

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:

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

All manufacturers’ batches from which spectra are used for the validation are listed by substance in this document: for substances included in the substance class *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

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

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

## Particularities of individual substance classes

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

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

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

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

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

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

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

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

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

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

## Significance of testing with *Apo-Ident*

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

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

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

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

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

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

## Conclusion

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



## Explanation of terminology

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

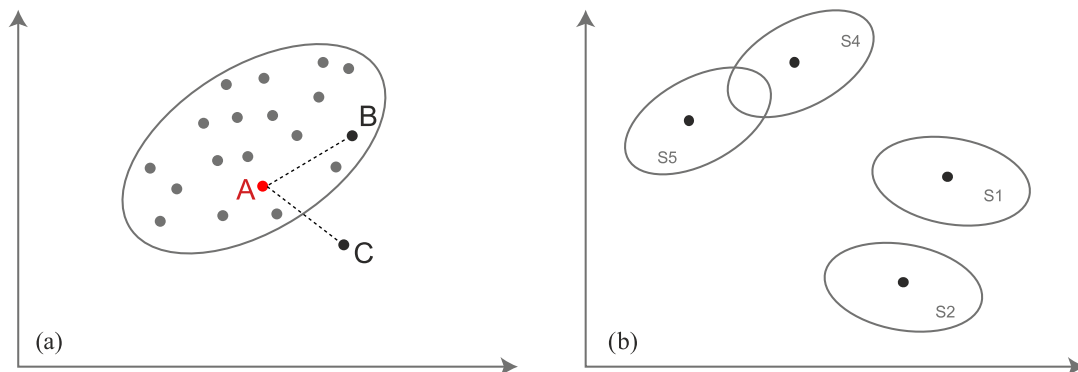


**Figure 1:** (a) The *Mahalanobis distance* from *A* to *B* is less than from *A* to *C*. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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



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

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

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

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

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

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

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



## Summary

A total of 34 694 spectra from 798 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) | 169        | 282     | 22 440  |

From category *A* a total of 22 440 spectra from 282 batches for a total of 169 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) | 169        | 282     | 11 397  |

From category *B* a total of 11 397 spectra from 282 batches for a total of 169 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 | 122            | 22 213        | 227            | 3 769 798     |
| Type B | 265            | 11 077        | 320            | 1 914 431     |
| Type C | 105            | 63            | 615            | 144 050       |

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 | 99.996 93 % (> 99.996 83 %) | 99.095 78 % (> 99.079 56 %) |
| Typ B | 99.985 96 % (> 99.985 77 %) | 97.227 84 % (> 97.195 90 %) |
| Typ C | 99.918 22 % (> 99.914 76 %) | 7.291 24 % (> 6.551 76 %)   |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 2.4-2022-02

Validated substance/substance group (Bai) Dou Kou  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002257-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | (Bai) Dou Kou | G016H0508921 | 62762 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Jiang Huang         | 13.94                     | —                                 |
| Sha Ren             | 14.00                     | —                                 |
| He Huan Pi          | 18.41                     | —                                 |
| E Zhu               | 20.20                     | —                                 |
| Sha Shen (Bei)      | 22.77                     | —                                 |
| Mang Xiao           | 23.52                     | —                                 |
| Chen Pi             | 27.00                     | —                                 |
| Di Gu Pi            | 27.68                     | —                                 |
| Shan Yao            | 31.16                     | —                                 |
| Yan Hu Suo          | 31.41                     | —                                 |
| Cang Er Zi          | 31.44                     | —                                 |
| Bai Hua She She Cao | 32.57                     | —                                 |
| Gan Jiang           | 32.69                     | —                                 |
| Niu Bang Zi         | 34.19                     | —                                 |
| Huang Lian          | 34.87                     | —                                 |
| Zi Su Zi            | 36.98                     | —                                 |
| Du Huo              | 37.70                     | —                                 |
| He Shou Wu          | 38.59                     | —                                 |
| Lai Fu Zi           | 39.05                     | —                                 |
| Wang Bu Liu Xing    | 39.87                     | —                                 |
| Dang Gui            | 40.45                     | —                                 |
| Wu Yao              | 40.50                     | —                                 |
| Yi Mu Cao           | 40.53                     | —                                 |
| Zhi Ke              | 40.66                     | —                                 |
| Chuan Niu Xi        | 40.91                     | —                                 |
| Xi Xian Cao         | 40.99                     | —                                 |
| Xin Yi              | 41.80                     | —                                 |
| Sang Zhi            | 42.04                     | —                                 |
| Sang Ji Shend       | 42.06                     | —                                 |
| Hu Zhang            | 42.57                     | —                                 |
| Hong Jing Tian      | 43.26                     | —                                 |
| Mi Huan Jun         | 43.72                     | —                                 |
| Yin Chen Hao        | 44.22                     | —                                 |
| (Huai) Niu Xi       | 44.45                     | —                                 |
| Chuan Lian Zi       | 44.88                     | —                                 |
| Tu Si Zi            | 45.18                     | —                                 |
| Du Zhong            | 45.31                     | —                                 |
| Gu Sui Bu           | 46.08                     | —                                 |
| Mao Dong Qing       | 46.15                     | —                                 |
| Ze Lan              | 46.67                     | —                                 |
| Shan Yu Rou         | 46.88                     | —                                 |
| Bai Xian Pi         | 46.90                     | —                                 |
| Xiang Fu            | 47.38                     | —                                 |
| Chuan Mu Tong       | 47.48                     | —                                 |
| Xiao Hui Xiang      | 48.00                     | —                                 |
| Fu Ling             | 48.35                     | —                                 |
| Tian Hua Fen        | 48.44                     | —                                 |
| Bu Gu Zhi           | 49.16                     | —                                 |
| Rou Gui             | 49.49                     | —                                 |
| (Shi) Chang Pu      | 50.02                     | —                                 |



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                         | 13.94                           |
| 62762     | 62762               | 0.00                         | 14.06                           |

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 2.4-2022-02

Validated substance/substance group (Fen) Bi Xie  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60111-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

(Fen) Bi Xie; Dioscoreae hypoglaucae rhizoma

### Special notes

When selecting the (Fen) Bi Xie substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| (Fen) Bi Xie              | 1      | 0      | 1      |

