi	20.19	—
Yu Zhu	20.38	—
Dang Gui	21.81	—
Dang Shen	22.06	—
Ci Wu Jia	22.16	—
Zhu Ru	22.22	—
Hong Jing Tian	22.28	—
Suan Zao Ren	22.32	—
Gui Zhi	22.48	—
Dang Gui Wei	23.29	—
Qiang Huo	23.33	—
Ma Huang	23.65	—
Gou Qi Zi	23.86	—
Zhi Ke	24.02	—
Ban Xia (Jiang)	24.05	—
Yi Yi Ren	25.02	—
Qing Pi	25.10	—
Rou Gui	27.53	—
Hong Hua	27.53	—
Bai Zhu	27.79	—
Da Zao	27.94	—
Sang Ye	28.13	—
Ma Huang Gen	28.34	—
Huang Qin	28.92	—
Zi Hua Di Ding	29.62	—
Chuang Mu Xiang	29.77	—
Wu Mei	30.10	—
Fu Xiao Mai	30.73	—
Fo Shou	31.35	—
Du Zhong	31.37	—
Huang Lian	32.07	—
Zhi Mu	33.05	—
Gan Cao	34.84	—
Sang Zhi	35.96	—
Tian Men Dong	36.04	—
Long Yan Rou	37.21	—
Chi Shao (Yao)	38.74	—
Huang Bai	40.28	—
Fu Shen	40.45	—
Mang Xiao	42.19	—
Jie Geng	43.55	—
Niu Bang Zi	44.13	—
Ku Shen	45.62	—
Chuan Lian Zi	45.93	—
Xi Xian Cao	46.44	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Shan Yao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62332	62332	0.00	12.20
62447	62447	0.00	3.84
62448	62448	0.00	3.95
62331	62331	0.00	12.03
62523	62523	0.00	10.35
62524	62524	0.00	9.93

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 2.3-2020-05

Validated substance/substance group **Shan Yu Rou**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60226-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Shan Yu Rou; Corni officinalis fructus

Special notes

When selecting the *Shan Yu Rou* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Shan Yu Rou	2	0	3

Second-stage model

For differentiation of the substance/substance group *Shan Yu Rou* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Shan Yu Rou*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Shan Yu Rou	G080HS027RH1	62269	40	from supplier
PhytoComm	Shan Yu Rou	G080HS027RH1	62270	40	from supplier
PhytoComm	Shan Yu Rou	G080HS027SK1	62571	40	from supplier
PhytoComm	Shan Yu Rou	G080HS027SK1	62572	40	from supplier

Validation samples

A total of 30 254 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 *Shan Yu Rou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Shan Yu Rou*.
- 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
PhytoComm	Shan Yu Rou	G080HS027RH1	62269 [†]	20
PhytoComm	Shan Yu Rou	G080HS027RH1	62270 [†]	20
PhytoComm	Shan Yu Rou	G080HS027SK1	62571 [†]	20
PhytoComm	Shan Yu Rou	G080HS027SK1	62572 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Shan Yu Rou*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Shan Yu Rou	G080H0333221	1
Phytocomm	Shan Yu Rou	G080H0333421	1
Phytocomm	Shan Yu Rou	g080h0333221	1
PhytoComm	Shan Yu Rou	G080H0333621	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Shan Yu Rou* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Shan Yu Rou* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	1	0	4	852

The substance/substance group *Shan Yu Rou* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.8450 % (> 99.2584 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Shan Yu Rou* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dang Shen	9.10	—
Cang Zhu	9.21	—
Chuan Xiong	10.01	—
San Qi	10.21	—
Lian Qiao	12.80	—
Zhe Bei Mu	13.35	—
Pi Pa Ye	13.59	—
Mu Dan Pi	13.88	—
Zhi Mu	13.95	—
Dang Gui	14.11	—
Dang Gui Wei	14.64	—
Jiao Gu Lan	14.74	—
Yuan Zhi	14.87	—
Bai Shao Yao	15.08	—
Jin Yin Hua	15.08	—
Gua Lou	16.64	—
Shan Yao	17.19	—
Wu Wei Zi	17.32	—
Gou Qi Zi	17.47	—
Bai Zi Ren	17.48	—
Di Gu Pi	18.04	—
Ren Dong Teng	18.85	—
Chen Pi	18.89	—
Chuang Mu Xiang	19.07	—
Yu Zhu	19.39	—
He Huan Pi	19.66	—
Zhi Ke	19.68	—
Tai Zi Shen	20.76	—
Ye Jiao Teng	21.07	—
Ji Li	21.37	—
Fu Zi	22.83	—
Gan Cao	23.34	—
Tian Hua Fen	23.65	—
Hou Po	23.80	—
Suan Zao Ren	23.91	—
Tao Ren	25.09	—
Huo Ma Ren	25.23	—
Huang Qin	26.46	—
Tu Fu Ling	26.48	—
Fu Ling	26.56	—
Ci Wu Jia	27.00	—
Dan Shen	27.32	—
Lian Zi	27.63	—

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Substanz	Distance in main model	Distance in second-stage model
Fo Shou	28.22	—
Ban Xia (Jiang)	28.65	—
Mao Dong Qing	28.98	—
Zhu Ru	29.10	—
Bai Zhu	29.67	—
Shen Qu	30.25	—
Ji Xue Teng	30.26	—
Long Yan Rou	31.10	—
Jie Geng	31.14	—
Da Zao	31.25	—
Gou Teng	31.44	—
Yi Yi Ren	31.89	—
Yin Yang Huo	32.15	—
Yan Hu Suo	32.27	—
Sheng Jiang	32.57	—
Ma Huang	32.73	—
Qing Pi	32.82	—
Che Qian Zi	33.23	—
Chi Shao (Yao)	34.16	—
Chai Hu	34.24	—
Rou Gui	34.57	—
Mai Men Dong	34.66	—
Sang Zhi	35.13	—
Hong Jing Tian	35.51	—
Tian Men Dong	35.70	—
Gui Zhi	36.02	—
Qiang Huo	37.00	—
Bai Xian Pi	37.03	—
Zi Hua Di Ding	37.30	—
Fu Xiao Mai	37.49	—
Ling Zhi	37.79	—
Hong Hua	38.08	—
Dan Dou Chi	41.14	—
Cang Er Zi	41.49	—
Huang Lian	41.81	—
Yu Jin	45.00	—
Mang Xiao	45.44	—
Du Zhong	46.20	—
Sang Ye	46.46	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Shan Yu Rou* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62572	62572	0.00	12.33
62269	62269	0.00	9.21

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62270	62270	0.00	9.10
62571	62571	0.00	11.97

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 2.3-2020-05

Validated substance/substance group **Shen Qu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60020-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Shen Qu; Massa fermentata medicinalis

Special notes

When selecting the *Shen Qu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Shen Qu	2	0	4

Second-stage model

For differentiation of the substance/substance group *Shen Qu* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Shen Qu*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Shen Qu	G156HS222RP1	62459	40	from supplier
PhytoComm	Shen Qu	G156HS222RP1	62460	40	from supplier
PhytoComm	Shen Qu	G156H0935821	62467	40	from supplier
PhytoComm	Shen Qu	G156H0935821	62468	40	from supplier

Validation samples

A total of 30 254 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 *Shen Qu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Shen Qu*.
- 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
PhytoComm	Shen Qu	G156HS222RP1	62459 [†]	20
PhytoComm	Shen Qu	G156HS222RP1	62460 [†]	20
PhytoComm	Shen Qu	G156H0935821	62467 [†]	20
PhytoComm	Shen Qu	G156H0935821	62468 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Shen Qu*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
phytocomm	Shen Qu	g156h0935421	1
Phytocomm	Shen Qu	G156H0935521	1
PhytoComm	Shen Qu	G156H0935121	1
PhytoComm	Shen Qu	G156H0935521	1
PhytoComm	Shen Qu	G156H0935522	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Shen Qu* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Shen Qu* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	1	0	5	851

The substance/substance group *Shen Qu* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.9070 % (> 99.3201 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Shen Qu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Huo Ma Ren	4.32	—
Ren Dong Teng	6.73	—
He Huan Pi	7.76	—
Ji Li	8.47	—
Lian Zi	8.68	—
Shan Yao	8.72	—
Tian Hua Fen	8.79	—
Ling Zhi	9.36	—
Pi Pa Ye	9.63	—
Tai Zi Shen	9.72	—
Tao Ren	9.93	—
Bai Shao Yao	9.99	—
Zhe Bei Mu	10.23	—
Lian Qiao	10.86	—
Fu Zi	11.24	—
Chuan Xiong	11.29	—
Bai Zi Ren	11.49	—
Ji Xue Teng	11.98	—
Ye Jiao Teng	12.06	—
Gou Teng	12.23	—
Gua Lou	12.28	—
Fu Ling	13.06	—
Sheng Jiang	13.29	—
Ci Wu Jia	13.71	—
Chen Pi	13.96	—
Bai Xian Pi	14.23	—
Gui Zhi	14.49	—
Di Gu Pi	14.72	—
Yu Jin	15.51	—
Dan Shen	16.17	—
Yuan Zhi	16.72	—
Yan Hu Suo	17.58	—
Dan Dou Chi	17.68	—
Tu Fu Ling	17.95	—
Rou Gui	17.97	—
Chai Hu	18.07	—
Ban Xia (Jiang)	18.22	—
Hou Po	18.38	—
Jiao Gu Lan	18.70	—
Ma Huang Gen	18.72	—
Zhu Ru	19.02	—
Yin Yang Huo	19.14	—
Mao Dong Qing	19.43	—

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Substanz	Distance in main model	Distance in second-stage model
Yi Yi Ren	19.94	—
Che Qian Zi	20.04	—
Jin Yin Hua	20.44	—
Hong Jing Tian	20.99	—
Fu Xiao Mai	21.00	—
Fo Shou	21.04	—
Yu Zhu	21.40	—
Cang Zhu	21.55	—
Ma Huang	21.57	—
San Qi	22.01	—
Dang Gui Wei	23.21	—
Da Zao	24.13	—
Dang Shen	25.37	—
Zhi Ke	25.71	—
Qiang Huo	25.84	—
Tian Men Dong	26.00	—
Wu Wei Zi	26.23	—
Dang Gui	26.98	—
Long Yan Rou	29.29	—
Gou Qi Zi	29.65	—
Shan Yu Rou	30.26	—
Suan Zao Ren	31.04	—
Fu Shen	31.26	—
Huang Qin	31.38	—
Cang Er Zi	31.64	—
Qing Pi	32.55	—
Mu Dan Pi	32.64	—
Huang Lian	34.19	—
Du Zhong	36.06	—
Sang Zhi	36.63	—
Bai Zhu	38.89	—
Zhi Zi	39.16	—
Zhi Mu	39.38	—
Zi Hua Di Ding	39.80	—
Chuang Mu Xiang	40.00	—
Gan Cao	40.29	—
Mang Xiao	40.56	—
Jie Geng	40.71	—
Chi Shao (Yao)	42.43	—
Chuan Lian Zi	44.35	—
Ku Shen	46.22	—
Yi Mu Cao	47.17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Shen Qu* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62459	62459	0.00	5.10
62467	62467	0.00	31.08
62460	62460	0.00	4.32
62468	62468	0.00	31.35

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 2.3-2020-05

Validated substance/substance group **Sheng Jiang**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60017-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sheng Jiang; Zingiberis rhizoma recens

Special notes

When selecting the *Sheng Jiang* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sheng Jiang	2	0	3

Second-stage model

For differentiation of the substance/substance group *Sheng Jiang* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sheng Jiang*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Sheng Jiang	G253H0534623	62141	40	from supplier
PhytoComm	Sheng Jiang	G253H0534623	62142	40	from supplier
PhytoComm	Sheng Jiang	G253HS085SK1	62549	40	from supplier
PhytoComm	Sheng Jiang	G253HS085SK1	62550	40	from supplier

Validation samples

A total of 30 254 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 *Sheng Jiang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Sheng Jiang*.
- 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
PhytoComm	Sheng Jiang	G253H0534623	62141 [†]	20
PhytoComm	Sheng Jiang	G253H0534623	62142 [†]	20
PhytoComm	Sheng Jiang	G253HS085SK1	62549 [†]	20
PhytoComm	Sheng Jiang	G253HS085SK1	62550 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Sheng Jiang*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Sheng Jiang	G253H0534221	1
Phytocomm	Sheng Jiang	G253H0534522	1
PhytoComm	Sheng Jiang	G253H0534321	1
PhytoComm	Sheng Jiang	G253H0534522	3

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sheng Jiang* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sheng Jiang* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	1	160	0	19 319
Type B	16	78	2	9821
Type C	1	0	6	850

The substance/substance group *Sheng Jiang* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9921 % (> 99.9737 %)	100.0000 % (> 96.2500 %)
Type B	99.8022 % (> 99.7663 %)	97.5000 % (> 93.7500 %)
Type C	99.8837 % (> 99.2966 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sheng Jiang* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Di Gu Pi	4.04	—
Gui Zhi	4.55	—
Fu Xiao Mai	5.53	—
Yi Yi Ren	5.91	—
Zhu Ru	6.26	—
Ban Xia (Jiang)	7.31	—
Tian Hua Fen	7.57	—
Ci Wu Jia	8.10	—
Fu Ling	8.99	—
He Huan Pi	9.11	—
Tao Ren	10.99	—
Rou Gui	11.24	—
Sang Zhi	11.41	—
Shen Qu	12.66	—
Zhe Bei Mu	12.87	—
Bai Shao Yao	13.15	—
San Qi	13.30	—
Bai Zi Ren	13.45	—
Ji Li	13.50	—
Gou Teng	14.22	—
Lian Zi	14.28	—
Ling Zhi	15.37	—
Chuan Lian Zi	16.29	—
Ji Xue Teng	16.34	—
Huo Ma Ren	16.57	—
Tai Zi Shen	16.84	—
Bai Xian Pi	17.67	—
Jie Geng	18.78	—
E Zhu	18.97	—
Lai Fu Zi	18.97	—
Ma Huang Gen	19.05	—
Fo Shou	19.14	—
Ye Jiao Teng	20.08	—
Fu Shen	20.75	—
Mai Ya	21.02	—
Gua Lou	21.11	—
Bai Zhu	23.05	—
Yuan Zhi	23.25	—
Long Yan Rou	23.29	—
Tian Men Dong	23.71	—
Pi Pa Ye	23.76	—
Da Zao	24.14	—
Qing Pi	24.27	—

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Substanz	Distance in main model	Distance in second-stage model
Yu Jin	24.32	—
Shan Yao	24.61	—
Xiang Fu	24.89	—
Bai He	25.64	—
Zi Su Zi	25.93	—
Chen Pi	26.00	—
Lian Qiao	26.22	—
(Shi) Chang Pu	27.04	—
Tu Fu Ling	27.29	—
Mu Dan Pi	27.33	—
Yan Hu Suo	27.85	—
Ren Dong Teng	27.95	—
Du Huo	27.99	—
Ban Zhi Lian	28.08	—
Mang Xiao	28.65	—
Chuan Xiong	28.91	—
Dang Gui	28.99	—
Qin Jiao	29.37	—
Mai Men Dong	30.05	—
Jiang Huang	30.74	—
Huang Qi	31.28	—
Dang Shen	31.55	—
Cang Er Zi	32.70	—
Bai Bian Dou	33.43	—
Qiang Huo	33.80	—
Chai Hu	34.11	—
Dan Dou Chi	34.14	—
Ba Ji Tian	34.20	—
Shan Yu Rou	34.37	—
Wu Wei Zi	34.49	—
Fu Zi	34.58	—
Sha Shen (Bei)	34.91	—
Bai Mao Gen	35.00	—
Long Dan (Cao)	35.23	—
Dan Shen	35.29	—
Jiao Gu Lan	35.36	—
Jin Yin Hua	36.21	—
Zhi Ke	36.67	—
(Huai) Niu Xi	37.68	—
Chi Shao (Yao)	38.39	—
Pu Gong Ying	38.53	—
Huang Qin	38.65	—
Mao Dong Qing	39.01	—
(Bai) Dou Kou	39.17	—
Yin Yang Huo	39.30	—
Zhu Ling	39.46	—
Xie Bai	39.61	—
Huang Lian	39.82	—
Dang Gui Wei	40.05	—
Ku Shen	40.06	—
Wang Bu Liu Xing	40.28	—
Du Zhong	41.10	—
Yu Zhu	41.13	—
Fang Feng	42.14	—
Niu Bang Zi	42.17	—
Hou Po	42.41	—
Zhi Mu	42.75	—
Cang Zhu	42.85	—
Sha Ren	44.78	—

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Substanz	Distance in main model	Distance in second-stage model
Ma Huang	46.43	—
Wu Yao	46.62	—
Che Qian Zi	46.85	—
Hong Jing Tian	49.06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sheng Jiang* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62550	62550	0.00	4.04
62142	62142	0.00	7.57
62549	62549	0.00	4.22
62141	62141	0.00	9.20

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Shi Gao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50368-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Shi Gao; Gypsum fibrosum

Special notes

When selecting the *Shi Gao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Shi Gao	1	0	1

Second-stage model

For differentiation of the substance/substance group *Shi Gao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Shi Gao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Shi Gao	G120HS081SH1	62561	40	from supplier
PhytoComm	Shi Gao	G120HS081SH1	62562	40	from supplier

Validation samples

A total of 30 254 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 *Shi Gao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Shi Gao*.
- 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
PhytoComm	Shi Gao	G120HS081SH1	62561 [†]	20
PhytoComm	Shi Gao	G120HS081SH1	62562 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 1 batches from the substance/substance group *Shi Gao*.
- 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
Phytocomm	Shi Gao	G120H0541223	1
PhytoComm	Shi Gao	G120H0541223	2

- 854 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Shi Gao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Shi Gao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	3	854

The substance/substance group *Shi Gao* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8280 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Shi Gao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hua Shi	53.84	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Shi Gao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62561	62561	0.00	54.32
62562	62562	0.00	53.84

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 2.3-2020-05

Validated substance/substance group **Shu Di (Huang)**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60006-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Shu Di (Huang); Rehmanniae radix praep.

Special notes

When selecting the *Shu Di (Huang)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Shu Di (Huang)	1	0	4

Second-stage model

For differentiation of the substance/substance group *Shu Di (Huang)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Shu Di (Huang)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Shu Di (Huang)	G210H1601823	62493	40	from supplier
PhytoComm	Shu Di (Huang)	G210H1601823	62494	40	from supplier

Validation samples

A total of 30 254 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 *Shu Di (Huang)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Shu Di (Huang)*.
- 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
PhytoComm	Shu Di (Huang)	G210H1601823	62493 [†]	20
PhytoComm	Shu Di (Huang)	G210H1601823	62494 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Shu Di (Huang)*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hedinger	Shu Di (Huang)	g210h1601221	4
Phytocomm	Shu Di (Huang)	G210H1601221	1
Phytocomm	Shu Di (Huang)	G210H1601421	6
Phytocomm	Shu Di (Huang)	G210H1601521	3
PhytoComm	Shu Di (Huang)	G210H1601121	1

- 842 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Shu Di (Huang)* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Shu Di (Huang)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	7	0	15	835

The substance/substance group *Shu Di (Huang)* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.3992 % (> 98.8115 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Shu Di (Huang)* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ai Ye	8.12	—
Jue Ming Zi	15.46	—
Yu Xing Cao	22.49	—
(Sheng) Di Huang	24.50	—
Guang Huo Xiang	26.53	—
Pu Gong Ying	29.73	—
Hua Shi	43.96	—
Jing Jie	50.37	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Shu Di (Huang)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62493	62493	0.00	8.39
62494	62494	0.00	8.12

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 2.3-2020-05

Validated substance/substance group **Suan Zao Ren**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60059-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Suan Zao Ren; Zizyphi spinosae semen

Special notes

When selecting the *Suan Zao Ren* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Suan Zao Ren	1	0	2

Second-stage model

For differentiation of the substance/substance group *Suan Zao Ren* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Suan Zao Ren*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Suan Zao Ren	G254HS310SM1	62717	40	from supplier
PhytoComm	Suan Zao Ren	G254HS310SM1	62718	40	from supplier

Validation samples

A total of 30 254 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 *Suan Zao Ren*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Suan Zao Ren*.
- 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
PhytoComm	Suan Zao Ren	G254HS310SM1	62717 [†]	20
PhytoComm	Suan Zao Ren	G254HS310SM1	62718 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Suan Zao Ren*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Suan Zao Ren	g254h1418121	2
Phytocomm	Suan Zao Ren	G254H1418421	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Suan Zao Ren* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Suan Zao Ren* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	1	40	0	9876
Type C	1	0	3	853

The substance/substance group *Suan Zao Ren* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	99.9947 % (> 99.9590 %)	100.0000 % (> 85.0000 %)
Type C	99.8837 % (> 99.2977 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Suan Zao Ren* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yuan Zhi	7.87	—
Lian Qiao	8.38	—
Cang Zhu	11.45	—
Ji Li	11.74	—
Bai Zi Ren	11.83	—
Jiao Gu Lan	12.34	—
Shan Yao	13.69	—
Mao Dong Qing	13.76	—
Lian Zi	14.02	—
San Qi	14.60	—
Ling Zhi	16.17	—
Dang Shen	18.23	—
Chen Pi	18.54	—
Bai Shao Yao	19.04	—
Shen Qu	19.94	—
Huo Ma Ren	19.97	—
Fu Ling	20.19	—
Shan Yu Rou	20.39	—
Pi Pa Ye	20.58	—
Zhe Bei Mu	20.63	—
Chuan Xiong	20.90	—
Jin Yin Hua	20.99	—
Wu Wei Zi	21.21	—
Yu Zhu	21.85	—
Dan Shen	22.48	—
Gou Qi Zi	22.99	—
Chuang Mu Xiang	23.06	—
Gua Lou	23.13	—
Hou Po	23.26	—
Tai Zi Shen	23.80	—
Fu Zi	24.15	—
Mu Dan Pi	24.22	—
Di Gu Pi	24.29	—
Sheng Jiang	24.68	—
Chai Hu	25.98	—
He Huan Pi	26.65	—
Zhu Ru	26.81	—
Ren Dong Teng	26.83	—
Zhi Ke	27.02	—
Dang Gui	27.48	—
Dang Gui Wei	27.91	—
Tu Fu Ling	28.02	—
Bai Xian Pi	28.07	—
Dan Dou Chi	28.48	—
Gui Zhi	29.01	—
Zhi Mu	29.08	—
Tian Hua Fen	30.58	—
Yan Hu Suo	31.04	—
Ye Jiao Teng	31.18	—
Yu Jin	32.08	—
Cang Er Zi	32.13	—
Gou Teng	32.41	—