### Second-stage model

For differentiation of the substance/substance group (Fen) Bi Xie 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 *(Fen) Bi Xie*:

| Supplier  | Substance    | Batch        | Sample ID | Spectra | Certificate   |
|-----------|--------------|--------------|-----------|---------|---------------|
| PhytoComm | (Fen) Bi Xie | G290HS286TH1 | 62815     | 40      | from supplier |
| PhytoComm | (Fen) Bi Xie | G290HS286TH1 | 62816     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *(Fen) Bi Xie*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *(Fen) Bi Xie*.
- 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 | (Fen) Bi Xie | G290HS286TH1 | 62815 <sup>†</sup> | 20      |
| PhytoComm | (Fen) Bi Xie | G290HS286TH1 | 62816 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *(Fen) Bi Xie*.
- 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 | (Fen) Bi Xie | G0290H1251121 | 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 *(Fen) Bi Xie* 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 *(Fen) Bi Xie* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 79            | 1              | 22 360        |
| <b>Type B</b> | 0              | 37            | 3              | 11 357        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

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

|               | Specificity              | Recognition rate        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 98.7500 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 92.5000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group (*Fen*) *Bi Xie* 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| She Gan         | 4.32                      | —                                 |
| Ren Dong Teng   | 5.95                      | —                                 |
| Lu Gen          | 6.35                      | —                                 |
| Bai Xian Pi     | 8.17                      | —                                 |
| Huo Ma Ren      | 8.38                      | —                                 |
| Ye Jiao Teng    | 8.53                      | —                                 |
| Bai Shao Yao    | 8.86                      | —                                 |
| He Huan Pi      | 8.96                      | —                                 |
| Gu Sui Bu       | 9.94                      | —                                 |
| Rou Gui         | 9.98                      | —                                 |
| Zhu Ling        | 10.14                     | —                                 |
| Gou Teng        | 10.15                     | —                                 |
| Gui Zhi         | 10.28                     | —                                 |
| Ling Zhi        | 10.56                     | —                                 |
| Tu Fu Ling      | 11.08                     | —                                 |
| Fo Shou         | 11.13                     | —                                 |
| Dan Dou Chi     | 11.21                     | —                                 |
| Lian Zi         | 11.40                     | —                                 |
| Ji Xue Teng     | 11.45                     | —                                 |
| Ce Bai Ye       | 11.82                     | —                                 |
| Mu Zei          | 12.31                     | —                                 |
| Ma Huang Gen    | 12.95                     | —                                 |
| Fu Ling         | 12.98                     | —                                 |
| Shen Qu         | 13.36                     | —                                 |
| Guang Huo Xiang | 13.47                     | —                                 |
| Suan Zao Ren    | 13.69                     | —                                 |
| Tao Ren         | 14.57                     | —                                 |
| Dan Shen        | 14.65                     | —                                 |
| Sheng Jiang     | 14.70                     | —                                 |
| Yin Yang Huo    | 15.13                     | —                                 |
| Yu Jin          | 15.59                     | —                                 |
| Ji Li           | 15.91                     | —                                 |
| Yi Yi Ren       | 16.02                     | —                                 |
| Ci Wu Jia       | 17.08                     | —                                 |
| Mao Dong Qing   | 17.32                     | —                                 |
| Ban Xia (Jiang) | 17.37                     | —                                 |
| Zhe Bei Mu      | 17.98                     | —                                 |
| Fu Zi           | 18.18                     | —                                 |
| Ma Huang        | 18.45                     | —                                 |
| Fu Xiao Mai     | 18.53                     | —                                 |
| Chai Hu         | 18.78                     | —                                 |
| Yan Hu Suo      | 18.90                     | —                                 |
| Shan Yao        | 19.11                     | —                                 |
| Pi Pa Ye        | 19.23                     | —                                 |
| Lian Qiao       | 19.91                     | —                                 |
| Fu Pen Zi       | 20.30                     | —                                 |
| Gan Cao         | 20.59                     | —                                 |
| Tian Hua Fen    | 20.89                     | —                                 |
| Jin Yin Hua     | 21.53                     | —                                 |
| Jing Jie        | 21.56                     | —                                 |
| Hou Po          | 22.28                     | —                                 |
| Hong Jing Tian  | 22.63                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bai Zi Ren      | 22.63                     | —                                 |
| Ban Lan Gen     | 22.86                     | —                                 |
| Di Gu Pi        | 22.93                     | —                                 |
| Qiang Huo       | 22.97                     | —                                 |
| Lai Fu Zi       | 23.73                     | —                                 |
| Zhu Ru          | 23.89                     | —                                 |
| Jiao Gu Lan     | 24.63                     | —                                 |
| Fu Shen         | 25.07                     | —                                 |
| Ze Xie          | 25.20                     | —                                 |
| Che Qian Zi     | 25.57                     | —                                 |
| Zi Hua Di Ding  | 26.23                     | —                                 |
| Cang Zhu        | 26.33                     | —                                 |
| Sha Ren         | 27.69                     | —                                 |
| Zhi Ke          | 29.34                     | —                                 |
| Ren Shen        | 31.36                     | —                                 |
| Mang Xiao       | 31.90                     | —                                 |
| Huang Lian      | 31.96                     | —                                 |
| Dang Gui        | 32.13                     | —                                 |
| Gua Lou         | 32.63                     | —                                 |
| Zhi Gan Cao     | 32.67                     | —                                 |
| Bo He           | 32.92                     | —                                 |
| Jie Geng        | 33.14                     | —                                 |
| Long Yan Rou    | 33.33                     | —                                 |
| Sang Zhi        | 33.83                     | —                                 |
| Chuang Mu Xiang | 33.96                     | —                                 |
| Huang Qin       | 34.89                     | —                                 |
| San Qi          | 35.04                     | —                                 |
| Du Zhong        | 35.50                     | —                                 |
| Huang Bai       | 36.79                     | —                                 |
| Qing Pi         | 36.89                     | —                                 |
| Chi Shao (Yao)  | 39.19                     | —                                 |
| Zhi Mu          | 39.36                     | —                                 |
| Mu Gua          | 43.14                     | —                                 |
| Xie Bai         | 43.78                     | —                                 |
| Hong Hua        | 44.81                     | —                                 |
| Bai Zhu         | 44.87                     | —                                 |
| Gou Qi Zi       | 45.63                     | —                                 |
| Yuan Zhi        | 47.47                     | —                                 |
| Ku Shen         | 48.02                     | —                                 |
| Bai Jiang Cao   | 48.73                     | —                                 |
| Ban Zhi Lian    | 50.61                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group (*Fen*) *Bi Xie* 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62815     | 62815               | 0.00                         | 4.32                            |
| 62816     | 62816               | 0.00                         | 4.94                            |