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Substanz	Distance in main model	Distance in second-stage model
Qing Pi	32.90	—
Yi Yi Ren	33.07	—
Du Zhong	33.10	—
Hong Jing Tian	33.38	—
Ji Xue Teng	33.59	—
Qiang Huo	33.89	—
Tao Ren	34.09	—
Yin Yang Huo	34.12	—
Bai Zhu	34.27	—
Ci Wu Jia	34.52	—
Che Qian Zi	36.18	—
Rou Gui	37.16	—
Fu Xiao Mai	37.69	—
Zi Hua Di Ding	39.55	—
Huang Qin	39.68	—
Ban Xia (Jiang)	40.59	—
Tian Men Dong	41.61	—
Chi Shao (Yao)	41.99	—
Da Zao	42.07	—
Ma Huang Gen	42.36	—
Sang Zhi	43.37	—
Huang Lian	43.43	—
Gan Cao	44.15	—
Ma Huang	44.19	—
Long Yan Rou	44.52	—
Mang Xiao	45.38	—
Chuan Lian Zi	45.69	—
Sang Ye	47.72	—
Jie Geng	48.88	—
Fo Shou	49.04	—
Zi Su Zi	49.67	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Suan Zao Ren* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62718	62718	0.00	8.26
62717	62717	0.00	7.87

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 2.3-2020-05

Validated substance/substance group **Tai Zi Shen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60114-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tai Zi Shen; Pseudostellariae heterophyllae radix

Special notes

When selecting the *Tai Zi Shen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tai Zi Shen	1	0	2

Second-stage model

For differentiation of the substance/substance group *Tai Zi Shen* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tai Zi Shen*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Tai Zi Shen	G204HM066SK1	62595	40	from supplier
PhytoComm	Tai Zi Shen	G204HM066SK1	62596	40	from supplier

Validation samples

A total of 30 254 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 *Tai Zi Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Tai Zi Shen*.
- 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
PhytoComm	Tai Zi Shen	G204HM066SK1	62595 [†]	20
PhytoComm	Tai Zi Shen	G204HM066SK1	62596 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Tai Zi Shen*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Tai Zi Shen	G204H0446221	1
Phytocomm	Tai Zi Shen	G204H0446521	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tai Zi Shen* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tai Zi Shen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	2	855

The substance/substance group *Tai Zi Shen* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tai Zi Shen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Shao Yao	5.46	—
Zhe Bei Mu	5.99	—
Shen Qu	6.52	—
He Huan Pi	7.43	—
Ye Jiao Teng	8.07	—
Ban Xia (Jiang)	8.27	—
Tian Hua Fen	9.00	—
Ji Li	9.20	—
Tao Ren	9.43	—
Huo Ma Ren	9.71	—
Ji Xue Teng	10.08	—
Ci Wu Jia	10.28	—
Gui Zhi	11.05	—
Gou Teng	11.14	—
Gua Lou	11.15	—
Di Gu Pi	11.17	—
Fo Shou	11.24	—
Rou Gui	11.38	—
Pi Pa Ye	12.06	—
Bai Zi Ren	12.23	—
Sheng Jiang	13.09	—
Lian Qiao	13.55	—
Chen Pi	15.00	—
Zhu Ru	15.79	—
Ling Zhi	16.15	—
Lian Zi	16.15	—
Shan Yao	17.01	—
Fu Zi	17.34	—
Ren Dong Teng	17.45	—
Da Zao	17.48	—
Yi Yi Ren	17.63	—
Fu Ling	17.80	—
Ma Huang Gen	17.86	—
Yuan Zhi	17.95	—
Yan Hu Suo	18.11	—
Bai Xian Pi	18.24	—
Long Yan Rou	18.65	—
Fu Xiao Mai	19.15	—
Chuan Xiong	19.27	—
Jin Yin Hua	19.81	—
Dang Gui Wei	20.22	—
Tian Men Dong	20.27	—
Yu Zhu	21.07	—
Dang Shen	22.14	—
Fu Shen	22.23	—
Yu Jin	22.42	—
Ma Huang	22.62	—
Tu Fu Ling	22.76	—
Jiao Gu Lan	22.87	—
Zhi Ke	23.34	—
Hou Po	23.46	—
Dan Shen	23.93	—

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Substanz	Distance in main model	Distance in second-stage model
Cang Zhu	24.39	—
Dang Gui	24.69	—
Dan Dou Chi	25.30	—
Yin Yang Huo	25.44	—
San Qi	25.79	—
Huang Qin	25.92	—
Shan Yu Rou	27.01	—
Wu Wei Zi	28.56	—
Che Qian Zi	29.76	—
Chai Hu	29.81	—
Mao Dong Qing	30.15	—
Hong Jing Tian	31.64	—
Gou Qi Zi	32.45	—
Qiang Huo	34.20	—
Zhi Mu	35.25	—
Bai Zhu	35.97	—
Gan Cao	37.58	—
Sang Zhi	38.33	—
Huang Lian	38.60	—
Mu Dan Pi	40.63	—
Jie Geng	41.08	—
Mang Xiao	41.12	—
Qing Pi	41.65	—
Chi Shao (Yao)	44.02	—
Suan Zao Ren	44.38	—
Du Zhong	47.12	—
Zi Hua Di Ding	47.20	—
Chuang Mu Xiang	47.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tai Zi Shen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62595	62595	0.00	6.16
62596	62596	0.00	5.46

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 2.3-2020-05

Validated substance/substance group **Tao Ren**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60454-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tao Ren; Persicae semen

Special notes

When selecting the *Tao Ren* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tao Ren	1	0	2

Second-stage model

For differentiation of the substance/substance group *Tao Ren* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tao Ren*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Tao Ren	G184HS220SK1	62609	40	from supplier
PhytoComm	Tao Ren	G184HS220SK1	62610	40	from supplier

Validation samples

A total of 30 254 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 *Tao Ren*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Tao Ren*.
- 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
PhytoComm	Tao Ren	G184HS220SK1	62609 [†]	20
PhytoComm	Tao Ren	G184HS220SK1	62610 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Tao Ren*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Tao Ren	g184h1007122	1
PhytoComm	Tao Ren	G184H1007321	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tao Ren* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tao Ren* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	2	76	4	19 398
Type B	0	30	10	9877
Type C	0	0	2	855

The substance/substance group *Tao Ren* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9881 % (> 99.9698 %)	95.0000 % (> 91.2500 %)
Type B	100.0000 % (> 99.9285 %)	75.0000 % (> 67.5000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tao Ren* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
He Huan Pi	3.68	—
Gui Zhi	5.93	—
Ci Wu Jia	6.01	—
Sheng Jiang	6.55	—
Lian Zi	8.67	—
Rou Gui	9.24	—
Bai Zi Ren	10.04	—
Huo Ma Ren	10.28	—
Bai Shao Yao	10.34	—
Fu Xiao Mai	10.52	—
Di Gu Pi	10.94	—
Gou Teng	11.26	—
Tai Zi Shen	11.77	—
Ling Zhi	11.81	—
Ban Xia (Jiang)	11.87	—
Yi Yi Ren	11.93	—
Bai Xian Pi	12.03	—
Ye Jiao Teng	12.62	—
Fu Ling	12.75	—
Ji Li	12.77	—
Fo Shou	12.86	—
Shen Qu	13.21	—
Zhu Ru	13.49	—
Zhe Bei Mu	15.07	—
Ma Huang Gen	16.13	—
Gua Lou	16.14	—
Ji Xue Teng	16.21	—
Tian Men Dong	17.08	—
Chen Pi	17.25	—
Tu Fu Ling	17.49	—
Tian Hua Fen	17.57	—
Ren Dong Teng	18.62	—
Chuan Xiong	20.50	—
Yuan Zhi	21.36	—
Pi Pa Ye	21.44	—
Yu Jin	21.45	—
Shan Yao	22.00	—
Long Yan Rou	22.75	—
Da Zao	23.12	—
Fu Shen	23.43	—
Dang Shen	23.98	—
Lian Qiao	24.41	—
Dan Dou Chi	24.58	—
Dan Shen	26.11	—
Mao Dong Qing	27.95	—
Yu Zhu	28.53	—
Chai Hu	28.94	—
San Qi	29.39	—
Jiao Gu Lan	29.40	—
Fu Zi	29.53	—
Yan Hu Suo	29.63	—
Dang Gui Wei	30.92	—

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Substanz	Distance in main model	Distance in second-stage model
Hong Jing Tian	30.93	—
Zhi Ke	31.16	—
Yin Yang Huo	31.80	—
Ma Huang	32.50	—
Cang Zhu	32.58	—
Shan Yu Rou	33.82	—
Dang Gui	35.08	—
Jin Yin Hua	35.30	—
Hou Po	36.13	—
Wu Wei Zi	39.13	—
Huang Qin	39.43	—
Che Qian Zi	39.62	—
Qiang Huo	40.21	—
Mang Xiao	40.31	—
Zhi Mu	41.21	—
Suan Zao Ren	42.57	—
Bai Zhu	43.73	—
Gou Qi Zi	44.12	—
Jie Geng	44.92	—
Sang Zhi	44.98	—
Huang Lian	46.39	—
Chuan Lian Zi	47.82	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tao Ren* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62610	62610	0.00	3.89
62609	62609	0.00	3.68

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 2.3-2020-05

Validated substance/substance group **Tian Hua Fen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60139-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tian Hua Fen; Trichosanthis radix

Special notes

When selecting the *Tian Hua Fen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tian Hua Fen	2	0	3

Second-stage model

For differentiation of the substance/substance group *Tian Hua Fen* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tian Hua Fen*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Tian Hua Fen	G242H0417821	62315	40	from supplier
PhytoComm	Tian Hua Fen	G242H0417821	62316	40	from supplier
PhytoComm	Tian Hua Fen	G242HS040SG1	62633	40	from supplier
PhytoComm	Tian Hua Fen	G242HS040SG1	62634	40	from supplier

Validation samples

A total of 30 254 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 *Tian Hua Fen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Tian Hua Fen*.
- 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
PhytoComm	Tian Hua Fen	G242H0417821	62315 [†]	20
PhytoComm	Tian Hua Fen	G242H0417821	62316 [†]	20
PhytoComm	Tian Hua Fen	G242HS040SG1	62633 [†]	20
PhytoComm	Tian Hua Fen	G242HS040SG1	62634 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Tian Hua Fen*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Tian Hua Fen	h0417022	1
Phytocomm	Tian Hua Fen	G242H0417423	2
Phytocomm	Tian Hua Fen	G242H0417522	1
PhytoComm	Tian Hua Fen	G242H0417522	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tian Hua Fen* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tian Hua Fen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	1	80	0	9836
Type C	1	0	5	851

The substance/substance group *Tian Hua Fen* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	99.9842 % (> 99.9483 %)	100.0000 % (> 92.5000 %)
Type C	99.8837 % (> 99.2969 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tian Hua Fen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tai Zi Shen	6.18	—
Zhe Bei Mu	8.13	—
Shen Qu	8.38	—
Ji Li	8.62	—
Huo Ma Ren	8.89	—
Sheng Jiang	8.94	—
Pi Pa Ye	9.11	—
Bai Shao Yao	9.43	—
Sang Zhi	9.69	—
Bai Zi Ren	9.74	—
He Huan Pi	9.75	—
Lian Qiao	9.87	—
Fu Zi	10.03	—
Shan Yao	11.02	—
Ji Xue Teng	11.11	—
Gua Lou	12.19	—
Tao Ren	12.20	—
Ren Dong Teng	12.73	—
Di Gu Pi	13.23	—
Ye Jiao Teng	13.39	—
Yan Hu Suo	14.04	—
Jin Yin Hua	14.27	—
Lian Zi	14.77	—
Ling Zhi	14.96	—
Ban Xia (Jiang)	15.01	—
Gou Teng	15.59	—
Hou Po	15.78	—
Gui Zhi	15.94	—
Xiang Fu	15.99	—
Ci Wu Jia	16.92	—
Chuan Xiong	17.25	—
Chen Pi	17.36	—
Jie Geng	17.73	—
Bai Xian Pi	18.59	—
(Shi) Chang Pu	18.61	—
Yu Jin	18.62	—
San Qi	18.65	—
Zhu Ru	18.91	—
Yuan Zhi	19.38	—
Jiao Gu Lan	19.54	—
Ma Huang	19.59	—
Fu Ling	19.76	—
Qing Pi	19.77	—

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Substanz	Distance in main model	Distance in second-stage model
Cang Zhu	19.94	—
Rou Gui	19.99	—
Yi Yi Ren	20.01	—
Dan Shen	20.74	—
Che Qian Zi	20.83	—
Lai Fu Zi	20.89	—
Chuan Lian Zi	20.99	—
Yu Zhu	21.30	—
Dan Dou Chi	21.48	—
Dang Gui	21.49	—
Sha Shen (Bei)	21.63	—
Zhi Ke	22.14	—
E Zhu	22.37	—
Da Zao	22.46	—
Dang Gui Wei	22.57	—
Yin Yang Huo	22.61	—
Ma Huang Gen	22.80	—
Fo Shou	22.91	—
Dang Shen	23.07	—
Wu Wei Zi	23.17	—
Fu Xiao Mai	23.27	—
Du Huo	24.12	—
Chai Hu	24.40	—
Cang Er Zi	25.24	—
Mao Dong Qing	25.53	—
Mai Ya	25.74	—
Huang Qin	25.94	—
Tu Fu Ling	26.22	—
Shan Yu Rou	26.39	—
Huang Qi	26.53	—
Zi Su Zi	27.09	—
Bai Zhu	27.65	—
Hong Jing Tian	27.66	—
Qin Jiao	27.75	—
Jiang Huang	28.07	—
Long Yan Rou	28.27	—
Bai Mao Gen	28.76	—
Qiang Huo	28.96	—
(Huai) Niu Xi	29.04	—
Mu Dan Pi	29.30	—
Gou Qi Zi	29.61	—
Mang Xiao	29.82	—
Tian Men Dong	30.07	—
(Bai) Dou Kou	30.80	—
Pu Gong Ying	31.01	—
Ban Zhi Lian	31.40	—
Fu Shen	31.69	—
Ba Ji Tian	32.07	—
Long Dan (Cao)	32.44	—
Ku Shen	33.58	—
Niu Bang Zi	34.38	—
Zhi Mu	34.75	—
Huang Lian	34.77	—
Mai Men Dong	34.94	—
Suan Zao Ren	35.38	—
Gan Cao	35.77	—
Fang Feng	36.67	—
Chi Shao (Yao)	36.76	—
Bai He	38.21	—

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Substanz	Distance in main model	Distance in second-stage model
Xie Bai	38.80	—
Wu Yao	38.90	—
Sha Ren	38.99	—
Zhu Ling	39.14	—
Du Zhong	39.45	—
Zi Hua Di Ding	39.68	—
Chuang Mu Xiang	39.75	—
Bai Bian Dou	42.36	—
Yi Mu Cao	42.70	—
Wang Bu Liu Xing	47.53	—
Xian He Cao	47.88	—
Sang Ye	49.54	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tian Hua Fen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62315	62315	0.00	8.95
62633	62633	0.00	6.34
62316	62316	0.00	8.94
62634	62634	0.00	6.18

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 2.3-2020-05

Validated substance/substance group **Tian Men Dong**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60156-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tian Men Dong; Asparagi cochinensis radix

Special notes

When selecting the *Tian Men Dong* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tian Men Dong	1	0	3

Second-stage model

For differentiation of the substance/substance group *Tian Men Dong* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tian Men Dong*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Tian Men Dong	G037HS041RR1	62437	40	from supplier
PhytoComm	Tian Men Dong	G037HS041RR1	62438	40	from supplier

Validation samples

A total of 30 254 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 *Tian Men Dong*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Tian Men Dong*.
- 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
PhytoComm	Tian Men Dong	G037HS041RR1	62437 [†]	20
PhytoComm	Tian Men Dong	G037HS041RR1	62438 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 4 batches from the substance/substance group *Tian Men Dong*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Tian Men Dong	G037H0415221	1
Phytocomm	Tian Men Dong	g037h0415221	1
Phytocomm	Tian Men Dong	g03h0415521	1
Phytocomm	Tian Men Dong	G037H0415321	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tian Men Dong* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tian Men Dong* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	39	1	9877
Type C	0	0	4	853

The substance/substance group *Tian Men Dong* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8269 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tian Men Dong* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fo Shou	8.01	—
Dang Shen	8.50	—
Chen Pi	8.52	—
Yuan Zhi	10.76	—
Da Zao	14.37	—
Gua Lou	14.67	—
Chuan Xiong	14.77	—
Ye Jiao Teng	14.79	—
Bai Shao Yao	15.70	—
Di Gu Pi	16.18	—
Rou Gui	16.79	—
Mai Men Dong	16.93	—
Pi Pa Ye	18.36	—
He Huan Pi	19.39	—
Shen Qu	19.49	—
Zhi Mu	19.77	—
Dang Gui Wei	20.16	—
Fu Ling	20.77	—
Fu Xiao Mai	20.96	—
Lian Zi	21.41	—
San Qi	22.45	—
Shan Yao	22.67	—
Ji Li	22.83	—
Ci Wu Jia	23.01	—
Dang Gui	23.71	—
Tai Zi Shen	24.17	—
Yu Zhu	24.66	—
Jie Geng	24.83	—
Shan Yu Rou	24.83	—
Cang Zhu	25.02	—
Gui Zhi	25.14	—
Tao Ren	25.18	—
Bai Zi Ren	25.70	—
Sheng Jiang	26.99	—
Ren Dong Teng	27.01	—
Tu Fu Ling	27.29	—
Bai Xian Pi	27.43	—
Ban Xia (Jiang)	28.38	—
Long Yan Rou	28.50	—
Bai Zhu	30.22	—
Gou Teng	30.51	—
Ling Zhi	30.97	—
Lian Qiao	31.48	—
Zhe Bei Mu	31.62	—
Gou Qi Zi	31.68	—
Tian Hua Fen	32.52	—
Chuang Mu Xiang	32.79	—
Zhi Ke	33.41	—
Zhu Ru	33.45	—
Jiao Gu Lan	33.96	—
Huo Ma Ren	34.40	—
Ji Xue Teng	34.81	—

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Substanz	Distance in main model	Distance in second-stage model
Huang Qin	35.58	—
Fu Shen	36.76	—
Yi Yi Ren	37.07	—
Ma Huang	38.03	—
Ma Huang Gen	38.17	—
Suan Zao Ren	38.61	—
Mao Dong Qing	39.95	—
Fu Zi	40.09	—
Dan Shen	40.21	—
Jin Yin Hua	40.51	—
Gan Cao	40.67	—
Wu Wei Zi	41.40	—
Hou Po	43.51	—
Mang Xiao	43.76	—
Hong Jing Tian	44.46	—
Yin Yang Huo	45.20	—
Dan Dou Chi	46.34	—
Yu Jin	47.25	—
Chai Hu	47.65	—
Yan Hu Suo	48.45	—
Sang Zhi	49.06	—
Che Qian Zi	49.30	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tian Men Dong* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62437	62437	0.00	8.04
62438	62438	0.00	8.01

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 2.3-2020-05

Validated substance/substance group **Tu Fu Ling**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50885-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tu Fu Ling; Smilacis glabrae rhizoma

Special notes

When selecting the *Tu Fu Ling* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tu Fu Ling	2	0	3

Second-stage model

For differentiation of the substance/substance group *Tu Fu Ling* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tu Fu Ling*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Tu Fu Ling	G231HS009RK1	62427	40	from supplier
PhytoComm	Tu Fu Ling	G231HS009RK1	62428	40	from supplier
PhytoComm	Tu Fu Ling	G231HS009SK1	62641	40	from supplier
PhytoComm	Tu Fu Ling	G231HS009SK1	62642	40	from supplier

Validation samples

A total of 30 254 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 *Tu Fu Ling*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Tu Fu Ling*.
- 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
PhytoComm	Tu Fu Ling	G231HS009RK1	62427 [†]	20
PhytoComm	Tu Fu Ling	G231HS009RK1	62428 [†]	20
PhytoComm	Tu Fu Ling	G231HS009SK1	62641 [†]	20
PhytoComm	Tu Fu Ling	G231HS009SK1	62642 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Tu Fu Ling*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Tu Fu Ling	G231H0325121	1
Phytocomm	Tu Fu Ling	G231H0325421	2
PhytoComm	Tu Fu Ling	G231H0325121	1
PhytoComm	Tu Fu Ling	G231H0325421	1
PhytoComm	Tu Fu Ling	G23H0325121	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tu Fu Ling* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tu Fu Ling* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	1	160	0	19 319
Type B	0	77	3	9837
Type C	1	0	6	850

The substance/substance group *Tu Fu Ling* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9960 % (> 99.9776 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	96.2500 % (> 92.5000 %)
Type C	99.8837 % (> 99.2966 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tu Fu Ling* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Xian Pi	5.30	—
Xi Xian Cao	8.23	—
Ye Jiao Teng	8.37	—
Dan Dou Chi	9.34	—
Ji Xue Teng	12.42	—
Rou Gui	12.69	—
Ling Zhi	13.36	—
Du Zhong	13.48	—
Mao Dong Qing	13.57	—
Pu Gong Ying	13.95	—
Yin Yang Huo	14.47	—
Lian Zi	14.62	—
Yuan Zhi	15.04	—
Chen Pi	15.81	—
Ren Dong Teng	16.78	—
Zhi Ke	16.93	—
Jiao Gu Lan	17.92	—
Huang Lian	17.94	—
Xin Yi	18.05	—
Yu Jin	18.65	—
Shan Yao	19.40	—
Gou Teng	19.56	—
Nü Zhen Zi	19.64	—
Dan Shen	19.81	—
Qiang Huo	19.96	—
Bai Shao Yao	20.63	—
Hou Po	21.07	—
Shen Qu	21.13	—
He Huan Pi	21.44	—
Ma Huang Gen	21.48	—
Fo Shou	21.60	—
Sang Ye	22.01	—
Jin Yin Hua	22.45	—
Huo Ma Ren	22.89	—
Chai Hu	23.85	—
Gui Zhi	23.94	—
Di Gu Pi	24.39	—
Ji Li	24.62	—
Fu Ling	25.26	—
Mu Dan Pi	25.31	—
Sheng Jiang	25.48	—
Jiang Huang	25.50	—
Ban Zhi Lian	25.64	—