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 2.4-2022-02

Validated substance/substance group (Huai) Niu Xi  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002255-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | (Huai) Niu Xi | G003H1905921 | 62760 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G003H190522  | 1       |
| Phytocomm | (Huai) Niu Xi | g003h1905222 | 1       |
| 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 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 7              | 0             | 9              | 841           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 99.2713 % (> 98.6839 %)  | n/a (n/a)                |

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

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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Yuan Zhi       | 11.09                     | —                                 |
| Huang Qi       | 15.45                     | —                                 |
| Jie Geng       | 15.94                     | —                                 |
| Sang Zhi       | 17.74                     | —                                 |
| Bai Zhu        | 17.94                     | —                                 |
| Lian Qiao      | 18.43                     | —                                 |
| Di Gu Pi       | 19.94                     | —                                 |
| Zhi Gan Cao    | 23.49                     | —                                 |
| Chuan Niu Xi   | 23.61                     | —                                 |
| Ku Shen        | 25.01                     | —                                 |
| Chuan Lian Zi  | 25.22                     | —                                 |
| Chi Shao (Yao) | 25.48                     | —                                 |
| Tian Hua Fen   | 25.63                     | —                                 |
| Niu Bang Zi    | 25.87                     | —                                 |
| Zi Su Zi       | 26.28                     | —                                 |
| Xiang Fu       | 27.95                     | —                                 |
| (Shi) Chang Pu | 28.14                     | —                                 |
| Du Huo         | 28.22                     | —                                 |
| Mang Xiao      | 29.43                     | —                                 |
| Mu Gua         | 29.80                     | —                                 |
| Yan Hu Suo     | 30.89                     | —                                 |
| Shan Yao       | 31.02                     | —                                 |
| Ju Hua         | 31.25                     | —                                 |
| Lai Fu Zi      | 31.72                     | —                                 |
| Dang Gui       | 32.87                     | —                                 |
| Bing Lang      | 34.06                     | —                                 |
| Qin Jiao       | 34.52                     | —                                 |
| Ba Ji Tian     | 35.61                     | —                                 |
| Chuan Mu Tong  | 35.88                     | —                                 |
| Zhi Ke         | 35.98                     | —                                 |
| E Zhu          | 36.13                     | —                                 |
| Chen Pi        | 36.22                     | —                                 |
| Bai Zhi        | 36.55                     | —                                 |
| Xiao Hui Xiang | 36.62                     | —                                 |
| Xu Duan        | 37.03                     | —                                 |
| Bai He         | 37.36                     | —                                 |
| Gan Cao        | 37.37                     | —                                 |
| Dong Gua Zi    | 37.38                     | —                                 |
| Long Dan (Cao) | 37.48                     | —                                 |
| Wu Yao         | 37.70                     | —                                 |
| Jin Yin Hua    | 38.07                     | —                                 |
| Shan Yu Rou    | 38.76                     | —                                 |
| Fang Feng      | 38.95                     | —                                 |
| Cang Er Zi     | 39.33                     | —                                 |
| Gan Jiang      | 40.11                     | —                                 |
| Sha Shen (Bei) | 40.52                     | —                                 |
| Jiang Huang    | 41.47                     | —                                 |
| Pu Gong Ying   | 41.59                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Lian Zi             | 42.27                     | —                                 |
| Yi Mu Cao           | 43.14                     | —                                 |
| Bai Xian Pi         | 44.35                     | —                                 |
| Fu Zi               | 44.69                     | —                                 |
| (Bai) Dou Kou       | 45.06                     | —                                 |
| Da Zao              | 45.17                     | —                                 |
| Mi Huan Jun         | 45.38                     | —                                 |
| Sha Ren             | 46.20                     | —                                 |
| Qiang Huo           | 46.77                     | —                                 |
| Ji Li               | 46.93                     | —                                 |
| Bai Shao Yao        | 47.97                     | —                                 |
| Bai Hua She She Cao | 48.55                     | —                                 |
| Chai Hu             | 48.62                     | —                                 |
| Zhe Bei Mu          | 49.13                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62759     | 62759                  | 0.00                            | 11.09                              |
| 62760     | 62760                  | 0.00                            | 12.79                              |

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 2.4-2022-02

Validated substance/substance group (Ku) Xing Ren  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50290-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | 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 |
| PhytoComm | (Ku) Xing Ren | G029H0708021 | 62969     | 40      | from supplier |
| PhytoComm | (Ku) Xing Ren | G029H0708021 | 62970     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G029H0708823 | 62509 <sup>†</sup> | 20      |
| PhytoComm | (Ku) Xing Ren | G029H0708823 | 62510 <sup>†</sup> | 20      |
| PhytoComm | (Ku) Xing Ren | G029H0708921 | 62767 <sup>†</sup> | 20      |
| PhytoComm | (Ku) Xing Ren | G029H0708921 | 62768 <sup>†</sup> | 20      |
| PhytoComm | (Ku) Xing Ren | G029H0708021 | 62969 <sup>†</sup> | 20      |
| PhytoComm | (Ku) Xing Ren | G029H0708021 | 62970 <sup>†</sup> | 20      |



- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | g029h0708122 | 1       |
| Phytocomm | (Ku) Xing Ren | G029H0708125 | 2       |
| PhytoComm | (Ku) Xing Ren | G029H0708125 | 1       |
| phytocomm | (Ku) Xing Ren | g029h0708322 | 2       |
| PhytoComm | (Ku) Xing Ren | G029H0708322 | 2       |
| PhytoComm | (Ku) Xing Ren | G029H0708622 | 1       |
| PhytoComm | (Ku) Xing Ren | G029H708125  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8250 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------|---------------------------|-----------------------------------|
| Mang Xiao | 50.54                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62509     | 62509                  | 0.00                            | 54.37                              |
| 62510     | 62510                  | 0.00                            | 54.45                              |
| 62767     | 62767                  | 0.00                            | 51.44                              |
| 62768     | 62768                  | 0.00                            | 51.44                              |
| 62969     | 62969                  | 0.00                            | 50.54                              |
| 62970     | 62970                  | 0.00                            | 50.60                              |