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Substanz	Distance in main model	Distance in second-stage model
Che Qian Zi	25.72	—
Ma Huang	25.84	—
Yi Yi Ren	26.57	—
Yan Hu Suo	27.16	—
Pi Pa Ye	27.68	—
Long Yan Rou	28.16	—
Lian Qiao	28.51	—
Fu Zi	28.60	—
Gua Lou	28.73	—
Chuan Xiong	28.87	—
Tian Men Dong	29.31	—
Zi Hua Di Ding	29.33	—
Da Zao	30.09	—
Tao Ren	30.52	—
Hu Zhang	31.15	—
Cang Er Zi	31.17	—
Wu Mei	31.22	—
Fu Shen	31.35	—
Qing Pi	32.25	—
Sang Zhi	32.81	—
Zhe Bei Mu	32.84	—
Bai Hua She She Cao	33.19	—
Cang Zhu	33.22	—
Tai Zi Shen	33.26	—
Gou Qi Zi	33.55	—
Ci Wu Jia	34.22	—
Ban Xia (Jiang)	34.27	—
Hong Jing Tian	34.71	—
Wu Wei Zi	34.96	—
Jie Geng	35.27	—
Mang Xiao	35.51	—
Xiang Fu	36.13	—
Fu Xiao Mai	36.19	—
Wu Yao	36.71	—
Tian Hua Fen	37.10	—
Han Lian Cao	37.28	—
Wang Bu Liu Xing	37.61	—
E Zhu	38.18	—
Chi Shao (Yao)	38.65	—
Chuan Lian Zi	39.41	—
Yi Mu Cao	39.78	—
Bai Zhu	40.23	—
Sha Ren	40.84	—
Zhu Ru	41.48	—
Dang Shen	42.22	—
Yu Zhu	42.36	—
Huang Bai	42.46	—
(Shi) Chang Pu	43.14	—
Huang Qin	43.89	—
Bai Zi Ren	43.89	—
San Qi	44.09	—
Dang Gui Wei	44.66	—
Niu Bang Zi	44.83	—
Bai Mao Gen	46.27	—
(Bai) Dou Kou	46.33	—
Zi Su Zi	46.70	—
Du Huo	46.85	—
Sha Shen (Bei)	47.38	—
Bai Bian Dou	47.90	—

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Substanz	Distance in main model	Distance in second-stage model
Sang Ji Shend	49.21	—
Hong Hua	50.06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tu Fu Ling* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62642	62642	0.00	9.93
62428	62428	0.00	6.54
62641	62641	0.00	8.23
62427	62427	0.00	5.30

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 2.3-2020-05

Validated substance/substance group **Tu Si Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60217-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tu Si Zi; Cuscutae semen

Special notes

When selecting the *Tu Si Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tu Si Zi	1	0	2

Second-stage model

For differentiation of the substance/substance group *Tu Si Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tu Si Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Tu Si Zi	G086H1243823	62521	40	from supplier
PhytoComm	Tu Si Zi	G086H1243823	62522	40	from supplier

Validation samples

A total of 30 254 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 *Tu Si Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Tu Si Zi*.
- 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
PhytoComm	Tu Si Zi	G086H1243823	62521 [†]	20
PhytoComm	Tu Si Zi	G086H1243823	62522 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 2 batches from the substance/substance group *Tu Si Zi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Tu Si Zi	G086H1243521	3
Phytocomm	Tu Si Zi	h1243022	1
PhytoComm	Tu Si Zi	G086H1243521	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tu Si Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tu Si Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	5	852

The substance/substance group *Tu Si Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tu Si Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bu Gu Zhi	25.51	—
Yu Xing Cao	25.67	—
Mang Xiao	32.05	—
Dan Zhu Ye	32.85	—
Sha Ren	33.13	—
(Sheng) Di Huang	40.54	—
Gu Sui Bu	41.78	—
Jing Jie	42.89	—
Sang Bai Pi	44.55	—
(Bai) Dou Kou	46.40	—
Sang Ji Shend	46.87	—
He Huan Pi	46.97	—
Hua Shi	47.10	—
Wu Jia Pi	49.59	—
Gui Zhi	49.99	—
E Zhu	53.18	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tu Si Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62522	62522	0.00	25.51
62521	62521	0.00	25.67

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Wang Bu Liu Xing**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50390-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Wang Bu Liu Xing; Vaccariae semen

Special notes

When selecting the *Wang Bu Liu Xing* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wang Bu Liu Xing	2	0	4

Second-stage model

For differentiation of the substance/substance group *Wang Bu Liu Xing* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Wang Bu Liu Xing*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Wang Bu Liu Xing	G281H0456821	62463	40	from supplier
PhytoComm	Wang Bu Liu Xing	G281H0456821	62464	40	from supplier
PhytoComm	Wang Bu Liu Xing	G281H0456921	62731	40	from supplier
PhytoComm	Wang Bu Liu Xing	G281H0456921	62732	40	from supplier

Validation samples

A total of 30 254 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 *Wang Bu Liu Xing*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Wang Bu Liu Xing*.
- 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
PhytoComm	Wang Bu Liu Xing	G281H0456821	62463 [†]	20
PhytoComm	Wang Bu Liu Xing	G281H0456821	62464 [†]	20
PhytoComm	Wang Bu Liu Xing	G281H0456921	62731 [†]	20
PhytoComm	Wang Bu Liu Xing	G281H0456921	62732 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 4 batches from the substance/substance group *Wang Bu Liu Xing*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Wang Bu Liu Xing	G281H0456521	1
PhytoComm	Wang Bu Liu Xing	G281H0456221	1
PhytoComm	Wang Bu Liu Xing	G281H456421	1
PhytoComm	Wang Bu Liu Xing	G281H0456322	1

- 853 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Wang Bu Liu Xing* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wang Bu Liu Xing* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	4	853

The substance/substance group *Wang Bu Liu Xing* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8269 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wang Bu Liu Xing* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
E Zhu	22.04	—
Qiang Huo	23.35	—
Bai Bian Dou	23.76	—
Cang Er Zi	24.52	—
He Huan Pi	26.63	—
Shan Yao	27.12	—
Jiang Huang	27.48	—
Mang Xiao	27.59	—
Gui Zhi	27.67	—
Zi Su Zi	27.88	—
Sha Ren	29.23	—
Du Zhong	29.50	—
Bai Xian Pi	30.41	—
Yu Jin	30.65	—
Ji Li	32.03	—
Dan Dou Chi	32.23	—
Yuan Zhi	32.33	—
Che Qian Zi	32.66	—
Mao Dong Qing	32.75	—
Ye Jiao Teng	33.03	—
Niu Bang Zi	33.92	—
Huang Lian	34.21	—
Xi Xian Cao	34.28	—
Chuan Lian Zi	34.45	—
Wu Mei	34.70	—
Tu Fu Ling	34.73	—
(Bai) Dou Kou	35.75	—
Sheng Jiang	36.02	—
Lian Zi	37.05	—
Sang Zhi	37.23	—
Di Gu Pi	37.56	—
Hou Po	37.69	—
Lian Qiao	37.77	—
Shen Qu	37.97	—
Rou Gui	38.39	—
Ren Dong Teng	38.85	—
Chen Pi	39.28	—
Fu Zi	39.29	—
Xiang Fu	39.38	—
Yan Hu Suo	39.53	—
Nü Zhen Zi	39.76	—
Xin Yi	39.89	—
Wu Wei Zi	39.98	—
Jiao Gu Lan	40.52	—
Fu Ling	40.61	—

continued on the next page

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Substanz	Distance in main model	Distance in second-stage model
Sha Shen (Bei)	40.74	—
Ling Zhi	41.17	—
Pu Gong Ying	41.72	—
Qing Pi	41.74	—
Jin Yin Hua	42.34	—
Xia Ku Cao	42.92	—
Yin Yang Huo	43.13	—
Zhi Ke	43.31	—
Hu Zhang	43.63	—
Wu Yao	43.67	—
Mu Dan Pi	44.26	—
Pi Pa Ye	44.40	—
Gou Teng	44.79	—
Tian Hua Fen	44.87	—
Ban Zhi Lian	45.08	—
Du Huo	45.55	—
Yi Mu Cao	45.96	—
Ji Xue Teng	46.10	—
Xie Bai	46.69	—
Ba Ji Tian	46.71	—
Lai Fu Zi	47.25	—
Jie Geng	47.39	—
Yi Yi Ren	47.88	—
Bai Shao Yao	48.16	—
San Qi	49.92	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wang Bu Liu Xing* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62732	62732	0.00	24.52
62464	62464	0.00	22.04
62463	62463	0.00	22.38
62731	62731	0.00	25.40

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Wu Jia Pi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002259-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Wu Jia Pi; Acanthopanax cortex

Special notes

When selecting the *Wu Jia Pi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wu Jia Pi	1	0	1

Second-stage model

For differentiation of the substance/substance group *Wu Jia Pi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Wu Jia Pi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Wu Jia Pi	G002H0402921	62757	40	from supplier
PhytoComm	Wu Jia Pi	G002H0402921	62758	40	from supplier

Validation samples

A total of 30 254 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 *Wu Jia Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Wu Jia Pi*.
- 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
PhytoComm	Wu Jia Pi	G002H0402921	62757 [†]	20
PhytoComm	Wu Jia Pi	G002H0402921	62758 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 2 batches from the substance/substance group *Wu Jia Pi*.
- 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
Phytocomm	Wu Jia Pi	G002H0402321	1
Phytocomm	Wu Jia Pi	g002h0402321	1
PhytoComm	Wu Jia Pi	G002H0402321	3

- 852 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Wu Jia Pi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wu Jia Pi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	5	852

The substance/substance group *Wu Jia Pi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wu Jia Pi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sha Ren	10.83	—
Sang Bai Pi	18.74	—
Yu Xing Cao	19.34	—
Jing Jie	20.88	—
Dan Zhu Ye	23.33	—
Du Zhong	25.62	—
Pu Gong Ying	29.23	—
Sang Ji Shend	31.56	—
Bu Gu Zhi	34.02	—
Ge Gen	34.93	—
(Sheng) Di Huang	35.66	—
Jin Qian Cao	35.89	—
Nü Zhen Zi	35.89	—
Xuan Shen	37.57	—
Xian He Cao	39.03	—
Qing Hao	41.84	—
Gu Sui Bu	45.79	—
He Shou Wu	46.41	—
Hua Shi	47.79	—
Zhi Shi	49.45	—
Yin Chen Hao	49.76	—
Shu Di (Huang)	51.89	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wu Jia Pi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62758	62758	0.00	10.83
62757	62757	0.00	11.37

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 2.3-2020-05

Validated substance/substance group **Wu Mei**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60021-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Wu Mei; Pruni mume fructus

Special notes

When selecting the *Wu Mei* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wu Mei	2	0	2

Second-stage model

For differentiation of the substance/substance group *Wu Mei* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Wu Mei*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Wu Mei	G167H1026821	62477	40	from supplier
PhytoComm	Wu Mei	G167H1026821	62478	40	from supplier
PhytoComm	Wu Mei	G167HS192SK1	62715	40	from supplier
PhytoComm	Wu Mei	G167HS192SK1	62716	40	from supplier

Validation samples

A total of 30 254 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 *Wu Mei*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Wu Mei*.
- 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
PhytoComm	Wu Mei	G167H1026821	62477 [†]	20
PhytoComm	Wu Mei	G167H1026821	62478 [†]	20
PhytoComm	Wu Mei	G167HS192SK1	62715 [†]	20
PhytoComm	Wu Mei	G167HS192SK1	62716 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Wu Mei*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Wu Mei	G167H1026221	1
Phytocomm	Wu Mei	G167H1026421	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Wu Mei* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wu Mei* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	2	855

The substance/substance group *Wu Mei* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8302 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wu Mei* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Wu Wei Zi	7.72	—
Sang Ye	16.15	—
Qing Pi	17.69	—
Shan Yao	18.36	—
Gui Zhi	21.83	—
Huang Bai	23.35	—
Qiang Huo	26.20	—
Cang Er Zi	27.42	—
Xi Xian Cao	27.55	—
Fu Zi	27.92	—
Huang Lian	29.59	—
Mao Dong Qing	29.98	—
Du Zhong	30.39	—
Jin Yin Hua	31.09	—
Xin Yi	31.67	—
Pu Gong Ying	31.90	—
Hou Po	32.05	—
Jiao Gu Lan	32.33	—
Jiang Huang	32.37	—
Hong Hua	33.43	—
Hong Jing Tian	33.49	—
Tu Fu Ling	34.65	—
Zi Hua Di Ding	35.50	—
Ma Huang	35.66	—
Yin Yang Huo	35.67	—
Guang Huo Xiang	35.87	—
Wu Yao	36.95	—
Yi Mu Cao	37.27	—
Nü Zhen Zi	38.59	—
Bai Zhu	38.61	—
Lian Qiao	38.99	—
Zhi Ke	39.88	—
Dan Shen	41.14	—
Chai Hu	42.90	—
Gan Cao	43.17	—
Ye Jiao Teng	43.25	—
Zhi Zi	43.83	—
He Huan Pi	44.04	—
Wang Bu Liu Xing	45.07	—
Shan Yu Rou	45.68	—
Hu Zhang	46.14	—
Hua Shi	46.80	—
Gua Lou	46.87	—
Shen Qu	47.09	—
Gou Teng	47.27	—
Yu Xing Cao	47.56	—
Niu Bang Zi	48.07	—
Qing Hao	48.72	—

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Substanz	Distance in main model	Distance in second-stage model
Ai Ye	48.89	—
Wu Jia Pi	53.47	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wu Mei* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62716	62716	0.00	8.65
62715	62715	0.00	7.72
62478	62478	0.00	35.88
62477	62477	0.00	35.87

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 2.3-2020-05

Validated substance/substance group **Wu Wei Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60001-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Wu Wei Zi; Schisandrae chinensis fructus

Special notes

When selecting the *Wu Wei Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wu Wei Zi	3	0	1

Second-stage model

For differentiation of the substance/substance group *Wu Wei Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Wu Wei Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Wu Wei Zi	G220HS048RP1	62265	40	from supplier
PhytoComm	Wu Wei Zi	G220HS048RP1	62266	40	from supplier
PhytoComm	Wu Wei Zi	G220HS048SK1	62551	40	from supplier
PhytoComm	Wu Wei Zi	G220HS048SK1	62552	40	from supplier
PhytoComm	Wu Wei Zi	G220HS048SN1	62705	40	from supplier
PhytoComm	Wu Wei Zi	G220HS048SN1	62706	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Wu Wei Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Wu Wei Zi*.
- 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
PhytoComm	Wu Wei Zi	G220HS048RP1	62265 [†]	20
PhytoComm	Wu Wei Zi	G220HS048RP1	62266 [†]	20
PhytoComm	Wu Wei Zi	G220HS048SK1	62551 [†]	20
PhytoComm	Wu Wei Zi	G220HS048SK1	62552 [†]	20
PhytoComm	Wu Wei Zi	G220HS048SN1	62705 [†]	20
PhytoComm	Wu Wei Zi	G220HS048SN1	62706 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 1 batches from the substance/substance group *Wu Wei Zi*.
- 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
Caelo	Wu Wei Zi	G220H0401421	2
Phytocomm	Wu Wei Zi	G220H0401421	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Wu Wei Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wu Wei Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	19 240
Type B	0	120	0	9797
Type C	0	0	3	854

The substance/substance group *Wu Wei Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9281 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8280 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wu Wei Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Jin Yin Hua	10.64	—
Jiao Gu Lan	12.72	—
Shan Yao	12.97	—
Qing Pi	13.52	—
Zhi Ke	14.67	—
Wu Mei	15.94	—
Huang Bai	16.06	—
Lian Qiao	16.27	—
Suan Zao Ren	16.96	—
Sang Ye	18.38	—
Cang Zhu	19.71	—
Shan Yu Rou	20.99	—
Yan Hu Suo	21.40	—
San Qi	22.90	—
Mu Dan Pi	23.70	—
Chuan Xiong	23.89	—
Zhe Bei Mu	24.27	—
Gui Zhi	25.69	—
Dan Shen	26.17	—
Hou Po	26.80	—
Fu Zi	27.19	—
Qiang Huo	27.35	—
Zi Hua Di Ding	27.45	—
Bai Zi Ren	27.81	—
Mao Dong Qing	28.26	—
Du Zhong	28.75	—
He Huan Pi	28.77	—
Bai Zhu	28.94	—
Hong Hua	29.15	—
Cang Er Zi	29.77	—
Zhi Mu	29.93	—
Dang Shen	30.53	—
Gou Qi Zi	30.60	—
Di Gu Pi	30.95	—
Ye Jiao Teng	31.00	—
Huang Lian	31.24	—
Ji Li	31.25	—
Pi Pa Ye	31.49	—
Yin Yang Huo	31.85	—
Tai Zi Shen	32.37	—
Yu Zhu	32.95	—
Tao Ren	33.39	—
Gua Lou	33.53	—

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Substanz	Distance in main model	Distance in second-stage model
Yuan Zhi	33.82	—
Xi Xian Cao	34.04	—
Chen Pi	34.09	—
Hong Jing Tian	34.20	—
Ma Huang	34.64	—
Chai Hu	34.75	—
Ren Dong Teng	34.82	—
Bai Shao Yao	34.91	—
Dang Gui	35.08	—
Shen Qu	35.92	—
Che Qian Zi	37.96	—
Huo Ma Ren	38.00	—
Gan Cao	38.14	—
Huang Qin	38.64	—
Chi Shao (Yao)	38.72	—
Ling Zhi	38.73	—
Chuang Mu Xiang	38.91	—
Lian Zi	39.61	—
Yi Yi Ren	40.40	—
Wu Yao	40.94	—
Tu Fu Ling	40.99	—
Sheng Jiang	41.60	—
Pu Gong Ying	41.96	—
Xin Yi	42.17	—
Bai Xian Pi	42.52	—
Jiang Huang	43.14	—
Ji Xue Teng	43.36	—
Yi Mu Cao	43.95	—
Dan Dou Chi	44.56	—
Nü Zhen Zi	45.37	—
Zhu Ru	45.98	—
Dang Gui Wei	46.07	—
Tian Hua Fen	47.32	—
Bai Mao Gen	47.67	—
Gou Teng	47.79	—
Fu Ling	48.07	—
Sang Zhi	48.57	—
Mang Xiao	49.62	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wu Wei Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62266	62266	0.00	13.82
62265	62265	0.00	13.52
62551	62551	0.00	11.74

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62552	62552	0.00	10.64
62706	62706	0.00	24.77
62705	62705	0.00	26.00

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Wu Yao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60040-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Wu Yao; Linderæ radix

Special notes

When selecting the *Wu Yao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wu Yao	2	0	2

Second-stage model

For differentiation of the substance/substance group *Wu Yao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Wu Yao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Wu Yao	G140H1025721	62233	40	from supplier
PhytoComm	Wu Yao	G140H1025721	62234	40	from supplier
PhytoComm	Wu Yao	G140H1025921	62741	40	from supplier
PhytoComm	Wu Yao	G140H1025921	62742	40	from supplier

Validation samples

A total of 30 254 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 *Wu Yao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Wu Yao*.
- 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
PhytoComm	Wu Yao	G140H1025721	62233 [†]	20
PhytoComm	Wu Yao	G140H1025721	62234 [†]	20
PhytoComm	Wu Yao	G140H1025921	62741 [†]	20
PhytoComm	Wu Yao	G140H1025921	62742 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 6 *Apo-Ident* customers from 3 batches from the substance/substance group *Wu Yao*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Wu Yao	G140H1025521	2
Phytocomm	Wu Yao	g140h1025221	1
PhytoComm	Wu Yao	G140H1025221	2
PhytoComm	Wu Yao	G140H1025521	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Wu Yao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wu Yao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	8	3	3	843

The substance/substance group *Wu Yao* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.3411 % (> 98.7540 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wu Yao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yu Jin	12.86	—
Sha Ren	12.89	—
Chen Pi	13.25	—
He Huan Pi	15.18	—
Gui Zhi	15.33	—
Xian He Cao	15.83	—
Ji Li	16.39	—
Jiang Huang	16.44	—
Fu Zi	18.57	—
Mu Dan Pi	20.09	—
Gu Sui Bu	20.52	—
Fang Feng	20.64	—
He Shou Wu	21.48	—
(Bai) Dou Kou	21.83	—
(Shi) Chang Pu	22.73	—
Xiang Fu	23.44	—
Qiang Huo	23.98	—
Ju Hua	25.24	—
Zi Su Zi	25.39	—
Du Huo	25.43	—
Yin Chen Hao	26.89	—
Yan Hu Suo	26.92	—
Sang Bai Pi	27.38	—
Hong Jing Tian	27.42	—
Ba Ji Tian	27.96	—
Mang Xiao	28.11	—
Dang Gui	28.53	—
Shan Yao	28.58	—
Sang Ji Shend	28.62	—
Qing Pi	29.01	—
Wu Zhu Yu	30.06	—
Nü Zhen Zi	30.51	—
Huang Bo	30.81	—
Chuan Lian Zi	31.16	—
E Zhu	31.53	—
Hu Zhang	31.77	—
Di Gu Pi	32.05	—
Xie Bai	32.50	—
Bai Mao Gen	33.14	—
Xu Duan	34.46	—
Xin Yi	35.21	—
Zhi Ke	35.80	—
Ge Gen	35.82	—

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Substanz	Distance in main model	Distance in second-stage model
Niu Bang Zi	36.16	—
Sang Zhi	36.46	—
Gua Lou	36.82	—
(Huai) Niu Xi	36.97	—
Yi Mu Cao	37.18	—
Tian Hua Fen	37.29	—
Huang Qi	37.38	—
Sheng Jiang	37.69	—
Huang Lian	38.37	—
Dan Zhu Ye	38.99	—
Bu Gu Zhi	39.14	—
Cang Er Zi	40.18	—
Ku Shen	41.48	—
Bai Bian Dou	41.64	—
Sang Ye	42.51	—
Lai Fu Zi	43.06	—
Mao Dong Qing	43.50	—
Xi Xian Cao	43.95	—
Du Zhong	44.26	—
San Qi	45.06	—
Zhi Shi	45.79	—
Jie Geng	45.89	—
Pu Gong Ying	46.00	—
Wang Bu Liu Xing	47.27	—
Wu Wei Zi	48.32	—
Xia Ku Cao	49.96	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wu Yao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62234	62234	0.00	12.89
62233	62233	0.00	13.46
62741	62741	0.00	13.07
62742	62742	0.00	12.86

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 2.3-2020-05

Validated substance/substance group **Wu Zhu Yu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002260-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Wu Zhu Yu; Evodiae rutecarpae fructus

Special notes

When selecting the *Wu Zhu Yu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wu Zhu Yu	1	0	2

Second-stage model

For differentiation of the substance/substance group *Wu Zhu Yu* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Wu Zhu Yu*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Wu Zhu Yu	G103H0766921	62781	40	from supplier
PhytoComm	Wu Zhu Yu	G103H0766921	62782	40	from supplier

Validation samples

A total of 30 254 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 *Wu Zhu Yu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Wu Zhu Yu*.
- 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
PhytoComm	Wu Zhu Yu	G103H0766921	62781 [†]	20
PhytoComm	Wu Zhu Yu	G103H0766921	62782 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Wu Zhu Yu*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Wu Zhu Yu	G103H0766022	1
PhytoComm	Wu Zhu Yu	G103H0766321	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Wu Zhu Yu* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wu Zhu Yu* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	1	1	855

The substance/substance group *Wu Zhu Yu* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wu Zhu Yu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Xian He Cao	20.63	—
Nü Zhen Zi	20.66	—
Huang Bo	21.08	—
Gu Sui Bu	22.10	—
Ju Hua	22.15	—
Qiang Huo	22.17	—
Xu Duan	23.20	—
Yin Chen Hao	24.19	—
Wu Yao	25.71	—
Sha Ren	26.77	—
Dan Zhu Ye	27.69	—
Yi Mu Cao	27.90	—
Ku Shen	27.99	—
Sang Ji Shend	30.79	—
Hong Jing Tian	31.78	—
Fang Feng	32.08	—
Fu Zi	33.54	—
Gui Zhi	35.03	—
Yu Jin	35.67	—
He Huan Pi	36.44	—
Cang Er Zi	37.47	—
Xie Bai	38.32	—
He Shou Wu	39.20	—
Xiang Fu	39.55	—
Qing Pi	41.00	—
Chen Pi	41.64	—
Jing Jie	42.25	—
Jiang Huang	43.38	—
Zhi Shi	44.28	—
Sang Bai Pi	45.02	—
Sang Ye	45.07	—
Rou Cong Rong	45.09	—
Gua Lou	45.49	—
Gou Teng	45.51	—
(Shi) Chang Pu	46.09	—
Shan Yao	46.43	—
Ge Gen	46.50	—
(Bai) Dou Kou	46.62	—
Mang Xiao	46.94	—
Niu Bang Zi	47.72	—
Pu Gong Ying	47.83	—
Han Lian Cao	48.13	—
Xin Yi	49.34	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wu Zhu Yu* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62782	62782	0.00	20.63
62781	62781	0.00	20.66

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 2.3-2020-05

Validated substance/substance group **Xi Xian Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60103-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xi Xian Cao; Siegesbeckiae herba

Special notes

When selecting the *Xi Xian Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xi Xian Cao	1	0	2

Second-stage model

For differentiation of the substance/substance group *Xi Xian Cao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xi Xian Cao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Xi Xian Cao	G229HS309SK1	62555	40	from supplier
PhytoComm	Xi Xian Cao	G229HS309SK1	62556	40	from supplier

Validation samples

A total of 30 254 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 *Xi Xian Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Xi Xian Cao*.
- 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
PhytoComm	Xi Xian Cao	G229HS309SK1	62555 [†]	20
PhytoComm	Xi Xian Cao	G229HS309SK1	62556 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Xi Xian Cao*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
PhytoComm	Xi Xian Cao	G229H1431321	1
PhytoComm	Xi Xian Cao	G229H1431521	1
PhytoComm	Xi Xian Cao	G229H1431321	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xi Xian Cao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xi Xian Cao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	3	854

The substance/substance group *Xi Xian Cao* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8280 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xi Xian Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tu Fu Ling	8.10	—
Xin Yi	9.25	—
Pu Gong Ying	14.48	—
Nü Zhen Zi	15.24	—
Huang Lian	16.67	—
Shan Yao	18.97	—
Du Zhong	19.10	—
Yu Jin	19.64	—
Sang Ye	19.99	—
Zhi Ke	23.60	—
Jiang Huang	23.76	—
Qiang Huo	24.77	—
Hu Zhang	25.73	—
Gui Zhi	26.18	—
Bai Hua She She Cao	26.41	—
Jiao Gu Lan	26.80	—
Han Lian Cao	27.47	—
Wu Mei	28.06	—
Dan Shen	28.73	—
Bai Xian Pi	28.95	—
Hou Po	28.98	—
Mao Dong Qing	29.02	—
Fu Zi	31.27	—
Qing Pi	32.22	—
Yin Yang Huo	32.46	—
Ye Jiao Teng	32.56	—
Cang Er Zi	32.89	—
Ling Zhi	33.61	—
Yan Hu Suo	34.69	—
Wang Bu Liu Xing	34.95	—
Che Qian Zi	36.71	—
Ma Huang	37.30	—
Hong Jing Tian	37.70	—
Dan Dou Chi	37.88	—
Sha Ren	38.42	—
Di Gu Pi	38.68	—
Jin Yin Hua	38.80	—
He Huan Pi	38.95	—
Wu Wei Zi	39.12	—
Yi Mu Cao	40.21	—
Wu Yao	40.48	—
Pi Pa Ye	40.49	—
Zi Hua Di Ding	40.75	—
Lian Zi	41.46	—
E Zhu	41.59	—
Xiang Fu	41.77	—
Xia Ku Cao	42.59	—
Mang Xiao	43.12	—
Ji Li	43.29	—
Huang Bai	43.90	—
Ren Dong Teng	45.26	—
Chai Hu	45.90	—

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Substanz	Distance in main model	Distance in second-stage model
Bai Shao Yao	47.05	—
Ji Xue Teng	47.15	—
Chuan Xiong	47.26	—
Mu Dan Pi	47.34	—
Lian Qiao	47.65	—
Niu Bang Zi	48.60	—
(Shi) Chang Pu	49.03	—
Hong Hua	49.50	—
Sang Ji Shend	49.96	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xi Xian Cao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62556	62556	0.00	8.71
62555	62555	0.00	8.10

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Xia Ku Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60080-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xia Ku Cao; Prunellae vulgaris spica

Special notes

When selecting the *Xia Ku Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xia Ku Cao	1	0	3

Second-stage model

For differentiation of the substance/substance group *Xia Ku Cao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xia Ku Cao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Xia Ku Cao	G202HS232RM1	62283	40	from supplier
PhytoComm	Xia Ku Cao	G202HS232RM1	62284	40	from supplier

Validation samples

A total of 30 254 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 *Xia Ku Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Xia Ku Cao*.
- 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
PhytoComm	Xia Ku Cao	G202HS232RM1	62283 [†]	20
PhytoComm	Xia Ku Cao	G202HS232RM1	62284 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Xia Ku Cao*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Xia Ku Cao	G202H1064221	2
Phytocomm	Xia Ku Cao	g202h1064121	1
Phytocomm	Xia Ku Cao	G202H1064421	1
PhytoComm	Xia Ku Cao	G202H1064221	2

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xia Ku Cao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xia Ku Cao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	6	851

The substance/substance group *Xia Ku Cao* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8258 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xia Ku Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zhi Shi	7.31	—
Hu Zhang	19.94	—
Bai Hua She She Cao	22.88	—
Han Lian Cao	23.99	—
Xin Yi	26.13	—
Sang Ye	27.90	—
Yi Mu Cao	29.67	—
Huang Bo	30.11	—
Qiang Huo	35.20	—
Xi Xian Cao	37.31	—
Dan Zhu Ye	38.43	—
He Shou Wu	38.58	—
Huang Lian	40.53	—
Gu Sui Bu	41.35	—
Sang Ji Shend	41.89	—
He Huan Pi	42.47	—
Jiang Huang	42.53	—
Sha Ren	43.51	—
Sang Bai Pi	43.56	—
Xian He Cao	43.63	—
Gou Teng	44.76	—
Xuan Shen	44.78	—
Jing Jie	46.04	—
Nü Zhen Zi	46.87	—
Bu Gu Zhi	47.59	—
Wu Zhu Yu	48.19	—
Pu Gong Ying	48.67	—
Rou Cong Rong	48.88	—
Fu Zi	49.48	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xia Ku Cao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62284	62284	0.00	7.32
62283	62283	0.00	7.31

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 2.3-2020-05

Validated substance/substance group **Xian He Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60591-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xian He Cao; Agrimoniae herba

Special notes

When selecting the *Xian He Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xian He Cao	1	0	2

Second-stage model

For differentiation of the substance/substance group *Xian He Cao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xian He Cao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Xian He Cao	G008H0547921	62585	40	from supplier
PhytoComm	Xian He Cao	G008H0547921	62586	40	from supplier

Validation samples

A total of 30 254 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 *Xian He Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Xian He Cao*.
- 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
PhytoComm	Xian He Cao	G008H0547921	62585 [†]	20
PhytoComm	Xian He Cao	G008H0547921	62586 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 batches from the substance/substance group *Xian He Cao*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
phytocomm	Xian He Cao	g008h0547321	1
Phytocomm	Xian He Cao	G008H0547121	1
Phytocomm	Xian He Cao	G008H0547321	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xian He Cao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xian He Cao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	3	854

The substance/substance group *Xian He Cao* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8280 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xian He Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yu Jin	12.39	—
Gu Sui Bu	13.47	—
He Huan Pi	14.66	—
Sang Ji Shend	16.86	—
He Shou Wu	17.53	—
Sha Ren	20.21	—
Wu Yao	20.94	—
Chen Pi	21.44	—
Fu Zi	23.68	—
Sang Bai Pi	23.80	—
Gui Zhi	24.70	—
Hong Jing Tian	25.51	—
Yin Chen Hao	25.59	—
Fang Feng	25.67	—
Wu Zhu Yu	27.02	—
Qiang Huo	29.23	—
Dan Zhu Ye	29.77	—
Nü Zhen Zi	29.98	—
Ge Gen	30.37	—
Huang Bo	31.89	—
Jiang Huang	32.22	—
Ji Li	33.22	—
(Bai) Dou Kou	36.23	—
Mang Xiao	36.49	—
Hu Zhang	38.55	—
Xu Duan	39.28	—
Bu Gu Zhi	39.52	—
Xiang Fu	39.64	—
Zhi Shi	39.82	—
Shan Yao	41.14	—
Sang Ye	41.14	—
Yi Mu Cao	42.72	—
Ju Hua	43.11	—
E Zhu	43.41	—
(Shi) Chang Pu	44.04	—
Ku Shen	49.14	—
Qing Pi	49.82	—
Gou Teng	49.98	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xian He Cao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62586	62586	0.00	12.39
62585	62585	0.00	14.05

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 2.3-2020-05

Validated substance/substance group **Xiang Fu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60185-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xiang Fu; Cyperi rotundi rhizoma

Special notes

When selecting the *Xiang Fu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xiang Fu	2	0	3

Second-stage model

For differentiation of the substance/substance group *Xiang Fu* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xiang Fu*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Xiang Fu	G088H0930821	62333	40	from supplier
PhytoComm	Xiang Fu	G088H0930821	62334	40	from supplier
PhytoComm	Xiang Fu	G088H0930921	62777	40	from supplier
PhytoComm	Xiang Fu	G088H0930921	62778	40	from supplier

Validation samples

A total of 30 254 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 *Xiang Fu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Xiang Fu*.
- 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
PhytoComm	Xiang Fu	G088H0930821	62333 [†]	20
PhytoComm	Xiang Fu	G088H0930821	62334 [†]	20
PhytoComm	Xiang Fu	G088H0930921	62777 [†]	20
PhytoComm	Xiang Fu	G088H0930921	62778 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 8 spectra from 5 *Apo-Ident* customers from 3 batches from the substance/substance group *Xiang Fu*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Xiang Fu	g088h0930123	1
Phytocomm	Xiang Fu	G088H0930521	5
PhytoComm	Xiang Fu	G088H0930321	1
PhytoComm	Xiang Fu	G088H0930521	1

- 849 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xiang Fu* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xiang Fu* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	5	3	849

The substance/substance group *Xiang Fu* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8253 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xiang Fu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
(Shi) Chang Pu	8.77	—
Qing Pi	11.41	—
Sang Zhi	12.54	—
Du Huo	14.03	—
Gua Lou	16.44	—
Tian Hua Fen	19.43	—
Di Gu Pi	19.94	—
Cang Er Zi	19.96	—
Dang Gui	20.14	—
Niu Bang Zi	20.22	—
Wu Yao	20.26	—
Bai Mao Gen	20.48	—
Gui Zhi	20.90	—
Shan Yao	21.23	—
Yi Mu Cao	21.39	—
Ku Shen	22.59	—
(Huai) Niu Xi	24.07	—
Fang Feng	24.24	—
Jiang Huang	24.37	—
Pu Gong Ying	24.80	—
Mu Dan Pi	24.81	—
Chi Shao (Yao)	25.50	—
Huang Qi	25.55	—
Ji Li	25.97	—
Zhi Ke	25.98	—
(Bai) Dou Kou	26.28	—
Yan Hu Suo	26.83	—
Jie Geng	27.47	—
E Zhu	27.68	—
Wu Wei Zi	28.32	—
Ju Hua	28.36	—
Xie Bai	28.37	—
Sha Ren	28.90	—
Fu Zi	29.47	—
Yuan Zhi	29.97	—
Chen Pi	30.09	—
Huang Lian	31.03	—
Zi Su Zi	31.54	—
Tu Fu Ling	31.88	—
Xin Yi	32.30	—
Sang Ye	32.39	—
Jin Yin Hua	32.97	—
Xu Duan	33.20	—
Mang Xiao	33.63	—
Mao Dong Qing	33.68	—

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Substanz	Distance in main model	Distance in second-stage model
Sha Shen (Bei)	34.00	—
Huang Bo	34.40	—
Ba Ji Tian	34.42	—
Chuan Lian Zi	35.13	—
Gan Cao	35.21	—
Xian He Cao	36.20	—
Qiang Huo	36.70	—
Shan Yu Rou	37.17	—
Zi Hua Di Ding	37.23	—
Du Zhong	37.33	—
He Huan Pi	37.53	—
Sheng Jiang	38.16	—
Hou Po	38.98	—
Dong Gua Zi	39.27	—
Dan Shen	39.48	—
Lai Fu Zi	39.60	—
Xi Xian Cao	40.12	—
Jiao Gu Lan	40.12	—
Gu Sui Bu	40.47	—
Nü Zhen Zi	40.79	—
Bai Zhu	40.83	—
Lian Zi	40.92	—
Huang Bai	41.09	—
Chai Hu	41.45	—
Qin Jiao	41.83	—
Dan Dou Chi	41.86	—
Bai Xian Pi	42.03	—
Yu Jin	42.11	—
Ye Jiao Teng	42.49	—
Che Qian Zi	42.81	—
Gou Qi Zi	43.52	—
Lian Qiao	44.01	—
Chuan Xiong	45.31	—
Ji Xue Teng	46.80	—
Wu Zhu Yu	47.26	—
Wang Bu Liu Xing	47.35	—
Hu Zhang	47.54	—
Wu Mei	47.59	—
Sang Ji Shend	47.96	—
Ban Zhi Lian	48.13	—
Gou Teng	48.20	—
Ren Dong Teng	48.95	—
He Shou Wu	49.03	—
Yin Yang Huo	49.18	—
Hong Jing Tian	49.68	—
San Qi	49.71	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xiang Fu* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62777	62777	0.00	11.42
62334	62334	0.00	8.77
62778	62778	0.00	11.41
62333	62333	0.00	9.00

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Xie Bai**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60362-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xie Bai; Allii bulbus

Special notes

When selecting the *Xie Bai* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xie Bai	1	0	3

Second-stage model

For differentiation of the substance/substance group *Xie Bai* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xie Bai*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Xie Bai	G504H1830821	62321	40	from supplier
PhytoComm	Xie Bai	G504H1830821	62322	40	from supplier

Validation samples

A total of 30 254 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 *Xie Bai*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Xie Bai*.
- 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
PhytoComm	Xie Bai	G504H1830821	62321 [†]	20
PhytoComm	Xie Bai	G504H1830821	62322 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 batches from the substance/substance group *Xie Bai*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Xie Bai	G504H1830421	1
Phytocomm	Xie Bai	G504H1830422	1
PhytoComm	Xie Bai	G504H1830321	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xie Bai* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xie Bai* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	3	854

The substance/substance group *Xie Bai* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8280 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xie Bai* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zi Su Zi	17.38	—
(Huai) Niu Xi	19.60	—
Gua Lou	20.59	—
Bai Bian Dou	24.51	—
Niu Bang Zi	24.67	—
Sang Zhi	24.83	—
Fang Feng	25.27	—
Jie Geng	25.63	—
Gui Zhi	25.65	—
Yan Hu Suo	26.26	—
Shan Yao	27.30	—
Ji Li	27.58	—
Qing Pi	27.82	—
Xiang Fu	28.50	—
Di Gu Pi	28.54	—
Huang Qi	28.71	—
Jiang Huang	28.79	—
(Shi) Chang Pu	30.24	—
Cang Er Zi	30.88	—
Du Huo	31.13	—
Dong Gua Zi	31.26	—
Ku Shen	31.38	—
Mang Xiao	31.50	—
Tian Hua Fen	32.48	—
Sha Ren	32.71	—
Chen Pi	33.05	—
(Bai) Dou Kou	33.14	—
Dang Gui	33.48	—
Sheng Jiang	33.55	—
Qiang Huo	33.60	—
Wang Bu Liu Xing	33.79	—
Ju Hua	34.73	—
Ba Ji Tian	35.13	—
Bai Mao Gen	35.39	—
Huang Bo	35.82	—
E Zhu	35.86	—
San Qi	35.97	—
Wu Yao	36.09	—
Yi Mu Cao	37.00	—
Lai Fu Zi	38.32	—
Bai Zhu	38.95	—
Yuan Zhi	39.71	—
He Huan Pi	39.82	—
Chi Shao (Yao)	40.35	—
Nü Zhen Zi	40.38	—
Chuan Lian Zi	40.91	—
Wu Wei Zi	41.46	—
Zhi Ke	41.90	—
Pu Gong Ying	42.43	—
Jin Yin Hua	42.50	—
Mu Dan Pi	42.97	—
Xian He Cao	42.97	—

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Substanz	Distance in main model	Distance in second-stage model
Xin Yi	44.15	—
Bai Xian Pi	45.33	—
Lian Zi	45.43	—
Sha Shen (Bei)	45.77	—
Long Dan (Cao)	47.20	—
Huang Lian	47.43	—
Fu Zi	47.54	—
Gu Sui Bu	47.67	—
Yu Jin	47.74	—
Xu Duan	48.54	—
Hong Jing Tian	48.72	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xie Bai* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62321	62321	0.00	17.74
62322	62322	0.00	17.38

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 2.3-2020-05

Validated substance/substance group **Xin Yi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60231-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xin Yi; Magnoliae flos

Special notes

When selecting the *Xin Yi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xin Yi	2	0	2

Second-stage model

For differentiation of the substance/substance group *Xin Yi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xin Yi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Xin Yi	G153HS139SH1	62603	40	from supplier
PhytoComm	Xin Yi	G153HS139SH1	62604	40	from supplier
PhytoComm	Xin Yi	G153HS139SP1	62725	40	from supplier
PhytoComm	Xin Yi	G153HS139SP1	62726	40	from supplier

Validation samples

A total of 30 254 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 *Xin Yi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Xin Yi*.
- 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
PhytoComm	Xin Yi	G153HS139SH1	62603 [†]	20
PhytoComm	Xin Yi	G153HS139SH1	62604 [†]	20
PhytoComm	Xin Yi	G153HS139SP1	62725 [†]	20
PhytoComm	Xin Yi	G153HS139SP1	62726 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Xin Yi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Xin Yi	G153H0758521	1
PhytoComm	Xin Yi	G153H0758321	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xin Yi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xin Yi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	2	855

The substance/substance group *Xin Yi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8302 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xin Yi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Xi Xian Cao	6.79	—
Pu Gong Ying	7.32	—
Tu Fu Ling	10.64	—
Nü Zhen Zi	13.52	—
Bai Hua She She Cao	15.25	—
Sang Ye	15.53	—
Han Lian Cao	16.66	—
Huang Lian	17.02	—
Zhi Shi	18.01	—
Shan Yao	18.06	—
Jiang Huang	19.68	—
Hu Zhang	20.07	—
Xia Ku Cao	20.72	—
Yi Mu Cao	23.33	—
Du Zhong	25.12	—
Rou Cong Rong	25.69	—
Huang Bo	25.86	—
Yu Jin	26.07	—
Gui Zhi	27.74	—
Qiang Huo	28.69	—
Fu Zi	29.84	—
Dan Shen	32.19	—
Wu Mei	33.25	—
Zhi Ke	33.30	—
Dan Zhu Ye	33.56	—
Sha Ren	33.56	—
Hou Po	34.29	—
Yan Hu Suo	34.97	—
Gou Teng	34.97	—
Cang Er Zi	35.12	—
Mao Dong Qing	35.44	—
He Huan Pi	36.25	—
Qing Pi	37.08	—
Bai Xian Pi	37.29	—
Jiao Gu Lan	37.36	—
Wang Bu Liu Xing	37.77	—
Yin Yang Huo	38.68	—
Ye Jiao Teng	39.22	—
Xuan Shen	39.70	—
Wu Yao	40.19	—
Hong Jing Tian	40.60	—
Wu Wei Zi	40.79	—
Jing Jie	41.02	—
Xiang Fu	41.15	—
Ma Huang	41.29	—
Sang Ji Shend	42.29	—
Che Qian Zi	43.62	—
Ji Li	43.77	—

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Substanz	Distance in main model	Distance in second-stage model
E Zhu	43.78	—
Ling Zhi	43.90	—
Di Gu Pi	45.09	—
Jin Yin Hua	45.42	—
Mang Xiao	45.49	—
Dan Dou Chi	45.75	—
Gua Lou	46.74	—
Niu Bang Zi	47.23	—
Gu Sui Bu	47.43	—
He Shou Wu	48.31	—
Xian He Cao	48.69	—
Pi Pa Ye	48.85	—
Huang Bai	48.94	—
Bu Gu Zhi	48.96	—
(Shi) Chang Pu	49.58	—
Sang Bai Pi	49.61	—
Zi Hua Di Ding	49.76	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xin Yi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62604	62604	0.00	6.79
62725	62725	0.00	15.37
62726	62726	0.00	15.25
62603	62603	0.00	6.85

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 2.3-2020-05

Validated substance/substance group **Xu Duan**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60245-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xu Duan; Dipsaci radix

Special notes

When selecting the *Xu Duan* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xu Duan	1	0	1

Second-stage model

For differentiation of the substance/substance group *Xu Duan* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xu Duan*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Xu Duan	G092H2106822	62525	40	from supplier
PhytoComm	Xu Duan	G092H2106822	62526	40	from supplier

Validation samples

A total of 30 254 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 *Xu Duan*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Xu Duan*.
- 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
PhytoComm	Xu Duan	G092H2106822	62525 [†]	20
PhytoComm	Xu Duan	G092H2106822	62526 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Xu Duan*.
- 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
PhytoComm	Xu Duan	G092H2106422	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xu Duan* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xu Duan* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	2	1	0	854