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 2.4-2022-02

Validated substance/substance group (Sheng) Di Huang  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60005-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| (Sheng) Di Huang          | 3      | 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 |
| PhytoComm | (Sheng) Di Huang | G211H0532021 | 62853     | 40      | from supplier |
| PhytoComm | (Sheng) Di Huang | G211H0532021 | 62854     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *(Sheng) Di Huang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *(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 <sup>†</sup> | 20      |
| PhytoComm | (Sheng) Di Huang | G211H0532822 | 62312 <sup>†</sup> | 20      |
| PhytoComm | (Sheng) Di Huang | G211H0532921 | 62749 <sup>†</sup> | 20      |
| PhytoComm | (Sheng) Di Huang | G211H0532921 | 62750 <sup>†</sup> | 20      |
| PhytoComm | (Sheng) Di Huang | G211H0532021 | 62853 <sup>†</sup> | 20      |
| PhytoComm | (Sheng) Di Huang | G211H0532021 | 62854 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|-----------|------------------|--------------|---------|
|           | (Sheng) Di Huang | g211h0532323 | 1       |
| Phytocomm | (Sheng) Di Huang | g211h0532121 | 1       |
| Phytocomm | (Sheng) Di Huang | g211h0532221 | 1       |
| Phytocomm | (Sheng) Di Huang | G211H0532521 | 4       |
| PhytoComm | (Sheng) Di Huang | G211H0532621 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 1              | 4             | 4              | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 99.9690 % (> 99.3816 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Yu Xing Cao     | 10.46                     | —                                 |
| Xian Mao        | 14.39                     | —                                 |
| Shu Di (Huang)  | 16.68                     | —                                 |
| Mang Xiao       | 18.54                     | —                                 |
| Wu Jia Pi       | 19.08                     | —                                 |
| Ding Xiang      | 32.15                     | —                                 |
| Guang Huo Xiang | 32.83                     | —                                 |
| Jing Jie        | 33.21                     | —                                 |
| Sang Ye         | 35.30                     | —                                 |
| Dan Zhu Ye      | 36.41                     | —                                 |
| Sang Ji Shend   | 41.14                     | —                                 |
| Hua Shi         | 45.12                     | —                                 |
| Ge Gen          | 46.18                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62311     | 62311                  | 0.00                            | 10.46                              |
| 62312     | 62312                  | 0.00                            | 10.56                              |
| 62749     | 62749                  | 0.00                            | 11.78                              |
| 62750     | 62750                  | 0.00                            | 12.13                              |
| 62853     | 62853                  | 0.00                            | 14.62                              |
| 62854     | 62854                  | 0.00                            | 14.80                              |

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 2.4-2022-02

Validated substance/substance group (Shi) Chang Pu  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60426-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G006H0544922 | 62945     | 40      | from supplier |
| PhytoComm | (Shi) Chang Pu | G006H0544922 | 62946     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G006H0544922 | 62945 <sup>†</sup> | 20      |
| PhytoComm | (Shi) Chang Pu | G006H0544922 | 62946 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | g006h0544023 | 1       |
| Phytocomm   | (Shi) Chang Pu | G006H0544122 | 1       |
| Phytocomm   | (Shi) Chang Pu | G006H0544322 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 1              | 40            | 0              | 11 356        |
| <b>Type C</b> | 2              | 0             | 5              | 850           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9851 % (> 99.9531 %)  | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 99.7674 % (> 99.1806 %)  | n/a (n/a)                |

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

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

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

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Chen Pi             | 6.59                      | —                                 |
| Wu Yao              | 8.03                      | —                                 |
| Shan Yu Rou         | 8.73                      | —                                 |
| Dang Gui            | 15.88                     | —                                 |
| Xiang Fu            | 16.69                     | —                                 |
| Ju Hua              | 17.57                     | —                                 |
| Sha Ren             | 18.20                     | —                                 |
| Mu Dan Pi           | 19.15                     | —                                 |
| Chuan Niu Xi        | 20.74                     | —                                 |
| Gu Sui Bu           | 21.85                     | —                                 |
| He Huan Pi          | 23.00                     | —                                 |
| Jiang Huang         | 23.20                     | —                                 |
| Xiao Hui Xiang      | 23.21                     | —                                 |
| Wu Zhu Yu           | 23.75                     | —                                 |
| Chuan Lian Zi       | 23.91                     | —                                 |
| Fang Feng           | 24.93                     | —                                 |
| Yi Mu Cao           | 25.93                     | —                                 |
| Hong Jing Tian      | 26.09                     | —                                 |
| Xu Duan             | 26.45                     | —                                 |
| Mang Xiao           | 27.94                     | —                                 |
| Sang Ji Shend       | 28.48                     | —                                 |
| Ku Shen             | 28.50                     | —                                 |
| Bai Zhi             | 29.05                     | —                                 |
| Ba Ji Tian          | 30.07                     | —                                 |
| (Bai) Dou Kou       | 30.12                     | —                                 |
| Shan Yao            | 30.18                     | —                                 |
| Tian Hua Fen        | 30.33                     | —                                 |
| Yan Hu Suo          | 30.47                     | —                                 |
| Zhi Gan Cao         | 30.77                     | —                                 |
| Huang Qi            | 31.21                     | —                                 |
| Di Gu Pi            | 31.30                     | —                                 |
| (Huai) Niu Xi       | 33.55                     | —                                 |
| Bai Hua She She Cao | 33.99                     | —                                 |
| Niu Bang Zi         | 34.15                     | —                                 |
| Sang Bai Pi         | 35.00                     | —                                 |
| Yin Chen Hao        | 35.11                     | —                                 |
| Cang Er Zi          | 36.36                     | —                                 |
| He Shou Wu          | 36.45                     | —                                 |
| Zi Su Zi            | 36.97                     | —                                 |
| Xin Yi              | 37.61                     | —                                 |
| Sang Zhi            | 37.94                     | —                                 |
| E Zhu               | 38.01                     | —                                 |
| Zhi Ke              | 38.14                     | —                                 |
| Du Huo              | 38.81                     | —                                 |
| Jie Geng            | 39.31                     | —                                 |
| Ge Gen              | 40.07                     | —                                 |
| Gan Jiang           | 41.34                     | —                                 |
| Bai Zhu             | 41.79                     | —                                 |
| Nü Zhen Zi          | 41.89                     | —                                 |
| Mi Huan Jun         | 42.00                     | —                                 |
| Bing Lang           | 42.98                     | —                                 |
| Sang Ye             | 43.16                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Suan Zao Ren   | 43.69                     | —                                 |
| Lian Qiao      | 43.82                     | —                                 |
| Hu Zhang       | 44.05                     | —                                 |
| Tu Si Zi       | 44.06                     | —                                 |
| Huang Lian     | 44.22                     | —                                 |
| Ze Lan         | 44.23                     | —                                 |
| Pu Gong Ying   | 45.10                     | —                                 |
| Da Zao         | 47.03                     | —                                 |
| Chi Shao (Yao) | 47.92                     | —                                 |
| Dong Gua Zi    | 49.28                     | —                                 |
| Lai Fu Zi      | 49.32                     | —                                 |
| Du Zhong       | 49.42                     | —                                 |
| Bu Gu Zhi      | 49.64                     | —                                 |
| Qin Jiao       | 49.69                     | —                                 |
| Mao Dong Qing  | 49.92                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62945     | 62945                  | 0.00                            | 6.59                               |
| 62946     | 62946                  | 0.00                            | 6.86                               |