The substance/substance group *Xu Duan* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.8450 % (> 99.2633 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xu Duan* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yi Mu Cao	15.20	—
Huang Bo	15.89	—
Ku Shen	21.84	—
Nü Zhen Zi	22.58	—
Gui Zhi	23.77	—
Cang Er Zi	25.10	—
Qiang Huo	25.60	—
Wu Zhu Yu	26.91	—
Rou Cong Rong	30.35	—
Fu Zi	30.59	—
Gu Sui Bu	31.87	—
Yin Chen Hao	33.30	—
Ju Hua	33.65	—
Qing Pi	34.22	—
Sha Ren	34.91	—
Gua Lou	35.37	—
He Huan Pi	35.72	—
Pu Gong Ying	36.72	—
Gan Cao	36.75	—
Dan Zhu Ye	37.07	—
Wu Yao	37.62	—
Xiang Fu	37.65	—
Shen Qu	40.98	—
Xie Bai	41.25	—
Fang Feng	41.31	—
Xian He Cao	41.39	—
Xin Yi	41.98	—
Hu Zhang	42.33	—
Chen Pi	42.36	—
Shan Yao	42.69	—
Jiang Huang	42.79	—
Niu Bang Zi	44.38	—
Jing Jie	44.73	—
(Shi) Chang Pu	44.91	—
Wu Wei Zi	45.18	—
Lian Qiao	45.36	—
Sang Ye	46.54	—
(Bai) Dou Kou	46.59	—
Han Lian Cao	46.61	—
Xi Xian Cao	46.66	—
Hong Jing Tian	48.21	—
Sang Zhi	48.31	—
Yu Jin	48.35	—
Mang Xiao	48.41	—
Bai Hua She She Cao	48.85	—
Huang Qi	49.06	—
Chi Shao (Yao)	49.53	—
Du Huo	49.83	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xu Duan* is separated from critical neighbours in a second-stage model, all

the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62526	62526	0.00	15.49
62525	62525	0.00	15.20

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Xuan Shen**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60095-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xuan Shen; Scrophulariae ningpoensis radix

Special notes

When selecting the *Xuan Shen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xuan Shen	2	0	3

Second-stage model

For differentiation of the substance/substance group *Xuan Shen* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xuan Shen*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Xuan Shen	G223HS092RN1	62273	40	from supplier
PhytoComm	Xuan Shen	G223HS092RN1	62274	40	from supplier
PhytoComm	Xuan Shen	G223HS092SH1	62553	40	from supplier
PhytoComm	Xuan Shen	G223HS092SH1	62554	40	from supplier

Validation samples

A total of 30 254 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 *Xuan Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Xuan Shen*.
- 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
PhytoComm	Xuan Shen	G223HS092RN1	62273 [†]	20
PhytoComm	Xuan Shen	G223HS092RN1	62274 [†]	20
PhytoComm	Xuan Shen	G223HS092SH1	62553 [†]	20
PhytoComm	Xuan Shen	G223HS092SH1	62554 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Xuan Shen*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Xuan Shen	H0537021	1
Phytocomm	Xuan Shen	g22h0537322	1
Phytocomm	Xuan Shen	G223H0537421	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xuan Shen* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xuan Shen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	3	854

The substance/substance group *Xuan Shen* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8280 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xuan Shen* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sha Ren	17.35	—
Pu Gong Ying	24.92	—
Du Zhong	24.93	—
Guang Huo Xiang	26.78	—
Jing Jie	26.96	—
Zhi Shi	28.20	—
Qing Hao	29.69	—
Wu Jia Pi	32.83	—
Jin Qian Cao	33.20	—
Xia Ku Cao	33.85	—
Yi Mu Cao	34.69	—
Dan Zhu Ye	38.72	—
Sang Bai Pi	41.34	—
Shu Di (Huang)	42.52	—
Yin Chen Hao	42.55	—
Huang Bo	42.60	—
Sang Ji Shend	43.96	—
Hong Jing Tian	44.32	—
Nü Zhen Zi	45.95	—
Hua Shi	46.70	—
Qiang Huo	47.35	—
Gou Teng	48.72	—
Xin Yi	49.01	—
Hu Zhang	50.41	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xuan Shen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62274	62274	0.00	24.92
62554	62554	0.00	17.63
62553	62553	0.00	17.35
62273	62273	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 2.3-2020-05

Validated substance/substance group **Yan Hu Suo**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60439-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yan Hu Suo; Corydalis rhizoma

Special notes

When selecting the *Yan Hu Suo* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yan Hu Suo	2	0	4

Second-stage model

For differentiation of the substance/substance group *Yan Hu Suo* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yan Hu Suo*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yan Hu Suo	G081H0805821	62371	40	from supplier
PhytoComm	Yan Hu Suo	G081H0805821	62372	40	from supplier
PhytoComm	Yan Hu Suo	G081HS161SG1	62677	40	from supplier
PhytoComm	Yan Hu Suo	G081HS161SG1	62678	40	from supplier

Validation samples

A total of 30 254 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 *Yan Hu Suo*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Yan Hu Suo*.
- 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
PhytoComm	Yan Hu Suo	G081H0805821	62371 [†]	20
PhytoComm	Yan Hu Suo	G081H0805821	62372 [†]	20
PhytoComm	Yan Hu Suo	G081HS161SG1	62677 [†]	20
PhytoComm	Yan Hu Suo	G081HS161SG1	62678 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 6 *Apo-Ident* customers from 4 batches from the substance/substance group *Yan Hu Suo*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Yan Hu Suo	g081f1000301	1
Phytocomm	Yan Hu Suo	G081H0805223	1
Phytocomm	Yan Hu Suo	G081H0805521	1
PhytoComm	Yan Hu Suo	G081H0805223	1
PhytoComm	Yan Hu Suo	G081H0805521	1
PhytoComm	Yan Hu Suo	G081H0805223	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yan Hu Suo* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yan Hu Suo* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	0	6	851

The substance/substance group *Yan Hu Suo* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8258 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yan Hu Suo* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hou Po	6.29	—
Shan Yao	9.54	—
Pi Pa Ye	10.17	—
Jiang Huang	10.95	—
Chai Hu	11.84	—
Ren Dong Teng	12.45	—
Yu Jin	12.50	—
(Bai) Dou Kou	13.11	—
Che Qian Zi	13.18	—
Bai Xian Pi	13.65	—
Xiang Fu	14.13	—
Jin Yin Hua	14.18	—
Fu Zi	14.89	—
Yin Yang Huo	15.13	—
Dan Shen	15.16	—
Ma Huang	15.40	—
Mu Dan Pi	15.77	—
Dan Dou Chi	15.80	—
Qiang Huo	16.63	—
Ye Jiao Teng	16.67	—
Qing Pi	16.87	—
Yuan Zhi	17.29	—
Shen Qu	17.44	—
Tu Fu Ling	17.95	—
Zi Hua Di Ding	17.97	—
Ji Li	18.13	—
Bai Shao Yao	18.20	—
Ji Xue Teng	18.36	—
Chuan Xiong	18.39	—
Ling Zhi	18.48	—
Sha Ren	19.01	—
Mao Dong Qing	19.05	—
Tian Hua Fen	19.11	—
Hong Jing Tian	19.22	—
He Huan Pi	19.28	—
Lian Qiao	19.31	—
Jiao Gu Lan	19.41	—
Wu Wei Zi	19.49	—
Gui Zhi	19.56	—
Lian Zi	19.87	—
Wu Yao	19.89	—
Du Zhong	21.54	—
Zhi Ke	21.78	—

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Substanz	Distance in main model	Distance in second-stage model
Huang Lian	21.88	—
Gua Lou	21.97	—
Tao Ren	22.63	—
Bai Zi Ren	23.15	—
Di Gu Pi	23.29	—
(Shi) Chang Pu	23.58	—
Cang Er Zi	24.62	—
Zi Su Zi	24.89	—
Niu Bang Zi	25.19	—
Huo Ma Ren	25.55	—
Tai Zi Shen	25.63	—
Dang Gui	26.63	—
Sang Zhi	26.70	—
Shan Yu Rou	26.74	—
Cang Zhu	27.06	—
Huang Bai	27.11	—
Sha Shen (Bei)	27.27	—
Chuan Lian Zi	27.43	—
Zhe Bei Mu	27.43	—
Sheng Jiang	27.57	—
Ba Ji Tian	27.59	—
E Zhu	27.87	—
Gou Teng	28.01	—
Chen Pi	28.04	—
Rou Gui	28.25	—
Wang Bu Liu Xing	28.53	—
Gou Qi Zi	28.60	—
(Huai) Niu Xi	28.99	—
Ma Huang Gen	29.44	—
Du Huo	29.74	—
Huang Qin	29.83	—
Xian He Cao	29.93	—
Xie Bai	29.94	—
Suan Zao Ren	30.35	—
Fu Ling	30.58	—
Pu Gong Ying	30.60	—
Mang Xiao	31.10	—
Ban Xia (Jiang)	32.05	—
Yu Zhu	32.99	—
Xin Yi	33.11	—
Sang Ye	33.49	—
Bai Zhu	33.98	—
San Qi	34.10	—
Yi Yi Ren	34.79	—
Jie Geng	34.86	—
Fang Feng	35.46	—
Dang Shen	35.55	—
Ku Shen	35.66	—
Da Zao	35.83	—
Nü Zhen Zi	36.05	—
Bai Mao Gen	36.22	—
Huang Bo	36.32	—
Gan Cao	37.03	—
Xi Xian Cao	37.11	—
Yi Mu Cao	37.12	—
Ci Wu Jia	37.17	—
Chuang Mu Xiang	37.38	—
Hu Zhang	37.52	—
Dang Gui Wei	38.94	—

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Substanz	Distance in main model	Distance in second-stage model
Fu Shen	39.37	—
Gu Sui Bu	40.38	—
Huang Qi	40.91	—
Ju Hua	40.92	—
Fu Xiao Mai	40.97	—
Sang Ji Shend	41.09	—
Chi Shao (Yao)	41.13	—
Zhu Ru	41.37	—
Sang Bai Pi	42.04	—
Lai Fu Zi	43.91	—
Xu Duan	44.32	—
Long Yan Rou	44.93	—
Hong Hua	45.36	—
Wu Zhu Yu	46.40	—
Fo Shou	46.63	—
Bai Bian Dou	47.38	—
Wu Mei	47.73	—
He Shou Wu	48.12	—
Zhi Mu	48.73	—
Zhu Ling	49.10	—
Qin Jiao	49.68	—
Ban Zhi Lian	50.18	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yan Hu Suo* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62371	62371	0.00	10.95
62677	62677	0.00	6.81
62678	62678	0.00	6.29
62372	62372	0.00	11.06

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 2.3-2020-05

Validated substance/substance group **Ye Jiao Teng**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60068-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ye Jiao Teng; Polygoni multiflori caulis

Special notes

When selecting the *Ye Jiao Teng* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ye Jiao Teng	2	0	3

Second-stage model

For differentiation of the substance/substance group *Ye Jiao Teng* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ye Jiao Teng*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Ye Jiao Teng	G288HS163RM1	62421	40	from supplier
PhytoComm	Ye Jiao Teng	G288HS163RM1	62422	40	from supplier
PhytoComm	Ye Jiao Teng	G288HS163SK1	62625	40	from supplier
PhytoComm	Ye Jiao Teng	G288HS163SK1	62626	40	from supplier

Validation samples

A total of 30 254 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 *Ye Jiao Teng*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Ye Jiao Teng*.
- 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
PhytoComm	Ye Jiao Teng	G288HS163RM1	62421 [†]	20
PhytoComm	Ye Jiao Teng	G288HS163RM1	62422 [†]	20
PhytoComm	Ye Jiao Teng	G288HS163SK1	62625 [†]	20
PhytoComm	Ye Jiao Teng	G288HS163SK1	62626 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 4 *Apo-Ident* customers from 3 batches from the substance/substance group *Ye Jiao Teng*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Ye Jiao Teng	G288H0885223	1
Phytocomm	Ye Jiao Teng	G288H0885522	2
Phytocomm	Ye Jiao Teng	g228h0085223	1
PhytoComm	Ye Jiao Teng	G288H0885522	2

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ye Jiao Teng* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ye Jiao Teng* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	2	157	3	19 318
Type B	0	79	1	9837
Type C	0	0	6	851

The substance/substance group *Ye Jiao Teng* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9921 % (> 99.9737 %)	98.1250 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	98.7500 % (> 95.0000 %)
Type C	100.0000 % (> 98.8258 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ye Jiao Teng* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ji Xue Teng	5.20	—
Bai Xian Pi	6.48	—
Tu Fu Ling	7.18	—
Dan Dou Chi	7.64	—
Yin Yang Huo	9.07	—
Rou Gui	9.13	—
Ren Dong Teng	10.50	—
Fo Shou	12.33	—
Ling Zhi	12.44	—
Ma Huang Gen	12.88	—
Gou Teng	13.51	—
Chen Pi	13.61	—
Huo Ma Ren	13.64	—
Dan Shen	13.74	—
Bai Shao Yao	14.07	—
Yuan Zhi	14.25	—
Mao Dong Qing	14.35	—
Yu Jin	14.50	—
Tai Zi Shen	14.67	—
Lian Zi	15.61	—
Shen Qu	15.66	—
He Huan Pi	15.79	—
Ma Huang	16.48	—
Tao Ren	16.53	—
Hou Po	17.48	—
Yan Hu Suo	17.51	—
Qiang Huo	19.09	—
Sheng Jiang	19.10	—
Jin Yin Hua	19.85	—
Chuan Xiong	20.19	—
Gui Zhi	20.40	—
Ci Wu Jia	20.62	—
Shan Yao	20.71	—
Pi Pa Ye	21.28	—
Ban Xia (Jiang)	21.63	—
Chai Hu	21.65	—
Fu Shen	22.10	—
Che Qian Zi	22.28	—
Long Yan Rou	22.50	—
Yi Yi Ren	22.55	—
Zhi Ke	22.87	—
Zhe Bei Mu	23.05	—
Da Zao	23.22	—

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Substanz	Distance in main model	Distance in second-stage model
Lian Qiao	23.47	—
Gua Lou	23.52	—
Ji Li	23.60	—
Hong Jing Tian	23.91	—
Di Gu Pi	23.95	—
Tian Men Dong	24.06	—
Fu Ling	24.11	—
Mu Dan Pi	24.26	—
Zi Hua Di Ding	24.35	—
Tian Hua Fen	24.65	—
Du Zhong	24.89	—
Fu Zi	25.56	—
Jiao Gu Lan	25.68	—
Huang Lian	25.74	—
Yu Zhu	26.22	—
Cang Zhu	28.15	—
Bai Zi Ren	28.53	—
Fu Xiao Mai	30.12	—
Dang Shen	31.21	—
Wu Wei Zi	32.22	—
Dang Gui Wei	32.28	—
Qing Pi	32.50	—
Zhu Ru	32.59	—
Huang Qin	32.66	—
Ban Zhi Lian	33.36	—
Gou Qi Zi	33.42	—
San Qi	36.03	—
Sang Zhi	36.74	—
Mang Xiao	37.37	—
Jie Geng	37.43	—
Shan Yu Rou	38.04	—
Dang Gui	38.38	—
Bai Zhu	38.78	—
Chi Shao (Yao)	39.12	—
Huang Bai	40.26	—
Gan Cao	40.94	—
Pu Gong Ying	42.27	—
Chuan Lian Zi	46.33	—
Suan Zao Ren	46.85	—
Chuang Mu Xiang	48.02	—
Bai Mao Gen	49.23	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ye Jiao Teng* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62422	62422	0.00	5.73
62421	62421	0.00	5.20
62625	62625	0.00	6.76
62626	62626	0.00	6.48

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Yi Mu Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60105-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yi Mu Cao; Leonuri heterophylli herba

Special notes

When selecting the *Yi Mu Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yi Mu Cao	2	0	4

Second-stage model

For differentiation of the substance/substance group *Yi Mu Cao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yi Mu Cao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yi Mu Cao	G134H1050821	62409	40	from supplier
PhytoComm	Yi Mu Cao	G134H1050821	62410	40	from supplier
PhytoComm	Yi Mu Cao	G134H1050822	62541	40	from supplier
PhytoComm	Yi Mu Cao	G134H1050822	62542	40	from supplier

Validation samples

A total of 30 254 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 *Yi Mu Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Yi Mu Cao*.
- 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
PhytoComm	Yi Mu Cao	G134H1050821	62409 [†]	20
PhytoComm	Yi Mu Cao	G134H1050821	62410 [†]	20
PhytoComm	Yi Mu Cao	G134H1050822	62541 [†]	20
PhytoComm	Yi Mu Cao	G134H1050822	62542 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 7 spectra from 5 *Apo-Ident* customers from 4 batches from the substance/substance group *Yi Mu Cao*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Yi Mu Cao	g134h1050024	1
Phytocomm	Yi Mu Cao	G134H1050521	1
PhytoComm	Yi Mu Cao	G134H1050521	3
PhytoComm	Yi Mu Cao	G134H1050321	1
PhytoComm	Yi Mu Cao	G134H1050621	1

- 850 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yi Mu Cao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yi Mu Cao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	3	0	7	847

The substance/substance group *Yi Mu Cao* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.5736 % (> 98.9864 %)	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

[†]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*.

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yi Mu Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Huang Bo	11.66	—
Xu Duan	14.79	—
Qiang Huo	15.72	—
Gui Zhi	16.04	—
Nü Zhen Zi	16.89	—
Dan Zhu Ye	21.40	—
Cang Er Zi	21.57	—
Fu Zi	24.87	—
Rou Cong Rong	28.23	—
He Huan Pi	29.02	—
Gou Teng	29.03	—
Pu Gong Ying	31.96	—
Ku Shen	32.06	—
Sha Ren	32.41	—
Yin Chen Hao	33.01	—
Bai Hua She She Cao	33.35	—
Jiang Huang	34.09	—
Shen Qu	34.43	—
Wu Yao	34.44	—
Wu Zhu Yu	35.16	—
Jing Jie	35.54	—
Wu Wei Zi	36.06	—
Hu Zhang	36.11	—
Han Lian Cao	36.75	—
Xi Xian Cao	36.84	—
Gu Sui Bu	37.14	—
Shan Yao	37.58	—
Xin Yi	38.57	—
Gua Lou	38.63	—
Qing Pi	38.90	—
Ju Hua	39.42	—
Xia Ku Cao	41.06	—
Sang Ye	41.26	—
Gan Cao	41.62	—
Sang Ji Shend	41.90	—
Sang Bai Pi	42.28	—
Bu Gu Zhi	42.80	—
Niu Bang Zi	43.05	—
Huang Lian	43.79	—
Qing Hao	43.84	—
Xiang Fu	43.86	—
Xian He Cao	44.59	—
Yu Jin	45.68	—

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Substanz	Distance in main model	Distance in second-stage model
Tu Fu Ling	46.95	—
Zhi Shi	47.12	—
Chen Pi	47.91	—
Wu Mei	48.42	—
(Bai) Dou Kou	49.12	—
Du Zhong	49.72	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yi Mu Cao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62410	62410	0.00	14.26
62542	62542	0.00	11.66
62541	62541	0.00	11.73
62409	62409	0.00	14.75

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 2.3-2020-05

Validated substance/substance group **Yi Yi Ren**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60174-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yi Yi Ren; Coicis semen

Special notes

When selecting the *Yi Yi Ren* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yi Yi Ren	3	0	2

Second-stage model

For differentiation of the substance/substance group *Yi Yi Ren* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yi Yi Ren*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yi Yi Ren	G078H1701622	62097	40	from supplier
PhytoComm	Yi Yi Ren	G078H1701622	62098	40	from supplier
PhytoComm	Yi Yi Ren	G078HS336RL1	62279	40	from supplier
PhytoComm	Yi Yi Ren	G078HS336RL1	62280	40	from supplier
PhytoComm	Yi Yi Ren	G078HS336SH1	62675	40	from supplier
PhytoComm	Yi Yi Ren	G078HS336SH1	62676	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Yi Yi Ren*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Yi Yi Ren*.
- 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
PhytoComm	Yi Yi Ren	G078H1701622	62097 [†]	20
PhytoComm	Yi Yi Ren	G078H1701622	62098 [†]	20
PhytoComm	Yi Yi Ren	G078HS336RL1	62279 [†]	20
PhytoComm	Yi Yi Ren	G078HS336RL1	62280 [†]	20
PhytoComm	Yi Yi Ren	G078HS336SH1	62675 [†]	20
PhytoComm	Yi Yi Ren	G078HS336SH1	62676 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Yi Yi Ren*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Yi Yi Ren	G078H1701323	1
Phytocomm	Yi Yi Ren	g078h1701323	1
Phytocomm	Yi Yi Ren	G078H1701522	3
PhytoComm	Yi Yi Ren	G078H1701323	6

- 846 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yi Yi Ren* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yi Yi Ren* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	11	233	7	19 229
Type B	14	116	4	9783
Type C	0	8	3	846

The substance/substance group *Yi Yi Ren* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	99.9407 % (> 99.9222 %)	97.0833 % (> 95.8333 %)
Type B	99.8734 % (> 99.8375 %)	96.6667 % (> 94.1667 %)
Type C	100.0000 % (> 98.8249 %)	n/a (n/a)

[†]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*.