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 2.4-2022-02

Validated substance/substance group **Ba Ji Tian**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60138-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G165H0445921 | 62823     | 40      | from supplier |
| PhytoComm | Ba Ji Tian | G165H0445921 | 62824     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G165H0445921 | 62823 <sup>†</sup> | 20      |
| PhytoComm | Ba Ji Tian | G165H0445921 | 62824 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

| Substance           | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| (Shi) Chang Pu      | 13.17                     | —                                 |
| Chen Pi             | 13.43                     | —                                 |
| Shan Yu Rou         | 16.44                     | —                                 |
| Mu Dan Pi           | 16.56                     | —                                 |
| Chuan Niu Xi        | 17.82                     | —                                 |
| Chuan Lian Zi       | 18.56                     | —                                 |
| He Huan Pi          | 21.04                     | —                                 |
| Sang Zhi            | 22.81                     | —                                 |
| Mang Xiao           | 23.37                     | —                                 |
| Fang Feng           | 23.47                     | —                                 |
| Ju Hua              | 23.97                     | —                                 |
| Wu Yao              | 24.00                     | —                                 |
| Dang Gui            | 24.30                     | —                                 |
| Xiang Fu            | 24.68                     | —                                 |
| Jiang Huang         | 26.97                     | —                                 |
| (Huai) Niu Xi       | 27.61                     | —                                 |
| Long Dan (Cao)      | 28.27                     | —                                 |
| E Zhu               | 28.54                     | —                                 |
| Du Huo              | 30.02                     | —                                 |
| Gu Sui Bu           | 31.24                     | —                                 |
| Da Zao              | 31.77                     | —                                 |
| Lai Fu Zi           | 31.82                     | —                                 |
| Sha Ren             | 33.11                     | —                                 |
| Huang Qi            | 33.58                     | —                                 |
| Zhi Gan Cao         | 33.95                     | —                                 |
| Bing Lang           | 35.46                     | —                                 |
| Hong Jing Tian      | 35.78                     | —                                 |
| Shan Yao            | 37.62                     | —                                 |
| Zi Su Zi            | 38.71                     | —                                 |
| Yin Chen Hao        | 39.10                     | —                                 |
| Xiao Hui Xiang      | 41.85                     | —                                 |
| (Bai) Dou Kou       | 42.23                     | —                                 |
| Dong Gua Zi         | 42.66                     | —                                 |
| Niu Bang Zi         | 42.69                     | —                                 |
| Tian Hua Fen        | 43.38                     | —                                 |
| Di Gu Pi            | 43.60                     | —                                 |
| Bai Zhu             | 43.75                     | —                                 |
| Sang Ji Shend       | 44.84                     | —                                 |
| Sang Bai Pi         | 45.46                     | —                                 |
| Jie Geng            | 45.47                     | —                                 |
| Yuan Zhi            | 45.69                     | —                                 |
| Yan Hu Suo          | 46.06                     | —                                 |
| Sha Shen (Bei)      | 46.49                     | —                                 |
| Xin Yi              | 46.82                     | —                                 |
| Suan Zao Ren        | 47.20                     | —                                 |
| Tu Si Zi            | 47.20                     | —                                 |
| He Shou Wu          | 47.30                     | —                                 |
| Xu Duan             | 47.50                     | —                                 |
| Mi Huan Jun         | 47.58                     | —                                 |
| Gan Jiang           | 47.59                     | —                                 |
| Bai Hua She She Cao | 48.11                     | —                                 |
| Qin Jiao            | 48.73                     | —                                 |
| Zhi Ke              | 48.75                     | —                                 |
| Wu Zhu Yu           | 48.87                     | —                                 |
| Ku Shen             | 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62823     | 62823               | 0.00                         | 13.43                           |
| 62824     | 62824               | 0.00                         | 13.17                           |

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 2.4-2022-02

Validated substance/substance group **Bai He**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60093-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bai He                    | 2      | 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 |
| PhytoComm | Bai He    | G139H0607922 | 62887     | 40      | from supplier |
| PhytoComm | Bai He    | G139H0607922 | 62888     | 40      | from supplier |

## Validation samples

A total of 34 694 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 He*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Bai He    | G139H0607921 | 62740 <sup>†</sup> | 20      |
| PhytoComm | Bai He    | G139H0607922 | 62887 <sup>†</sup> | 20      |
| PhytoComm | Bai He    | G139H0607922 | 62888 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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    | G139H0607221 | 1       |
| Phytocomm | Bai He    | G139H0607421 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Sang Zhi       | 9.74                      | —                                 |
| Chuan Lian Zi  | 13.18                     | —                                 |
| Sha Shen (Bei) | 16.80                     | —                                 |
| Lai Fu Zi      | 17.15                     | —                                 |
| Long Dan (Cao) | 18.00                     | —                                 |
| Da Zao         | 18.39                     | —                                 |
| Di Gu Pi       | 19.24                     | —                                 |
| Dang Gui       | 19.94                     | —                                 |
| Tian Hua Fen   | 20.62                     | —                                 |
| Mi Huan Jun    | 21.50                     | —                                 |
| Mang Xiao      | 23.06                     | —                                 |
| Chuan Mu Tong  | 23.64                     | —                                 |
| Gan Jiang      | 24.35                     | —                                 |
| Jie Geng       | 25.02                     | —                                 |
| Bai Zhu        | 26.99                     | —                                 |
| Qin Jiao       | 27.04                     | —                                 |
| E Zhu          | 27.86                     | —                                 |
| Huang Qi       | 28.47                     | —                                 |
| Zhi Gan Cao    | 34.48                     | —                                 |
| Zi Su Zi       | 35.90                     | —                                 |
| Mu Gua         | 36.72                     | —                                 |
| Jiang Huang    | 37.75                     | —                                 |
| Shan Yao       | 38.57                     | —                                 |
| Cang Er Zi     | 38.59                     | —                                 |
| (Huai) Niu Xi  | 38.83                     | —                                 |
| Ban Zhi Lian   | 39.35                     | —                                 |
| Suan Zao Ren   | 39.65                     | —                                 |
| Yi Yi Ren      | 41.65                     | —                                 |
| Rou Gui        | 41.68                     | —                                 |
| Chi Shao (Yao) | 43.11                     | —                                 |
| Ji Li          | 43.17                     | —                                 |
| Fu Ling        | 43.89                     | —                                 |
| Lian Zi        | 44.04                     | —                                 |
| Tu Fu Ling     | 45.03                     | —                                 |
| Chuan Niu Xi   | 45.22                     | —                                 |
| Bai Xian Pi    | 45.42                     | —                                 |
| Bai Zhi        | 45.57                     | —                                 |
| Sheng Jiang    | 45.90                     | —                                 |
| Lian Qiao      | 46.74                     | —                                 |
| Yuan Zhi       | 47.33                     | —                                 |
| Bing Lang      | 48.35                     | —                                 |
| Ma Huang Gen   | 48.48                     | —                                 |
| Chai Hu        | 48.81                     | —                                 |
| Bai Shao Yao   | 49.87                     | —                                 |
| Niu Bang Zi    | 50.01                     | —                                 |



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                         | 9.74                            |
| 62740     | 62740               | 0.00                         | 10.43                           |
| 62887     | 62887               | 0.00                         | 14.33                           |
| 62888     | 62888               | 0.00                         | 13.18                           |

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 2.4-2022-02

Validated substance/substance group **Bai Hua She She Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60039-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bai Hua She She Cao       | 2      | 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 |
| PhytoComm | Bai Hua She She ... | G173HS078SP1 | 62827     | 40      | from supplier |
| PhytoComm | Bai Hua She She ... | G173HS078SP1 | 62828     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Hua She She Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Bai Hua She She Cao | G173HS078RW1 | 62576 <sup>†</sup> | 20      |
| PhytoComm | Bai Hua She She Cao | G173HS078SP1 | 62827 <sup>†</sup> | 20      |
| PhytoComm | Bai Hua She She Cao | G173HS078SP1 | 62828 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 1              | 80            | 0              | 11 316        |
| <b>Type C</b> | 0              | 0             | 7              | 850           |

The substance/substance group *Bai Hua She She 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 99.9950 % (> 99.9629 %)  | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| Xin Yi        | 6.84                      | —                                 |
| Han Lian Cao  | 9.88                      | —                                 |
| Zhi Shi       | 10.35                     | —                                 |
| Xi Xian Cao   | 11.26                     | —                                 |
| Xia Ku Cao    | 12.15                     | —                                 |
| Yu Xing Cao   | 12.82                     | —                                 |
| Huang Lian    | 14.34                     | —                                 |
| Hu Zhang      | 14.65                     | —                                 |
| Jiang Huang   | 15.59                     | —                                 |
| Sang Ye       | 16.54                     | —                                 |
| Tu Fu Ling    | 19.48                     | —                                 |
| Ze Lan        | 20.44                     | —                                 |
| Pu Gong Ying  | 21.71                     | —                                 |
| Shan Yao      | 21.84                     | —                                 |
| Xiang Fu      | 22.79                     | —                                 |
| Sha Ren       | 24.55                     | —                                 |
| Yi Mu Cao     | 26.87                     | —                                 |
| He Huan Pi    | 27.46                     | —                                 |
| Mang Xiao     | 27.79                     | —                                 |
| Nü Zhen Zi    | 28.20                     | —                                 |
| Yin Chen Hao  | 31.02                     | —                                 |
| Du Zhong      | 33.63                     | —                                 |
| Gu Sui Bu     | 34.50                     | —                                 |
| Zhi Ke        | 36.19                     | —                                 |
| Gou Teng      | 37.06                     | —                                 |
| Jiao Gu Lan   | 37.23                     | —                                 |
| E Zhu         | 38.33                     | —                                 |
| Dan Shen      | 38.57                     | —                                 |
| Yu Jin        | 38.75                     | —                                 |
| Cang Er Zi    | 40.91                     | —                                 |
| Fu Zi         | 41.38                     | —                                 |
| (Bai) Dou Kou | 41.83                     | —                                 |
| Qiang Huo     | 42.66                     | —                                 |
| Bai Jiang Cao | 43.66                     | —                                 |
| Che Qian Zi   | 44.56                     | —                                 |
| Bo He         | 44.66                     | —                                 |
| Chen Pi       | 45.71                     | —                                 |
| Bai Xian Pi   | 46.06                     | —                                 |
| Niu Bang Zi   | 47.00                     | —                                 |
| Ju Hua        | 47.14                     | —                                 |
| Mao Dong Qing | 47.63                     | —                                 |
| Wu Yao        | 47.93                     | —                                 |
| Hou Po        | 48.22                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62575     | 62575               | 0.00                         | 6.84                            |
| 62576     | 62576               | 0.00                         | 7.52                            |
| 62827     | 62827               | 0.00                         | 11.88                           |
| 62828     | 62828               | 0.00                         | 11.26                           |

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





# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Bai Jiang Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50319-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Bai Jiang Cao; Patriniae herba