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yi Yi Ren* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fu Xiao Mai	2.08	—
Zhu Ru	3.61	—
Sheng Jiang	5.40	—
Rou Gui	6.48	—
Fu Ling	7.54	—
Gui Zhi	8.23	—
Di Gu Pi	8.30	—
Fu Shen	9.47	—
Ci Wu Jia	9.55	—
He Huan Pi	10.44	—
Ma Huang Gen	11.43	—
Tao Ren	12.20	—
Ji Li	12.70	—
Ban Xia (Jiang)	12.84	—
Shen Qu	13.39	—
Lian Zi	13.46	—
Bai Shao Yao	14.35	—
Bai Zi Ren	14.48	—
Gou Teng	14.51	—
Ling Zhi	14.88	—
Ji Xue Teng	14.90	—
Zhe Bei Mu	17.19	—
Bai Xian Pi	18.69	—
Huo Ma Ren	19.00	—
Tian Hua Fen	20.61	—
Gua Lou	20.99	—
Fo Shou	21.28	—
Tai Zi Shen	21.33	—
Ye Jiao Teng	21.75	—
Yuan Zhi	22.65	—
Yu Jin	23.00	—
Shan Yao	23.09	—
Pi Pa Ye	24.69	—
Tian Men Dong	24.89	—
Long Yan Rou	26.32	—
Chen Pi	26.67	—
Da Zao	27.13	—
Tu Fu Ling	27.27	—
Ren Dong Teng	27.99	—
Lian Qiao	29.22	—
Chuan Xiong	31.11	—

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Substanz	Distance in main model	Distance in second-stage model
Dang Shen	31.65	—
Yan Hu Suo	32.45	—
Shan Yu Rou	34.66	—
Fu Zi	36.63	—
Dan Dou Chi	36.75	—
Jiao Gu Lan	37.36	—
San Qi	38.00	—
Dan Shen	38.29	—
Mao Dong Qing	38.75	—
Dang Gui Wei	39.79	—
Wu Wei Zi	39.90	—
Zhi Ke	40.24	—
Jin Yin Hua	40.32	—
Chai Hu	40.35	—
Mang Xiao	40.81	—
Zhi Mu	41.03	—
Yin Yang Huo	42.23	—
Huang Qin	42.36	—
Yu Zhu	44.14	—
Dang Gui	45.15	—
Hou Po	45.52	—
Suan Zao Ren	46.49	—
Cang Zhu	46.59	—
Che Qian Zi	46.67	—
Jie Geng	49.51	—
Hong Jing Tian	49.78	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yi Yi Ren* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62098	62098	0.00	54.15
62280	62280	0.00	4.15
62675	62675	0.00	2.14
62676	62676	0.00	2.08
62279	62279	0.00	3.37
62097	62097	0.00	55.47

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Yin Chen Hao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60163-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yin Chen Hao; Artemisiae scopariae herba

Special notes

When selecting the *Yin Chen Hao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yin Chen Hao	1	0	1

Second-stage model

For differentiation of the substance/substance group *Yin Chen Hao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yin Chen Hao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yin Chen Hao	G034H1030721	62397	40	from supplier
PhytoComm	Yin Chen Hao	G034H1030721	62398	40	from supplier

Validation samples

A total of 30 254 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 *Yin Chen Hao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Yin Chen Hao*.
- 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
PhytoComm	Yin Chen Hao	G034H1030721	62397 [†]	20
PhytoComm	Yin Chen Hao	G034H1030721	62398 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Yin Chen Hao*.
- 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
Fagron	Yin Chen Hao	G034H1030421	2

- 855 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yin Chen Hao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yin Chen Hao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	3	0	2	852

The substance/substance group *Yin Chen Hao* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	99.7209 % (> 99.1360 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yin Chen Hao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Nü Zhen Zi	10.79	—
Dan Zhu Ye	14.10	—
Jing Jie	15.62	—
Qiang Huo	18.05	—
Gou Teng	19.28	—
Pu Gong Ying	22.82	—
Sha Ren	24.14	—
Wu Zhu Yu	24.23	—
Sang Ji Shend	24.29	—
Hong Jing Tian	25.45	—
Xian He Cao	27.84	—
Yi Mu Cao	27.92	—
Huang Bo	28.10	—
Sang Bai Pi	28.67	—
Gu Sui Bu	29.77	—
He Shou Wu	30.87	—
He Huan Pi	31.47	—
Wu Jia Pi	32.47	—
Yu Jin	33.24	—
Du Zhong	33.39	—
Bu Gu Zhi	33.51	—
Chen Pi	33.88	—
Gui Zhi	34.85	—
Zhi Shi	35.21	—
Jin Qian Cao	35.27	—
Fang Feng	36.54	—
Xu Duan	37.83	—
Fu Zi	39.35	—
Qing Hao	39.65	—
Wu Yao	40.09	—
Ge Gen	41.71	—
Sang Ye	42.45	—
Ku Shen	42.56	—
Xin Yi	44.49	—
Hu Zhang	44.83	—
Ju Hua	45.79	—
Bai Hua She She Cao	46.49	—
Jiang Huang	46.86	—
Han Lian Cao	47.14	—
Xia Ku Cao	47.74	—
Cang Er Zi	49.99	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yin Chen Hao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62398	62398	0.00	11.20
62397	62397	0.00	10.79

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 2.3-2020-05

Validated substance/substance group **Yin Yang Huo**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60228-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yin Yang Huo; Epimedii herba

Special notes

When selecting the *Yin Yang Huo* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yin Yang Huo	1	0	1

Second-stage model

For differentiation of the substance/substance group *Yin Yang Huo* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yin Yang Huo*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yin Yang Huo	G098HS241SH1	62683	40	from supplier
PhytoComm	Yin Yang Huo	G098HS241SH1	62684	40	from supplier

Validation samples

A total of 30 254 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 *Yin Yang Huo*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Yin Yang Huo*.
- 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
PhytoComm	Yin Yang Huo	G098HS241SH1	62683 [†]	20
PhytoComm	Yin Yang Huo	G098HS241SH1	62684 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 1 batches from the substance/substance group *Yin Yang Huo*.
- 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
Phytocomm	Yin Yang Huo	G098H1114422	2

- 855 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yin Yang Huo* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yin Yang Huo* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	1	80	0	19 399
Type B	0	39	1	9877
Type C	0	0	2	855

The substance/substance group *Yin Yang Huo* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9960 % (> 99.9777 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yin Yang Huo* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bai Xian Pi	4.45	—
Mao Dong Qing	5.16	—
Hou Po	6.86	—
Ling Zhi	7.05	—
Dan Dou Chi	7.23	—
Yu Jin	7.59	—
Ye Jiao Teng	8.59	—
Che Qian Zi	8.85	—
Qiang Huo	9.49	—
Ren Dong Teng	11.56	—
Yuan Zhi	11.98	—
Yan Hu Suo	12.02	—
Tu Fu Ling	12.14	—
Shen Qu	12.49	—
Du Zhong	13.98	—
Lian Zi	14.57	—
Shan Yao	14.66	—
Chai Hu	15.50	—
Ji Xue Teng	15.59	—
Dan Shen	16.19	—
Pi Pa Ye	16.64	—
Zi Hua Di Ding	16.67	—
Ma Huang	17.51	—
Chuan Xiong	17.55	—
Mu Dan Pi	17.87	—
Ji Li	18.50	—
Ma Huang Gen	18.74	—
Rou Gui	19.02	—
Qing Pi	19.55	—
Jin Yin Hua	20.76	—
He Huan Pi	21.46	—
Hong Jing Tian	21.57	—
Jiao Gu Lan	21.88	—
Gou Teng	21.94	—
Lian Qiao	22.12	—
Huang Lian	22.94	—
Bai Shao Yao	23.12	—
Chen Pi	23.14	—
Zhi Ke	23.45	—
Sheng Jiang	24.42	—
Fu Zi	24.58	—
Huo Ma Ren	24.99	—
Gui Zhi	26.08	—
Gua Lou	26.12	—
Di Gu Pi	26.22	—
Yi Yi Ren	26.96	—
Tian Hua Fen	28.31	—
Wu Wei Zi	28.49	—
Fu Ling	28.51	—
Cang Zhu	28.92	—
Huang Bai	29.18	—
Tao Ren	31.18	—

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Substanz	Distance in main model	Distance in second-stage model
Zhe Bei Mu	31.29	—
Gou Qi Zi	31.81	—
Tai Zi Shen	33.92	—
Pu Gong Ying	34.53	—
Da Zao	34.65	—
Fu Shen	35.12	—
Ban Zhi Lian	35.80	—
Bai Zi Ren	35.84	—
Ban Xia (Jiang)	37.06	—
Long Yan Rou	37.39	—
Mang Xiao	38.26	—
Ci Wu Jia	38.33	—
Fo Shou	38.53	—
Fu Xiao Mai	39.06	—
Suan Zao Ren	39.23	—
Sang Zhi	39.31	—
Huang Qin	40.87	—
Yu Zhu	41.19	—
Chi Shao (Yao)	41.19	—
Jie Geng	41.29	—
Wang Bu Liu Xing	41.68	—
Tian Men Dong	42.99	—
San Qi	43.29	—
Zhu Ru	43.57	—
Dang Shen	43.69	—
Sang Ye	43.86	—
Chuang Mu Xiang	44.56	—
Dang Gui	44.58	—
Xi Xian Cao	44.72	—
Dang Gui Wei	44.98	—
Chuan Lian Zi	45.82	—
Shan Yu Rou	45.99	—
E Zhu	46.57	—
Cang Er Zi	46.95	—
Zi Su Zi	47.26	—
Jiang Huang	47.57	—
Bai Zhu	47.65	—
Bai Bian Dou	48.78	—
Bai Mao Gen	49.34	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yin Yang Huo* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62684	62684	0.00	4.45
62683	62683	0.00	4.50

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Yu Jin**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60171-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yu Jin; Curcumae tuber

Special notes

When selecting the *Yu Jin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yu Jin	2	0	0

Second-stage model

For differentiation of the substance/substance group *Yu Jin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yu Jin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yu Jin	G084HS357RN1	62277	40	from supplier
PhytoComm	Yu Jin	G084HS357RN1	62278	40	from supplier
PhytoComm	Yu Jin	G084H2201821	62517	40	from supplier
PhytoComm	Yu Jin	G084H2201821	62518	40	from supplier

Validation samples

A total of 30 254 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 *Yu Jin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Yu Jin*.
- 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
PhytoComm	Yu Jin	G084HS357RN1	62277 [†]	20
PhytoComm	Yu Jin	G084HS357RN1	62278 [†]	20
PhytoComm	Yu Jin	G084H2201821	62517 [†]	20
PhytoComm	Yu Jin	G084H2201821	62518 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Yu Jin*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yu Jin* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yu Jin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	1	80	0	9836
Type C	0	0	0	857

The substance/substance group *Yu Jin* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	99.9947 % (> 99.9588 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8345 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yu Jin* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ling Zhi	5.50	—
Mao Dong Qing	5.94	—
Yin Yang Huo	6.60	—
Hou Po	6.80	—
Qiang Huo	7.46	—
Du Zhong	8.32	—
Bai Xian Pi	8.41	—
Dan Dou Chi	9.69	—
Xian He Cao	9.70	—
Che Qian Zi	10.39	—
Wu Yao	10.98	—
Ye Jiao Teng	12.34	—
Ren Dong Teng	13.52	—
Yan Hu Suo	13.97	—
Chen Pi	14.09	—
Shen Qu	14.57	—
Shan Yao	14.86	—
Chai Hu	15.00	—
He Huan Pi	15.22	—
Sha Ren	15.44	—
Gui Zhi	15.56	—
Qing Pi	15.60	—
Zi Hua Di Ding	15.99	—
Dan Shen	16.17	—
Ji Li	16.80	—
Fu Zi	17.15	—
Mu Dan Pi	17.33	—
Pi Pa Ye	17.89	—
Jiao Gu Lan	17.97	—
Ji Xue Teng	18.75	—
Lian Zi	19.05	—
Jiang Huang	19.24	—
Yuan Zhi	19.37	—
He Shou Wu	19.54	—
Chuan Xiong	19.93	—
Hong Jing Tian	20.06	—
Lian Qiao	20.97	—
Gu Sui Bu	21.40	—
Ma Huang	22.11	—
Huang Lian	22.40	—
Zhi Ke	22.67	—
Fang Feng	22.91	—
(Bai) Dou Kou	23.24	—
Jin Yin Hua	23.54	—
Huang Bai	24.16	—
Sang Ji Shend	25.11	—
Gou Teng	25.60	—
Tu Fu Ling	26.14	—
Wu Wei Zi	26.17	—
Bai Shao Yao	26.41	—
Sang Bai Pi	26.92	—
Di Gu Pi	27.45	—

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Substanz	Distance in main model	Distance in second-stage model
Ma Huang Gen	27.64	—
Sheng Jiang	28.63	—
Yin Chen Hao	29.17	—
Huo Ma Ren	29.25	—
Mang Xiao	29.61	—
Rou Gui	29.97	—
Gua Lou	31.21	—
Tao Ren	31.95	—
Cang Zhu	32.34	—
Wu Zhu Yu	32.66	—
Tian Hua Fen	32.96	—
Nü Zhen Zi	33.06	—
Pu Gong Ying	33.17	—
Xiang Fu	33.20	—
Dan Zhu Ye	33.60	—
Yi Yi Ren	33.71	—
Zi Su Zi	34.04	—
Huang Bo	34.61	—
Xi Xian Cao	34.80	—
Tai Zi Shen	35.09	—
(Shi) Chang Pu	35.38	—
Bu Gu Zhi	35.60	—
Fu Ling	35.90	—
Gou Qi Zi	36.24	—
E Zhu	36.49	—
Zhe Bei Mu	36.58	—
Ge Gen	37.16	—
Suan Zao Ren	37.21	—
Sang Ye	37.36	—
Wang Bu Liu Xing	37.55	—
Ba Ji Tian	37.67	—
Hu Zhang	39.39	—
Ban Zhi Lian	39.42	—
Bai Zi Ren	40.13	—
Xu Duan	41.10	—
Du Huo	41.25	—
Shan Yu Rou	42.05	—
Ban Xia (Jiang)	42.69	—
Fu Shen	42.82	—
Xie Bai	42.83	—
Dang Gui	43.02	—
Ci Wu Jia	43.18	—
Ju Hua	43.40	—
Cang Er Zi	43.52	—
Sang Zhi	43.80	—
San Qi	43.94	—
Huang Qin	43.95	—
Bai Mao Gen	44.29	—
Da Zao	44.50	—
Yu Zhu	45.57	—
Chi Shao (Yao)	45.73	—
Ku Shen	45.81	—
Wu Mei	45.95	—
Huang Qi	46.42	—
Yi Mu Cao	46.73	—
Xin Yi	46.73	—
Chuan Lian Zi	47.48	—
Zhu Ru	47.56	—
Zhi Shi	47.57	—

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Substanz	Distance in main model	Distance in second-stage model
Fu Xiao Mai	47.78	—
Jie Geng	47.90	—
Niu Bang Zi	48.15	—
Chuang Mu Xiang	48.40	—
Bai Zhu	48.41	—
(Huai) Niu Xi	48.63	—
Dang Shen	48.64	—
Bai Bian Dou	49.65	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yu Jin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62278	62278	0.00	5.86
62277	62277	0.00	5.50
62518	62518	0.00	10.06
62517	62517	0.00	9.70

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 2.3-2020-05

Validated substance/substance group **Yu Xing Cao**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60606-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yu Xing Cao; Houlttuyniae herba

Special notes

When selecting the *Yu Xing Cao* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yu Xing Cao	1	0	3

Second-stage model

For differentiation of the substance/substance group *Yu Xing Cao* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yu Xing Cao*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yu Xing Cao	G124H1149823	62583	40	from supplier
PhytoComm	Yu Xing Cao	G124H1149823	62584	40	from supplier

Validation samples

A total of 30 254 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 *Yu Xing Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Yu Xing Cao*.
- 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
PhytoComm	Yu Xing Cao	G124H1149823	62583 [†]	20
PhytoComm	Yu Xing Cao	G124H1149823	62584 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 3 *Apo-Ident* customers from 4 batches from the substance/substance group *Yu Xing Cao*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Yu Xing Cao	g124h1149122	1
Phytocomm	Yu Xing Cao	G124H1149222	1
Phytocomm	Yu Xing Cao	G124H1149423	2
Phytocomm	Yu Xing Cao	g124h1149222	1

- 852 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yu Xing Cao* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yu Xing Cao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	5	852

The substance/substance group *Yu Xing Cao* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yu Xing Cao* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
(Sheng) Di Huang	14.00	—
Wu Jia Pi	15.20	—
Sha Ren	28.06	—
Shu Di (Huang)	29.64	—
Jing Jie	30.23	—
Pu Gong Ying	31.52	—
Ai Ye	31.93	—
Sang Bai Pi	37.27	—
Dan Zhu Ye	37.61	—
Du Zhong	43.49	—
Guang Huo Xiang	44.20	—
Hua Shi	45.55	—
Jue Ming Zi	47.68	—
Qing Hao	50.77	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yu Xing Cao* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62583	62583	0.00	14.38
62584	62584	0.00	14.00

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Yu Zhu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60056-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yu Zhu; Polygonati odorati rhizoma

Special notes

When selecting the *Yu Zhu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yu Zhu	1	0	2

Second-stage model

For differentiation of the substance/substance group *Yu Zhu* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yu Zhu*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yu Zhu	G195HS087SK1	62605	40	from supplier
PhytoComm	Yu Zhu	G195HS087SK1	62606	40	from supplier

Validation samples

A total of 30 254 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 *Yu Zhu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Yu Zhu*.
- 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
PhytoComm	Yu Zhu	G195HS087SK1	62605 [†]	20
PhytoComm	Yu Zhu	G195HS087SK1	62606 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Yu Zhu*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Yu Zhu	G195H0517421	2
PhytoComm	Yu Zhu	G195H0517121	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yu Zhu* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yu Zhu* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	3	854

The substance/substance group *Yu Zhu* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8280 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yu Zhu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dang Gui Wei	8.02	—
Gua Lou	8.39	—
Chen Pi	8.78	—
Chuan Xiong	11.67	—
Dang Shen	12.66	—
Cang Zhu	13.16	—
Gou Qi Zi	13.24	—
Tai Zi Shen	13.74	—
Zhe Bei Mu	13.85	—
Yuan Zhi	14.35	—
Dang Gui	14.42	—
Bai Shao Yao	14.68	—
Pi Pa Ye	14.77	—
Long Yan Rou	15.45	—
San Qi	15.47	—
Ye Jiao Teng	16.73	—
Fo Shou	17.13	—
Di Gu Pi	17.86	—
Ren Dong Teng	18.03	—
Da Zao	18.33	—
Tao Ren	18.62	—
He Huan Pi	18.67	—
Shen Qu	18.74	—
Lian Zi	19.20	—
Zhi Ke	19.40	—
Lian Qiao	19.42	—
Ma Huang	19.43	—
Hong Jing Tian	20.46	—
Ci Wu Jia	20.81	—
Tian Men Dong	20.85	—
Bai Zi Ren	21.38	—
Chuang Mu Xiang	22.16	—
Ji Li	22.73	—
Gou Teng	22.76	—
Shan Yao	22.76	—
Rou Gui	22.84	—
Jiao Gu Lan	23.56	—
Gui Zhi	23.84	—
Dan Shen	23.94	—
Jin Yin Hua	24.21	—
Shan Yu Rou	24.39	—
Sheng Jiang	24.49	—
Ji Xue Teng	24.52	—
Bai Xian Pi	24.80	—
Tu Fu Ling	24.95	—
Tian Hua Fen	25.50	—
Hou Po	25.66	—
Fu Zi	26.15	—
Jie Geng	26.92	—
Ling Zhi	27.43	—
Bai Zhu	27.50	—
Huo Ma Ren	27.84	—

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Substanz	Distance in main model	Distance in second-stage model
Huang Qin	28.54	—
Yin Yang Huo	29.28	—
Gan Cao	30.10	—
Ban Xia (Jiang)	30.13	—
Dan Dou Chi	30.48	—
Suan Zao Ren	30.50	—
Wu Wei Zi	30.55	—
Fu Ling	30.65	—
Zhi Mu	30.65	—
Mu Dan Pi	30.67	—
Chai Hu	31.34	—
Mao Dong Qing	31.77	—
Fu Xiao Mai	32.01	—
Ma Huang Gen	32.96	—
Yan Hu Suo	33.81	—
Che Qian Zi	34.89	—
Zhu Ru	35.00	—
Mai Men Dong	35.14	—
Zi Hua Di Ding	35.90	—
Yi Yi Ren	36.12	—
Sang Zhi	36.23	—
Yu Jin	37.08	—
Fu Shen	37.10	—
Qiang Huo	38.76	—
Chi Shao (Yao)	40.29	—
Mang Xiao	42.75	—
Qing Pi	44.24	—
Huang Lian	46.29	—
Huang Qi	48.03	—
Cang Er Zi	48.53	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yu Zhu* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62606	62606	0.00	8.02
62605	62605	0.00	8.39

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 2.3-2020-05

Validated substance/substance group **Yuan Zhi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60100-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Yuan Zhi; Polygalae radix

Special notes

When selecting the *Yuan Zhi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yuan Zhi	3	0	3

Second-stage model

For differentiation of the substance/substance group *Yuan Zhi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Yuan Zhi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Yuan Zhi	G194HS306RP1	62431	40	from supplier
PhytoComm	Yuan Zhi	G194HS306RP1	62432	40	from supplier
PhytoComm	Yuan Zhi	G194HS306SH1	62557	40	from supplier
PhytoComm	Yuan Zhi	G194HS306SH1	62558	40	from supplier
PhytoComm	Yuan Zhi	G194H1406921	62743	40	from supplier
PhytoComm	Yuan Zhi	G194H1406921	62744	40	from supplier

Validation samples

A total of 30 254 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Yuan Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 19 240 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 6 reference samples from the substance/substance group *Yuan Zhi*.
- 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
PhytoComm	Yuan Zhi	G194HS306RP1	62431 [†]	20
PhytoComm	Yuan Zhi	G194HS306RP1	62432 [†]	20
PhytoComm	Yuan Zhi	G194HS306SH1	62557 [†]	20
PhytoComm	Yuan Zhi	G194HS306SH1	62558 [†]	20
PhytoComm	Yuan Zhi	G194H1406921	62743 [†]	20
PhytoComm	Yuan Zhi	G194H1406921	62744 [†]	20

- 9797 spectra from a total of 241 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 6 *Apo-Ident* customers from 3 batches from the substance/substance group *Yuan Zhi*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Yuan Zhi	g194h140622	1
Phytocomm	Yuan Zhi	G194H1406222	1
Phytocomm	Yuan Zhi	G194H1406522	2
PhytoComm	Yuan Zhi	G194H1406222	1
PhytoComm	Yuan Zhi	G194H1406522	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Yuan Zhi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yuan Zhi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	19 240
Type B	4	118	2	9793
Type C	1	2	4	850

The substance/substance group *Yuan Zhi* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9631 %)	100.0000 % (> 97.5000 %)
Type B	99.9684 % (> 99.9324 %)	98.3333 % (> 95.8333 %)
Type C	99.9225 % (> 99.3354 %)	n/a (n/a)

[†]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*.