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bai Jiang Cao             | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Bai Jiang 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 Jiang Cao*:

| Supplier  | Substance     | Batch        | Sample ID | Spectra | Certificate   |
|-----------|---------------|--------------|-----------|---------|---------------|
| PhytoComm | Bai Jiang Cao | G181HS381TH1 | 62833     | 40      | from supplier |
| PhytoComm | Bai Jiang Cao | G181HS381TH1 | 62834     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Jiang Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 Jiang 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 Jiang Cao | G181HS381TH1 | 62833 <sup>†</sup> | 20      |
| PhytoComm | Bai Jiang Cao | G181HS381TH1 | 62834 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 Jiang 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 Jiang Cao | G181H1180321 | 1       |
| Phytocomm | Bai Jiang Cao | G181H1180422 | 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 Jiang 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 Jiang 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 39            | 1              | 11 357        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Bai Jiang 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 97.5000 % (> 90.0000 %)  |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai Jiang 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Sha Ren         | 6.69                      | —                                 |
| Du Zhong        | 9.47                      | —                                 |
| Jiao Gu Lan     | 9.86                      | —                                 |
| Bo He           | 10.43                     | —                                 |
| Yu Jin          | 11.36                     | —                                 |
| Mao Dong Qing   | 11.99                     | —                                 |
| Pu Gong Ying    | 12.52                     | —                                 |
| Fu Zi           | 12.90                     | —                                 |
| Tu Fu Ling      | 12.93                     | —                                 |
| Chai Hu         | 13.05                     | —                                 |
| Dan Shen        | 13.27                     | —                                 |
| Qiang Huo       | 13.33                     | —                                 |
| Zhi Ke          | 14.10                     | —                                 |
| Huang Lian      | 14.22                     | —                                 |
| Qing Hao        | 15.79                     | —                                 |
| Huang Bai       | 16.14                     | —                                 |
| Ze Lan          | 16.42                     | —                                 |
| Zi Hua Di Ding  | 16.76                     | —                                 |
| Hou Po          | 18.31                     | —                                 |
| Che Qian Zi     | 18.62                     | —                                 |
| Bai Xian Pi     | 18.84                     | —                                 |
| Yin Yang Huo    | 18.86                     | —                                 |
| Shan Yao        | 19.46                     | —                                 |
| Jing Jie        | 19.46                     | —                                 |
| Ye Jiao Teng    | 20.28                     | —                                 |
| Xi Xian Cao     | 20.38                     | —                                 |
| Qing Pi         | 20.85                     | —                                 |
| Sang Ye         | 21.95                     | —                                 |
| Fu Pen Zi       | 22.14                     | —                                 |
| Ce Bai Ye       | 22.18                     | —                                 |
| Ling Zhi        | 22.81                     | —                                 |
| Hong Jing Tian  | 22.88                     | —                                 |
| Dan Dou Chi     | 23.06                     | —                                 |
| Jin Yin Hua     | 23.35                     | —                                 |
| Pi Pa Ye        | 24.21                     | —                                 |
| Ma Huang        | 25.40                     | —                                 |
| Yan Hu Suo      | 25.55                     | —                                 |
| Ji Xue Teng     | 26.38                     | —                                 |
| Zhi Shi         | 26.44                     | —                                 |
| Di Gu Pi        | 26.50                     | —                                 |
| Nü Zhen Zi      | 27.23                     | —                                 |
| Lian Zi         | 27.41                     | —                                 |
| Tian Hua Fen    | 28.14                     | —                                 |
| Ren Dong Teng   | 28.50                     | —                                 |
| Chuang Mu Xiang | 28.84                     | —                                 |
| Bai Shao Yao    | 29.45                     | —                                 |
| Yin Chen Hao    | 30.26                     | —                                 |
| Gu Sui Bu       | 30.48                     | —                                 |
| Mang Xiao       | 30.56                     | —                                 |
| He Huan Pi      | 31.29                     | —                                 |
| Suan Zao Ren    | 31.61                     | —                                 |
| Shen Qu         | 31.92                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Ren Shen            | 33.83                     | —                                 |
| Gan Cao             | 33.95                     | —                                 |
| Ji Li               | 34.00                     | —                                 |
| Xin Yi              | 34.09                     | —                                 |
| Jiang Huang         | 34.20                     | —                                 |
| Ban Lan Gen         | 34.58                     | —                                 |
| Lian Qiao           | 34.89                     | —                                 |
| Guang Huo Xiang     | 35.63                     | —                                 |
| Cang Er Zi          | 35.69                     | —                                 |
| Zhu Ling            | 36.78                     | —                                 |
| (Fen) Bi Xie        | 36.89                     | —                                 |
| Lu Gen              | 37.72                     | —                                 |
| Hong Hua            | 37.96                     | —                                 |
| Gou Teng            | 38.58                     | —                                 |
| E Zhu               | 39.69                     | —                                 |
| Mu Zei              | 40.32                     | —                                 |
| Cang Zhu            | 40.63                     | —                                 |
| Yi Mu Cao           | 41.18                     | —                                 |
| Chi Shao (Yao)      | 41.22                     | —                                 |
| Zhe Bei Mu          | 41.39                     | —                                 |
| Sheng Jiang         | 41.48                     | —                                 |
| Bai Hua She She Cao | 42.29                     | —                                 |
| Rou Gui             | 42.47                     | —                                 |
| Zhi Gan Cao         | 42.63                     | —                                 |
| She Gan             | 43.15                     | —                                 |
| Ban Zhi Lian        | 43.77                     | —                                 |
| Zi Su Zi            | 43.90                     | —                                 |
| Wang Bu Liu Xing    | 43.99                     | —                                 |
| Tao Ren             | 44.16                     | —                                 |
| Niu Bang Zi         | 44.60                     | —                                 |
| Huang Qin           | 44.82                     | —                                 |
| Sha Shen (Bei)      | 44.85                     | —                                 |
| Ma Huang Gen        | 44.85                     | —                                 |
| Jie Geng            | 46.49                     | —                                 |
| Hu Zhang            | 46.71                     | —                                 |
| Yu Xing Cao         | 47.75                     | —                                 |
| Huo Ma Ren          | 48.72                     | —                                 |
| Chuan Mu Tong       | 50.06                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Bai Jiang 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62833     | 62833                  | 0.00                            | 7.33                               |
| 62834     | 62834                  | 0.00                            | 6.69                               |