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Yuan Zhi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cang Zhu	4.82	—
Bai Shao Yao	5.11	—
Dang Shen	6.64	—
Lian Qiao	7.78	—
Suan Zao Ren	8.10	—
Chuan Xiong	8.69	—
(Huai) Niu Xi	9.01	—
Jiao Gu Lan	10.45	—
Shan Yao	11.01	—
Ji Li	11.44	—
Pi Pa Ye	12.09	—
Chen Pi	12.09	—
Ye Jiao Teng	12.12	—
Mao Dong Qing	12.57	—
Zhi Mu	12.86	—
Bai Zi Ren	12.96	—
Huang Qi	13.10	—
Gua Lou	13.17	—
San Qi	13.30	—
Gou Qi Zi	13.31	—
Di Gu Pi	13.62	—
Fo Shou	13.91	—
Jin Yin Hua	14.01	—
Tian Men Dong	14.44	—
He Huan Pi	16.18	—
Shan Yu Rou	16.25	—
Chuang Mu Xiang	16.57	—
Dang Gui Wei	16.69	—
Lian Zi	16.76	—
Shen Qu	17.16	—
Dan Shen	17.34	—
Mu Dan Pi	17.49	—
Bai Mao Gen	17.87	—
Fu Xiao Mai	17.99	—
Ling Zhi	18.18	—
Fu Zi	18.49	—
Huo Ma Ren	18.50	—
Ci Wu Jia	18.77	—
Rou Gui	19.23	—
Wu Wei Zi	19.23	—
Yu Zhu	19.37	—

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Substanz	Distance in main model	Distance in second-stage model
Fu Ling	19.38	—
Chi Shao (Yao)	19.47	—
Hou Po	19.76	—
Sang Zhi	20.09	—
Zhe Bei Mu	20.20	—
Chai Hu	20.30	—
Ren Dong Teng	20.61	—
Dang Gui	21.76	—
Tu Fu Ling	21.87	—
Qing Pi	21.92	—
Jie Geng	22.07	—
Tian Hua Fen	22.08	—
Gui Zhi	22.10	—
Tai Zi Shen	22.22	—
Sheng Jiang	22.79	—
Da Zao	23.10	—
Xiang Fu	23.96	—
Hong Jing Tian	24.12	—
Ku Shen	24.40	—
Zhu Ru	24.48	—
Niu Bang Zi	24.56	—
Mai Men Dong	24.81	—
Tao Ren	24.91	—
Ban Xia (Jiang)	26.25	—
Dan Dou Chi	26.40	—
Zhi Ke	26.72	—
Bai Xian Pi	26.82	—
Gou Teng	27.72	—
Bai Zhu	27.89	—
Yan Hu Suo	27.98	—
Yi Yi Ren	28.00	—
Qiang Huo	28.71	—
Ji Xue Teng	28.79	—
Gan Cao	28.98	—
Cang Er Zi	29.02	—
Yin Yang Huo	29.30	—
Yu Jin	31.39	—
Che Qian Zi	31.87	—
Huang Qin	32.14	—
(Shi) Chang Pu	32.21	—
Long Yan Rou	32.84	—
Zi Hua Di Ding	33.03	—
Du Zhong	33.64	—
Qin Jiao	35.00	—
Du Huo	35.28	—
Lai Fu Zi	35.50	—
Ma Huang	36.67	—
Ma Huang Gen	36.98	—
Mang Xiao	37.20	—
Pu Gong Ying	39.05	—
Huang Lian	39.23	—
Sha Shen (Bei)	40.17	—
Fu Shen	40.91	—
Dong Gua Zi	41.20	—
Chuan Lian Zi	41.64	—
E Zhu	42.00	—
Fang Feng	42.00	—
Ju Hua	42.48	—
Hong Hua	42.83	—

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Substanz	Distance in main model	Distance in second-stage model
Sang Ye	42.91	—
Huang Bai	43.19	—
Zi Su Zi	44.41	—
Yi Mu Cao	44.62	—
Wu Yao	46.50	—
Xie Bai	46.86	—
Ban Zhi Lian	48.63	—
Jiang Huang	49.24	—
(Bai) Dou Kou	49.67	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yuan Zhi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62743	62743	0.00	9.01
62431	62431	0.00	4.82
62432	62432	0.00	5.25
62744	62744	0.00	9.21
62557	62557	0.00	5.11
62558	62558	0.00	5.42

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Zhe Bei Mu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50388-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zhe Bei Mu; Fritillariae thunbergii bulbus

Special notes

When selecting the *Zhe Bei Mu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zhe Bei Mu	1	0	2

Second-stage model

For differentiation of the substance/substance group *Zhe Bei Mu* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zhe Bei Mu*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zhe Bei Mu	G108HS138SG1	62687	40	from supplier
PhytoComm	Zhe Bei Mu	G108HS138SG1	62688	40	from supplier

Validation samples

A total of 30 254 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 *Zhe Bei Mu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Zhe Bei Mu*.
- 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
PhytoComm	Zhe Bei Mu	G108HS138SG1	62687 [†]	20
PhytoComm	Zhe Bei Mu	G108HS138SG1	62688 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Zhe Bei Mu*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Zhe Bei Mu	G108H0712422	1
PhytoComm	Zhe Bei Mu	G108H0712321	1

- 855 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zhe Bei Mu* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zhe Bei Mu* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	39	1	9877
Type C	0	0	2	855

The substance/substance group *Zhe Bei Mu* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zhe Bei Mu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tian Hua Fen	8.00	—
Bai Shao Yao	8.43	—
Pi Pa Ye	8.88	—
Tai Zi Shen	9.41	—
He Huan Pi	10.56	—
Di Gu Pi	10.95	—
Shan Yao	11.50	—
Bai Zi Ren	11.63	—
Ban Xia (Jiang)	12.05	—
Ye Jiao Teng	12.18	—
Lian Qiao	12.30	—
Gua Lou	13.06	—
Shen Qu	13.36	—
Ji Li	13.61	—
Tao Ren	14.25	—
Sheng Jiang	15.04	—
Ji Xue Teng	15.49	—
Yi Yi Ren	15.68	—
Huo Ma Ren	16.00	—
Fu Zi	16.40	—
Chuan Xiong	17.03	—
Zhu Ru	17.16	—
Ci Wu Jia	17.35	—
Jin Yin Hua	17.36	—
Gui Zhi	17.89	—
Yuan Zhi	18.01	—
Yan Hu Suo	18.32	—
Lian Zi	19.10	—
Fu Xiao Mai	20.38	—
Ling Zhi	20.98	—
Rou Gui	21.01	—
Gou Teng	21.13	—
Fu Ling	21.15	—
Ren Dong Teng	21.16	—
Dang Shen	21.71	—
Zhi Ke	22.17	—
Shan Yu Rou	22.60	—
Chen Pi	22.74	—
Fo Shou	22.77	—
Jiao Gu Lan	23.87	—
Hou Po	23.88	—
Bai Xian Pi	24.09	—
Huang Qin	24.34	—
Dang Gui Wei	24.52	—
Cang Zhu	24.76	—
Dang Gui	24.86	—
Yu Jin	25.21	—
Wu Wei Zi	25.36	—
Da Zao	25.84	—
Yu Zhu	26.20	—
San Qi	26.57	—
Ma Huang	29.13	—

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Substanz	Distance in main model	Distance in second-stage model
Long Yan Rou	29.37	—
Che Qian Zi	29.50	—
Yin Yang Huo	30.80	—
Fu Shen	30.93	—
Zhi Mu	31.13	—
Tian Men Dong	31.42	—
Dan Shen	32.05	—
Tu Fu Ling	32.18	—
Ma Huang Gen	32.41	—
Dan Dou Chi	32.81	—
Chai Hu	35.29	—
Mu Dan Pi	36.14	—
Gou Qi Zi	36.94	—
Mao Dong Qing	37.01	—
Qiang Huo	39.23	—
Gan Cao	39.78	—
Huang Lian	40.59	—
Bai Zhu	40.69	—
Suan Zao Ren	41.86	—
Hong Jing Tian	41.92	—
Qing Pi	42.13	—
Sang Zhi	43.39	—
Mang Xiao	44.09	—
Chuang Mu Xiang	46.40	—
Chi Shao (Yao)	46.82	—
Jie Geng	46.84	—
Du Zhong	49.12	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zhe Bei Mu* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62687	62687	0.00	8.00
62688	62688	0.00	8.43

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 2.3-2020-05

Validated substance/substance group **Zhi Ke**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60158-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zhi Ke; Citri aurantii fructus

Special notes

When selecting the *Zhi Ke* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zhi Ke	2	0	2

Second-stage model

For differentiation of the substance/substance group *Zhi Ke* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zhi Ke*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zhi Ke	G043HS169RR1	62439	40	from supplier
PhytoComm	Zhi Ke	G043HS169RR1	62440	40	from supplier
PhytoComm	Zhi Ke	G043HS169SL1	62703	40	from supplier
PhytoComm	Zhi Ke	G043HS169SL1	62704	40	from supplier

Validation samples

A total of 30 254 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 *Zhi Ke*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Zhi Ke*.
- 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
PhytoComm	Zhi Ke	G043HS169RR1	62439 [†]	20
PhytoComm	Zhi Ke	G043HS169RR1	62440 [†]	20
PhytoComm	Zhi Ke	G043HS169SL1	62703 [†]	20
PhytoComm	Zhi Ke	G043HS169SL1	62704 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 2 batches from the substance/substance group *Zhi Ke*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Zhi Ke	G043H0921422	2
Phytocomm	Zhi Ke	G043H0921221	1

- 854 spectra from 13 *Apo-Ident* customers from a total of 517 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zhi Ke* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zhi Ke* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	1	0	3	853

The substance/substance group *Zhi Ke* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	99.7674 % (> 99.1814 %)	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.)

[†]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*.

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zhi Ke* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Jin Yin Hua	9.59	—
Ma Huang	13.12	—
Jiao Gu Lan	13.37	—
Lian Qiao	13.40	—
Hou Po	13.71	—
Zi Hua Di Ding	15.30	—
Wu Wei Zi	15.80	—
Yan Hu Suo	17.01	—
Shan Yu Rou	17.30	—
Bai Zhu	17.54	—
San Qi	18.45	—
Fu Zi	18.49	—
Cang Zhu	18.62	—
Pi Pa Ye	18.86	—
Hong Jing Tian	19.16	—
Dan Shen	19.70	—
Yin Yang Huo	19.91	—
Ye Jiao Teng	20.04	—
Gou Qi Zi	20.11	—
Zhe Bei Mu	20.43	—
Yu Zhu	20.43	—
Shan Yao	20.46	—
Qing Pi	20.47	—
Gua Lou	21.58	—
Chuang Mu Xiang	21.66	—
Dang Gui	22.56	—
Tai Zi Shen	22.90	—
Chuan Xiong	23.23	—
Mu Dan Pi	23.72	—
Qiang Huo	24.04	—
Chai Hu	24.17	—
Bai Shao Yao	24.20	—
Huang Qin	24.38	—
Ren Dong Teng	24.70	—
He Huan Pi	24.92	—
Dang Shen	25.30	—
Gan Cao	25.84	—
Huang Lian	26.33	—
Huang Bai	26.62	—
Zhi Mu	26.79	—
Bai Zi Ren	27.51	—
Suan Zao Ren	28.01	—
Ji Li	28.93	—
Tian Hua Fen	29.43	—
Di Gu Pi	29.58	—

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Substanz	Distance in main model	Distance in second-stage model
Sang Ye	29.70	—
Chen Pi	29.84	—
Tao Ren	30.26	—
Lian Zi	30.88	—
Yuan Zhi	30.98	—
Bai Xian Pi	31.64	—
Dang Gui Wei	31.94	—
Ji Xue Teng	32.29	—
Che Qian Zi	32.35	—
Hong Hua	33.17	—
Du Zhong	33.20	—
Mao Dong Qing	34.78	—
Dan Dou Chi	35.06	—
Chi Shao (Yao)	35.15	—
Cang Er Zi	35.55	—
Huo Ma Ren	38.18	—
Yu Jin	38.47	—
Gui Zhi	38.79	—
Sheng Jiang	38.83	—
Ci Wu Jia	39.76	—
Shen Qu	41.35	—
Yi Yi Ren	42.36	—
Gou Teng	42.39	—
Ling Zhi	43.07	—
Tu Fu Ling	43.79	—
Bai Mao Gen	43.85	—
Rou Gui	44.21	—
Wu Yao	44.83	—
Mang Xiao	46.99	—
Fu Ling	47.11	—
Long Yan Rou	48.40	—
Ban Zhi Lian	49.18	—
Pu Gong Ying	49.30	—
Wu Mei	49.61	—
Sang Zhi	49.95	—
Ban Xia (Jiang)	49.98	—
Fu Xiao Mai	50.19	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zhi Ke* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62704	62704	0.00	13.52
62439	62439	0.00	10.58
62440	62440	0.00	9.59
62703	62703	0.00	13.40

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 2.3-2020-05

Validated substance/substance group **Zhi Mu**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60196-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zhi Mu; Anemarrhenae rhizoma

Special notes

When selecting the *Zhi Mu* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zhi Mu	1	0	1

Second-stage model

For differentiation of the substance/substance group *Zhi Mu* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zhi Mu*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zhi Mu	G019HS153SG1	62647	40	from supplier
PhytoComm	Zhi Mu	G019HS153SG1	62648	40	from supplier

Validation samples

A total of 30 254 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 *Zhi Mu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Zhi Mu*.
- 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
PhytoComm	Zhi Mu	G019HS153SG1	62647 [†]	20
PhytoComm	Zhi Mu	G019HS153SG1	62648 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Zhi Mu*.
- 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
PhytoComm	Zhi Mu	G019H0824321	1

- 856 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zhi Mu* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zhi Mu* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	1	856

The substance/substance group *Zhi Mu* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8367 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zhi Mu* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yuan Zhi	9.23	—
Dang Shen	9.32	—
Bai Shao Yao	11.10	—
Shan Yu Rou	12.50	—
Chuan Xiong	12.65	—
Shan Yao	15.23	—
Pi Pa Ye	16.11	—
Chen Pi	17.56	—
San Qi	18.00	—
Cang Zhu	18.74	—
Tian Men Dong	19.86	—
Dang Gui Wei	20.34	—
Ye Jiao Teng	20.42	—
Di Gu Pi	20.52	—
Ji Li	21.85	—
Dang Gui	22.86	—
Fo Shou	22.87	—
Lian Zi	23.25	—
Lian Qiao	23.48	—
Mai Men Dong	24.06	—
Gou Qi Zi	24.44	—
Bai Zi Ren	24.98	—
Gua Lou	25.01	—
He Huan Pi	25.17	—
Fu Xiao Mai	25.22	—
Shen Qu	25.31	—
Jiao Gu Lan	25.70	—
Zhe Bei Mu	26.72	—
Suan Zao Ren	26.99	—
Ren Dong Teng	27.06	—
Yu Zhu	27.50	—
Zhi Ke	27.64	—
Jie Geng	28.19	—
Fu Ling	28.26	—
Rou Gui	28.45	—
Huo Ma Ren	28.78	—
Ci Wu Jia	28.85	—
Tai Zi Shen	29.25	—
Tian Hua Fen	29.27	—
Mu Dan Pi	29.29	—
Tu Fu Ling	29.32	—
Da Zao	29.96	—
Jin Yin Hua	30.29	—
Gui Zhi	30.84	—
Wu Wei Zi	31.23	—
Chuang Mu Xiang	31.38	—
Mao Dong Qing	31.68	—
Sheng Jiang	31.75	—
Ling Zhi	31.99	—
Hou Po	33.30	—
Zhu Ru	33.88	—
Yi Yi Ren	35.73	—

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Substanz	Distance in main model	Distance in second-stage model
Gan Cao	35.93	—
Gou Teng	36.02	—
Tao Ren	36.17	—
Bai Zhu	36.54	—
Long Yan Rou	36.90	—
Ji Xue Teng	36.95	—
Huang Qin	37.56	—
Ban Xia (Jiang)	37.93	—
Fu Zi	37.97	—
Dan Shen	38.64	—
Bai Xian Pi	40.37	—
Che Qian Zi	43.35	—
Sang Zhi	44.53	—
Hong Jing Tian	45.60	—
Yin Yang Huo	46.24	—
Mang Xiao	46.32	—
Chai Hu	46.89	—
Yan Hu Suo	47.28	—
Dan Dou Chi	47.59	—
Ma Huang	47.66	—
Chi Shao (Yao)	48.71	—
Yu Jin	49.78	—
Ma Huang Gen	50.37	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zhi Mu* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62647	62647	0.00	9.23
62648	62648	0.00	9.50

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Zhi Shi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60145-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zhi Shi; Aurantii fructus immaturus

Special notes

When selecting the *Zhi Shi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zhi Shi	2	0	3

Second-stage model

For differentiation of the substance/substance group *Zhi Shi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zhi Shi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zhi Shi	G044H0922821	62389	40	from supplier
PhytoComm	Zhi Shi	G044H0922821	62390	40	from supplier
PhytoComm	Zhi Shi	G044HS168SK1	62655	40	from supplier
PhytoComm	Zhi Shi	G044HS168SK1	62656	40	from supplier

Validation samples

A total of 30 254 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 *Zhi Shi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 19 320 spectra from a total of 242 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 4 reference samples from the substance/substance group *Zhi Shi*.
- 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
PhytoComm	Zhi Shi	G044H0922821	62389 [†]	20
PhytoComm	Zhi Shi	G044H0922821	62390 [†]	20
PhytoComm	Zhi Shi	G044HS168SK1	62655 [†]	20
PhytoComm	Zhi Shi	G044HS168SK1	62656 [†]	20

- 9837 spectra from a total of 242 batches from further 158 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 14 spectra from 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Zhi Shi*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
phytocomm	Zhi Shi	g044h0922321	1
Phytocomm	Zhi Shi	G044H0922221	2
Phytocomm	Zhi Shi	g044h0922221	1
Phytocomm	Zhi Shi	G044H0922321	2
Phytocomm	Zhi Shi	G044H0922521	3
PhytoComm	Zhi Shi	G044H0922321	2
PhytoComm	Zhi Shi	G044H0922221	3

- 843 spectra from 13 *Apo-Ident* customers from a total of 514 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zhi Shi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zhi Shi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	19 320
Type B	0	80	0	9837
Type C	0	1	13	843

The substance/substance group *Zhi Shi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9632 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9282 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8246 %)	n/a (n/a)

[†]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*.

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zhi Shi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Xia Ku Cao	10.84	—
Hu Zhang	14.12	—
Bai Hua She She Cao	19.29	—
Ge Gen	21.55	—
Han Lian Cao	25.89	—
Huang Bo	26.98	—
Sang Ye	27.04	—
Xin Yi	27.97	—
Yi Mu Cao	28.60	—
Qiang Huo	30.94	—
Dan Zhu Ye	35.62	—
Sang Ji Shend	36.97	—
Gu Sui Bu	37.77	—
Xi Xian Cao	38.87	—
Jing Jie	38.89	—
Gou Teng	38.90	—
Xian He Cao	39.00	—
Huang Lian	39.40	—
Sha Ren	39.44	—
Rou Cong Rong	40.84	—
He Shou Wu	41.15	—
Nü Zhen Zi	41.51	—
He Huan Pi	41.99	—
Wu Zhu Yu	42.12	—
Sang Bai Pi	43.01	—
Jiang Huang	44.44	—
Fu Zi	44.54	—
Pu Gong Ying	44.55	—
Yin Chen Hao	47.53	—
Yu Jin	48.66	—
Xuan Shen	49.28	—
Shan Yao	49.50	—
Bu Gu Zhi	49.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zhi Shi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62390	62390	0.00	22.46
62655	62655	0.00	11.59
62656	62656	0.00	10.84
62389	62389	0.00	21.55

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Zhi Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60367-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zhi Zi; Gardeniae fructus

Special notes

When selecting the *Zhi Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zhi Zi	1	0	2

Second-stage model

For differentiation of the substance/substance group *Zhi Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zhi Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zhi Zi	G110H1137922	62733	40	from supplier
PhytoComm	Zhi Zi	G110H1137922	62734	40	from supplier

Validation samples

A total of 30 254 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 *Zhi Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Zhi Zi*.
- 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
PhytoComm	Zhi Zi	G110H1137922	62733 [†]	20
PhytoComm	Zhi Zi	G110H1137922	62734 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 6 *Apo-Ident* customers from 3 batches from the substance/substance group *Zhi Zi*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Zhi Zi	g110h1137121	1
Phytocomm	Zhi Zi	G110H1137521	3
PhytoComm	Zhi Zi	G110H1137121	1
PhytoComm	Zhi Zi	G110H1137521	1

- 851 spectra from 13 *Apo-Ident* customers from a total of 516 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zhi Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zhi Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	6	851

The substance/substance group *Zhi Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8258 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zhi Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ku Shen	22.48	—
Dong Gua Zi	23.83	—
Shen Qu	28.61	—
Shan Yao	32.06	—
Gui Zhi	36.61	—
Gua Lou	36.92	—
Cang Er Zi	37.41	—
Niu Bang Zi	37.65	—
Lian Qiao	37.67	—
Yi Mu Cao	39.43	—
Huang Bo	39.55	—
Wu Wei Zi	43.54	—
Mang Xiao	43.72	—
Bai Bian Dou	45.52	—
Di Gu Pi	45.58	—
Jiang Huang	46.17	—
Xie Bai	47.61	—
Jin Yin Hua	48.57	—
Wu Mei	49.04	—
Sang Zhi	49.72	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zhi Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62733	62733	0.00	22.48
62734	62734	0.00	23.17

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 2.3-2020-05

Validated substance/substance group **Zhu Ling**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 10002254-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zhu Ling; Polypori umbellati sclerotium

Special notes

When selecting the *Zhu Ling* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zhu Ling	1	0	3

Second-stage model

For differentiation of the substance/substance group *Zhu Ling* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zhu Ling*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zhu Ling	G199H1509921	62747	40	from supplier
PhytoComm	Zhu Ling	G199H1509921	62748	40	from supplier

Validation samples

A total of 30 254 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 *Zhu Ling*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Zhu Ling*.
- 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
PhytoComm	Zhu Ling	G199H1509921	62747 [†]	20
PhytoComm	Zhu Ling	G199H1509921	62748 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Zhu Ling*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Phytocomm	Zhu Ling	G199H1509421	2
PhytoComm	Zhu Ling	G199H1509022	1
PhytoComm	Zhu Ling	G199H1509521	1
Mediherb	Zhu Ling		1

- 852 spectra from 12 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zhu Ling* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zhu Ling* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	5	852

The substance/substance group *Zhu Ling* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8263 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zhu Ling* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Mang Xiao	17.60	—
Mai Ya	29.24	—
Sheng Jiang	30.25	—
E Zhu	30.92	—
Ji Li	32.92	—
San Qi	34.11	—
Sha Shen (Bei)	35.72	—
Jiang Huang	35.90	—
Bai He	36.38	—
(Bai) Dou Kou	36.44	—
Gui Zhi	37.15	—
Sha Ren	38.61	—
Xian He Cao	40.39	—
Sang Zhi	40.44	—
Long Dan (Cao)	40.46	—
Di Gu Pi	41.24	—
Jie Geng	42.14	—
Fu Ling	42.16	—
He Huan Pi	44.10	—
Yu Jin	47.37	—
Cang Er Zi	47.57	—
Du Huo	49.17	—
Shan Yao	50.56	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zhu Ling* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62747	62747	0.00	17.66
62748	62748	0.00	17.60

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 2.3-2020-05

Validated substance/substance group **Zhu Ru**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60241-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zhu Ru; Bambusae in taeniae caulis

Special notes

When selecting the *Zhu Ru* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zhu Ru	1	0	3

Second-stage model

For differentiation of the substance/substance group *Zhu Ru* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zhu Ru*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zhu Ru	G047HS109SK1	62657	40	from supplier
PhytoComm	Zhu Ru	G047HS109SK1	62658	40	from supplier

Validation samples

A total of 30 254 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 *Zhu Ru*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Zhu Ru*.
- 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
PhytoComm	Zhu Ru	G047HS109SK1	62657 [†]	20
PhytoComm	Zhu Ru	G047HS109SK1	62658 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 9 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Zhu Ru*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
phytocomm	Zhu Ru	g047h0625321	1
Phytocomm	Zhu Ru	G047H0625321	2
Phytocomm	Zhu Ru	g047h0625321	1
Phytocomm	Zhu Ru	G047h625321	1
Phytocomm	Zhu Ru	G047H0625422	3
PhytoComm	Zhu Ru	G047H0625321	1

- 848 spectra from 13 *Apo-Ident* customers from a total of 515 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zhu Ru* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zhu Ru* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	76	4	19 400
Type B	1	32	8	9876
Type C	0	0	9	848

The substance/substance group *Zhu Ru* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	95.0000 % (> 91.2500 %)
Type B	99.9921 % (> 99.9563 %)	80.0000 % (> 72.5000 %)
Type C	100.0000 % (> 98.8251 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zhu Ru* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Yi Yi Ren	3.16	—
Fu Xiao Mai	4.62	—
Sheng Jiang	5.77	—
Di Gu Pi	6.96	—
He Huan Pi	7.69	—
Fu Ling	8.02	—
Ci Wu Jia	8.30	—
Gui Zhi	8.51	—
Ji Li	9.06	—
Bai Shao Yao	10.67	—
Shen Qu	11.85	—
Lian Zi	12.02	—
Ban Xia (Jiang)	12.04	—
Tao Ren	12.07	—
Bai Zi Ren	12.53	—
Rou Gui	13.58	—
Ling Zhi	13.66	—
Zhe Bei Mu	13.77	—
Gua Lou	16.05	—
Gou Teng	16.46	—
Huo Ma Ren	16.65	—
Tai Zi Shen	16.90	—
Tian Hua Fen	17.52	—
Bai Xian Pi	18.86	—
Yuan Zhi	19.32	—
Ye Jiao Teng	19.69	—
Shan Yao	19.96	—
Ji Xue Teng	20.53	—
Pi Pa Ye	20.56	—
Fo Shou	20.56	—
Tian Men Dong	21.62	—
Yu Jin	21.98	—
Long Yan Rou	22.64	—
Chen Pi	22.82	—
Ma Huang Gen	22.90	—
Da Zao	23.36	—
Ren Dong Teng	23.75	—
Lian Qiao	24.26	—
Tu Fu Ling	25.43	—
Chuan Xiong	26.29	—
Fu Shen	26.92	—
Dang Shen	27.00	—
Yan Hu Suo	28.18	—
Shan Yu Rou	30.62	—
Fu Zi	30.82	—
Dang Gui Wei	32.19	—
Dan Shen	32.78	—
San Qi	32.78	—

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Substanz	Distance in main model	Distance in second-stage model
Jiao Gu Lan	33.36	—
Dan Dou Chi	33.91	—
Mao Dong Qing	34.11	—
Jin Yin Hua	34.45	—
Wu Wei Zi	36.38	—
Zhi Ke	36.43	—
Yu Zhu	36.80	—
Zhi Mu	37.01	—
Huang Qin	37.06	—
Dang Gui	38.21	—
Yin Yang Huo	38.40	—
Chai Hu	38.45	—
Hou Po	38.50	—
Cang Zhu	40.03	—
Che Qian Zi	40.20	—
Mang Xiao	42.23	—
Suan Zao Ren	43.18	—
Ma Huang	44.83	—
Jie Geng	47.09	—
Qiang Huo	47.24	—
Bai Zhu	47.77	—
Hong Jing Tian	48.62	—
Huang Lian	49.41	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zhu Ru* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62657	62657	0.00	3.24
62658	62658	0.00	3.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.3-2020-05

Validated substance/substance group **Zi Hua Di Ding**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 50376-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zi Hua Di Ding; Viola herba

Special notes

When selecting the *Zi Hua Di Ding* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zi Hua Di Ding	1	0	1

Second-stage model

For differentiation of the substance/substance group *Zi Hua Di Ding* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zi Hua Di Ding*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zi Hua Di Ding	G249HS269SK1	62627	40	from supplier
PhytoComm	Zi Hua Di Ding	G249HS269SK1	62628	40	from supplier

Validation samples

A total of 30 254 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 *Zi Hua Di Ding*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Zi Hua Di Ding*.
- 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
PhytoComm	Zi Hua Di Ding	G249HS269SK1	62627 [†]	20
PhytoComm	Zi Hua Di Ding	G249HS269SK1	62628 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Zi Hua Di Ding*.
- 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
PhytoComm	Zi Hua Di Ding	G249H1216321	2

- 855 spectra from 13 *Apo-Ident* customers from a total of 518 batches from a further 215 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zi Hua Di Ding* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zi Hua Di Ding* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	1	80	0	19 399
Type B	1	39	1	9876
Type C	0	0	2	855

The substance/substance group *Zi Hua Di Ding* can be distinguished from other substances with some limitations. (*False-positive* classifications were obtained.) In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	99.9921 % (> 99.9737 %)	100.0000 % (> 92.5000 %)
Type B	99.9842 % (> 99.9484 %)	97.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.8302 %)	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.

[†]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*.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zi Hua Di Ding* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dan Shen	4.70	—
Mu Dan Pi	6.25	—
Qing Pi	7.04	—
Jiao Gu Lan	8.24	—
Hong Jing Tian	8.31	—
Hou Po	9.65	—
Jin Yin Hua	9.85	—
Qiang Huo	10.23	—
Huang Bai	10.30	—
Chai Hu	11.57	—
Yin Yang Huo	12.27	—
Zhi Ke	13.32	—
Ye Jiao Teng	14.28	—
Chuan Xiong	14.44	—
Ma Huang	14.56	—
Shan Yao	14.74	—
Wu Wei Zi	15.09	—
Mao Dong Qing	15.70	—
Pi Pa Ye	15.89	—
Yan Hu Suo	16.40	—
Yu Jin	16.82	—
Dan Dou Chi	16.98	—
Ren Dong Teng	17.32	—
Du Zhong	17.37	—
Huang Lian	17.84	—
Bai Xian Pi	18.08	—
Gua Lou	18.38	—
Bai Shao Yao	18.89	—
Fu Zi	19.29	—
Ji Li	19.76	—
Che Qian Zi	19.85	—
Gou Qi Zi	20.46	—
Cang Zhu	20.46	—
Sang Ye	20.84	—
Ji Xue Teng	20.97	—
Shan Yu Rou	21.23	—
Yuan Zhi	21.60	—
Bai Zhu	22.02	—
Lian Qiao	22.16	—
Shen Qu	23.08	—
Lian Zi	23.12	—
Di Gu Pi	23.60	—
He Huan Pi	24.14	—
Hong Hua	24.46	—
Ling Zhi	25.72	—
Cang Er Zi	27.05	—
Tu Fu Ling	27.65	—
Chen Pi	29.22	—
Gou Teng	29.34	—
Tao Ren	29.41	—
Pu Gong Ying	29.49	—
Chi Shao (Yao)	30.36	—

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Substanz	Distance in main model	Distance in second-stage model
Gui Zhi	30.99	—
Huang Qin	31.04	—
Zhe Bei Mu	31.19	—
Suan Zao Ren	31.21	—
Huo Ma Ren	31.94	—
San Qi	32.54	—
Gan Cao	32.63	—
Tian Hua Fen	32.91	—
Rou Gui	33.01	—
Bai Zi Ren	33.70	—
Dang Shen	33.74	—
Dang Gui	34.59	—
Bai Mao Gen	34.98	—
Tai Zi Shen	35.04	—
Xi Xian Cao	35.71	—
Chuang Mu Xiang	36.07	—
Da Zao	36.15	—
Ma Huang Gen	36.82	—
Sheng Jiang	36.93	—
Sang Zhi	37.46	—
Long Yan Rou	37.58	—
Wu Mei	37.89	—
Yu Zhu	38.19	—
Ban Zhi Lian	38.53	—
Jie Geng	39.07	—
Fu Ling	39.40	—
Dang Gui Wei	40.09	—
Ci Wu Jia	40.37	—
Mang Xiao	41.30	—
Ban Xia (Jiang)	41.37	—
Jiang Huang	41.40	—
Wu Yao	42.97	—
Yi Yi Ren	45.65	—
Zhu Ru	46.46	—
Fu Shen	46.50	—
E Zhu	46.97	—
Yi Mu Cao	47.35	—
(Shi) Chang Pu	47.66	—
Niu Bang Zi	47.72	—
Nü Zhen Zi	48.08	—
Chuan Lian Zi	48.70	—
Zhi Mu	49.66	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zi Hua Di Ding* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62627	62627	0.00	7.04
62628	62628	0.00	4.70

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 2.3-2020-05

Validated substance/substance group **Zi Su Zi**
Substance class TCM - Granulated herbal extracts (PhytoComm)
Report date 25/11/2020
Report number 60133-2020-11-25
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zi Su Zi; Perillae fructus

Special notes

When selecting the *Zi Su Zi* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zi Su Zi	1	0	0

Second-stage model

For differentiation of the substance/substance group *Zi Su Zi* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zi Su Zi*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
PhytoComm	Zi Su Zi	G183H1213822	62483	40	from supplier
PhytoComm	Zi Su Zi	G183H1213822	62484	40	from supplier

Validation samples

A total of 30 254 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 *Zi Su Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 19 400 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite 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 2 reference samples from the substance/substance group *Zi Su Zi*.
- 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
PhytoComm	Zi Su Zi	G183H1213822	62483 [†]	20
PhytoComm	Zi Su Zi	G183H1213822	62484 [†]	20

- 9877 spectra from a total of 243 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *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 *Zi Su Zi*.
- 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.
- 857 spectra from 13 *Apo-Ident* customers from a total of 519 batches from a further 216 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zi Su Zi* can be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zi Su Zi* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	19 400
Type B	0	40	0	9877
Type C	0	0	0	857

The substance/substance group *Zi Su Zi* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9633 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9285 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8345 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zi Su Zi* in the substance class *TCM - Granulated herbal extracts (PhytoComm)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Substance	Distance in main model	Distance in second-stage model
Cang Er Zi	9.13	—
San Qi	18.07	—
Bai Bian Dou	18.31	—
Xie Bai	19.86	—
Niu Bang Zi	22.88	—
Sang Zhi	23.43	—
Ji Li	23.85	—
Sha Shen (Bei)	24.13	—
Di Gu Pi	24.43	—
Jiang Huang	24.66	—
Xiang Fu	25.22	—
E Zhu	26.00	—
Wang Bu Liu Xing	26.33	—
Shan Yao	26.69	—
Tian Hua Fen	27.36	—
Jie Geng	28.18	—
Chen Pi	28.38	—
Yan Hu Suo	28.48	—
Mang Xiao	28.57	—
Sheng Jiang	28.98	—
Gua Lou	29.42	—
Chuan Lian Zi	29.60	—
Fang Feng	31.20	—
Sha Ren	31.67	—
(Huai) Niu Xi	31.89	—
Ba Ji Tian	32.01	—
(Bai) Dou Kou	32.04	—
(Shi) Chang Pu	32.55	—
Ku Shen	34.66	—
Qing Pi	34.91	—
Lai Fu Zi	35.00	—
Huang Qi	36.73	—
Dong Gua Zi	37.33	—
Dang Gui	37.87	—
Long Dan (Cao)	38.54	—
Du Huo	38.94	—
Gui Zhi	39.37	—
Qiang Huo	39.54	—
Yi Mu Cao	40.32	—
Yuan Zhi	40.44	—
Pu Gong Ying	41.40	—
Bai Zhu	42.19	—
Bai Mao Gen	43.10	—
Fu Zi	44.02	—
Bai Xian Pi	44.38	—
Xian He Cao	44.69	—
Wu Yao	44.95	—
Fu Ling	45.15	—
Yu Jin	45.18	—
Mai Men Dong	45.24	—
He Huan Pi	45.32	—
Mai Ya	46.38	—
Huang Lian	47.03	—
Wu Wei Zi	47.29	—
Nü Zhen Zi	47.49	—
Jin Yin Hua	47.65	—
Huang Bo	48.12	—
Mu Dan Pi	48.31	—
Lian Zi	49.06	—

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Substanz	Distance in main model	Distance in second-stage model
Tu Fu Ling	49.11	—
Wu Mei	50.01	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zi Su Zi* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
62484	62484	0.00	9.15
62483	62483	0.00	9.13

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.

Appendix A: Additional calibration samples (Type A)

Not required.

Appendix B: Additional validation samples (Type B)

Not required.

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 139 batches. From these, 194 spectra were recorded. The spectra recorded on independent samples of substances from the field which can be identified with the model are listed respectively in the section *Type C* for the individual substances and do not appear again elsewhere in this list.

Supplier	Substance	Batch	Spectra
Phytocomm	(Bai) Jiang Can	g144h1708221	1
Phytocomm	(Bai) Jiang Can	g269h0513222	1
Phytocomm	(Bai) Jiang Can	G269H0513321	2
PhytoComm	(Bai) Jiang Can	G269H0513222	1
PhytoComm	(Fen) Bi Xie	G0290H1251121	1
Phytocomm	Bai Bu	G235H0608321	1
PhytoComm	Bai Bu	G235H0608221	1
Phytocomm	Bai Guo	G114H0509321	2
Phytocomm	Bai Guo	G114H0509521	1
Phytocomm	Bai Jiang Cao	G181H1180321	1
Phytocomm	Bai Jiang Cao	G181H1180422	1
Phytocomm	Bai Tou Weng	G207H0511521	4
PhytoComm	Bai Tou Weng	G207H0511221	3
Phytocomm	Bai Zhi	G020H0503421	1
Phytocomm	Ban Lan Gen	G128H0816421	2
PhytoComm	Bie Jia	G507H2401121	1
PhytoComm	Bie Jia	G507H2401321	1
Phytocomm	Bo He	g158h1712022	1
PhytoComm	Bo He	G158H1712121	1
PhytoComm	Cao Guo	E241050	1
phytocomm	Ce Bai Ye	g050h0975321	2
Phytocomm	Ce Bai Ye	G050H0975321	1
Phytocomm	Ce Bai Ye	G050HS245	1
phytocomm	Chan Tui	g067h1817322	1
Phytocomm	Chan Tui	G067H1817322	3
Phytocomm	Chan Tui	G067H1817323	2
Phytocomm	Chong Wei Zi	g317bp021046	1
Phytocomm	Chuan Bei Mu	g107f110721	1
Phytocomm	Chuan Bei Mu	G107BP020722A	1
Phytocomm	Chuan Bei Mu	g107f11021	1
PhytoComm	Chuan Bei Mu	G107F110721	1
Phytocomm	Chuan Mu Tong	g009h0310321	1
Phytocomm	Chuan Mu Tong	G009H0310321	1
PhytoComm	Chuan Mu Tong	G009H0310521	1
Phytocomm	Chuan Niu Xi	g318h0431321	1
PhytoComm	Chuan Niu Xi	G318H0431321	1
Phytocomm	Da Fu Pi	G293H0321221	1
Phytocomm	Da Qing Ye	G127H0318421	2
Phytocomm	Deng Xin Cao	f100707	1
phytocomm	Di Long	g148h603321	1
Phytocomm	Di Long	G148H0603321	2
Phytocomm	Di Long	G148H0603421	2
PhytoComm	Di Long	G148H0603022	1
Phytocomm	Di Yu	G215H0604322	2
Phytocomm	Ding Xiang	G058H0210021	1
PhytoComm	E Bu Shi Cao	G061H180122	1
Phytocomm	E Jiao	g036h0861121	1

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Supplier	Substance	Batch	Spectra
Phytocomm	E Jiao	g036h0861221	1
Phytocomm	E Jiao	G036H0861421	2
PhytoComm	E Jiao	G036H0861221	4
Phytocomm	Fang Ji	G236H0727321	1
PhytoComm	Fang Ji	G236H0727123	1
Phytocomm	Fu Pen Zi	g213h1813122	1
Phytocomm	Gan Jiang	G252H1145221	1
Phytocomm	Gan Jiang	g252h01145221	1
Phytocomm	Gan Jiang	G252H1145421	1
Phytocomm	Gan Jiang	G252H1145521	1
PhytoComm	Geng Mi	G329H1320121	1
Phytocomm	Gua Lou Ren	g243h1095123	1
PhytoComm	Gua Lou Ren	G243H1095421	1
PhytoComm	He Zi	G291H1239221	2
Phytocomm	Huai Hua	G263H1423421	1
Phytocomm	Huang Jing	g196h1206121	1
Phytocomm	Huang Jing	G196H1206121	1
Phytocomm	Ji Nei Jin	G259H2102321	1
Phytocomm	Ji Nei Jin	g259h2102321	1
Phytocomm	Jie Cao	H2111921	1
PhytoComm	Kuan Dong Hua	H1219921	1
Phytocomm	Long Gu	g0251706122	1
PhytoComm	Long Gu	G025H1706122	1
Phytocomm	Lu Gen	G189H2014221	1
Phytocomm	Lu Gen	G189H2014521	3
Bios	Lu Hui	424263	1
phytocomm	Lu Jiao Jiao	G323H1158321	1
Phytocomm	Lu Jiao Shuang	FB1419901	1
Phytocomm	Lu Jiao Shuang	G062H1419421	1
Phytocomm	Lu Lu Tong	G142H1336321	1
Phytocomm	Lu Lu Tong	G142H1336521	2
PhytoComm	Lu Lu Tong	G142H1336122	1
Phytocomm	Ma Bian Cao	G248H1085221	1
PhytoComm	Ma Chi Xian	G255F110310	1
Phytocomm	Mi Huan Jun	G510H0418221	1
Phytocomm	Mi Huan Jun	G510H0418422	1
Phytocomm	Mo Yao	G1690732222	1
PhytoComm	Mo Yao	G169H0732222	2
Phytocomm	Mu Gua	G063H0424521	4
PhytoComm	Mu Gua	G063H0424221	2
Phytocomm	Mu Zei	G265H0427421	1
PhytoComm	Mu Zei	G265H0427823	1
Phytocomm	Qian Hu	G185H0926322	4
Phytocomm	Qian Shi	G102H0836422	1
PhytoComm	Qian Shi	G102H0836121	1
Phytocomm	Quan Xie	G222F110314	1
Phytocomm	Ren Shen	g115ho562121	1
Phytocomm	Ru Xiang	G174H0820231	1
Phytocomm	Ru Xiang	G174H0820421	3
Phytocomm	San Leng	g270h0311221	1
PhytoComm	San Leng	G270H0311221	1
Phytocomm	Sang Piao Xiao	G282H421029201	1
Phytocomm	Sang Shen	G163H1047121	1
Phytocomm	Sang Shen	G163H1047221	2
Phytocomm	Shan Zha	G082H0331324	1
Phytocomm	Shan Zha	G082H0331521	1
Phytocomm	She Chuang Zi	G076H1154122	1
PhytoComm	She Chuang Zi	G076H1154021	1
Phytocomm	She Gan	G048H1034422	1
Phytocomm	Sheng Ma	g068h04317121	1

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Supplier	Substance	Batch	Spectra
Phytocomm	Sheng Ma	G068H0437421	2
PhytoComm	Suo Yang	G260H1831121	1
Phytocomm	Wei Ling Xian	G075H0943223	3
Phytocomm	Wei Ling Xian	g075h0943223	1
Phytocomm	Wei Ling Xian	G075H0943422	1
PhytoComm	Wei Ling Xian	G075H0943223	1
Phytocomm	Wu Gong	G311H1411321	1
Phytocomm	Wu Gong	G311H411321	1
Phytocomm	Xi Yang Shen	G324H0647321	1
Phytocomm	Xi Yang Shen	g324h0647321	1
Phytocomm	Xi Yang Shen	G324HS4070L1	1
Phytocomm	Xian Mao	G304H0549321	2
Phytocomm	Xian Mao	G304H0549521	2
Phytocomm	Xiao Hui Xiang	g104h0339321	1
Phytocomm	Xiao Hui Xiang	G104H0339522	3
Phytocomm	Xuan Fu Hua	G126H1168521	1
Phytocomm	Yi Zhi Ren	G015H1051321	2
Phytocomm	Yi Zhi Ren	G015H1051521	1
Phytocomm	Ze Lan	g268h1606221	1
Phytocomm	Ze Lan	G268H1606421	1
PhytoComm	Ze Lan	G268H1606221	2
Phytocomm	Ze Xie	g011h1605122	1
Phytocomm	Ze Xie	G011H1605521	6
Phytocomm	Ze Xie	G011H1605422	1
PhytoComm	Ze Xie	G011H1605122	1
Phytocomm	Zhen Zhu Mu	g155h0979221	1
Phytocomm	Zhi Gan Cao	g118h0881322	1
Phytocomm	Zhi Gan Cao	G118H0881522	4
PhytoComm	Zhi Gan Cao	G118H0881322	1
PhytoComm	Zi Su Ye	G182H1214321	3
PhytoComm	Zi Su Ye	G182HS2680P1	1
Phytocomm	Zi Wan	G038H1215321	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).

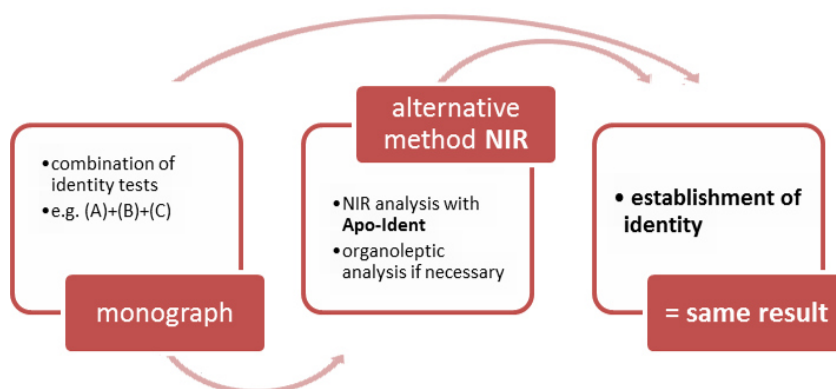


Figure 2: The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

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, Grundwerk 2017*. 9. Ausgabe. Deutscher Apotheker Verlag (978-3-7692-6679-5)
- [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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