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 2.4-2022-02

Validated substance/substance group **Bai Shao Yao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60007-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bai Shao Yao              | 4      | 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 |
| PhytoComm | Bai Shao Yao | G179HS065TK1 | 62829     | 40      | from supplier |
| PhytoComm | Bai Shao Yao | G179HS065TK1 | 62830     | 40      | from supplier |

## Validation samples

A total of 34 694 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

**Type A** All calibration spectra.

- 280 spectra of 7 reference samples from the substance/substance group *Bai Shao Yao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 160 spectra from a total of 278 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 199 spectra of 8 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 <sup>†</sup> | 20      |
| PhytoComm | Bai Shao Yao | G179HS065RQ1 | 62276              | 59      |
| PhytoComm | Bai Shao Yao | G179HS065RT1 | 62435 <sup>†</sup> | 20      |
| PhytoComm | Bai Shao Yao | G179HS065RT1 | 62436 <sup>†</sup> | 20      |
| PhytoComm | Bai Shao Yao | G179HS065RW1 | 62601 <sup>†</sup> | 20      |

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| Supplier  | Substance    | Batch        | Sample ID          | Spectra |
|-----------|--------------|--------------|--------------------|---------|
| PhytoComm | Bai Shao Yao | G179HS065RW1 | 62602 <sup>†</sup> | 20      |
| PhytoComm | Bai Shao Yao | G179HS065TK1 | 62829 <sup>†</sup> | 20      |
| PhytoComm | Bai Shao Yao | G179HS065TK1 | 62830 <sup>†</sup> | 20      |

- 11 198 spectra from a total of 278 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | 1214401      | 1       |
| Phytocomm | Bai Shao Yao | G179H0502121 | 1       |
| Phytocomm | Bai Shao Yao | g179h0502322 | 1       |
| Phytocomm | Bai Shao Yao | G179H0502322 | 1       |
| PhytoComm | Bai Shao Yao | G179H0502322 | 1       |
| Phytocomm | Bai Shao Yao | G179H0502521 | 5       |
| Phytocomm | Bai Shao Yao | g17h0502323  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 280           | 0              | 22 159        |
| <b>Type B</b> | 2              | 190           | 9              | 11 196        |
| <b>Type C</b> | 1              | 0             | 11             | 845           |

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

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:

|               | <b>Specificity</b>      | <b>Recognition rate</b>  |
|---------------|-------------------------|--------------------------|
| <b>Type A</b> | 99.9926 % (> 99.9762 %) | 100.0000 % (> 97.8571 %) |
| <b>Type B</b> | 99.9777 % (> 99.9454 %) | 95.4774 % (> 93.9698 %)  |
| <b>Type C</b> | 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.

| <b>Substance</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|------------------|-----------------------------------|-------------------------------------------|
| Ban Xia (Jiang)  | 3.12                              | —                                         |
| Di Gu Pi         | 6.23                              | —                                         |
| Ye Jiao Teng     | 7.10                              | —                                         |
| He Huan Pi       | 7.70                              | —                                         |
| Zhu Ru           | 7.85                              | —                                         |
| Rou Gui          | 7.87                              | —                                         |
| Pi Pa Ye         | 8.01                              | —                                         |
| Zhe Bei Mu       | 9.13                              | —                                         |
| Gui Zhi          | 9.97                              | —                                         |
| Ci Wu Jia        | 10.01                             | —                                         |
| Ji Li            | 10.01                             | —                                         |
| Shen Qu          | 10.11                             | —                                         |
| Sheng Jiang      | 10.22                             | —                                         |
| Shan Yao         | 10.61                             | —                                         |
| Fu Xiao Mai      | 10.82                             | —                                         |
| Tian Hua Fen     | 10.98                             | —                                         |
| Fo Shou          | 11.77                             | —                                         |
| Bai Zi Ren       | 12.01                             | —                                         |
| Tao Ren          | 12.13                             | —                                         |
| Lai Fu Zi        | 12.32                             | —                                         |
| Ji Xue Teng      | 13.39                             | —                                         |
| Yi Yi Ren        | 13.97                             | —                                         |
| Gou Teng         | 14.22                             | —                                         |
| Jin Yin Hua      | 14.24                             | —                                         |
| Mu Zei           | 14.54                             | —                                         |
| Lian Qiao        | 14.73                             | —                                         |
| Lian Zi          | 15.10                             | —                                         |
| Zhi Mu           | 15.33                             | —                                         |
| Fu Ling          | 15.34                             | —                                         |
| Huo Ma Ren       | 16.78                             | —                                         |
| Ling Zhi         | 17.41                             | —                                         |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ren Dong Teng   | 18.27                     | —                                 |
| San Qi          | 18.40                     | —                                 |
| Lu Gen          | 19.45                     | —                                 |
| Ze Xie          | 19.56                     | —                                 |
| Dang Gui        | 19.98                     | —                                 |
| Ku Shen         | 20.12                     | —                                 |
| Bai Xian Pi     | 20.21                     | —                                 |
| Gua Lou         | 20.26                     | —                                 |
| Ren Shen        | 20.30                     | —                                 |
| Fu Zi           | 20.62                     | —                                 |
| Gu Sui Bu       | 20.66                     | —                                 |
| Jie Geng        | 20.94                     | —                                 |
| Fu Shen         | 21.86                     | —                                 |
| Ma Huang Gen    | 22.22                     | —                                 |
| Cang Zhu        | 23.20                     | —                                 |
| Yuan Zhi        | 23.99                     | —                                 |
| Jiao Gu Lan     | 24.49                     | —                                 |
| Fu Pen Zi       | 24.57                     | —                                 |
| Zhi Ke          | 24.70                     | —                                 |
| Ban Lan Gen     | 24.70                     | —                                 |
| Yan Hu Suo      | 24.77                     | —                                 |
| Tu Fu Ling      | 25.29                     | —                                 |
| Suan Zao Ren    | 25.38                     | —                                 |
| Huang Qin       | 26.38                     | —                                 |
| Yu Jin          | 26.92                     | —                                 |
| Mu Gua          | 27.07                     | —                                 |
| Gou Qi Zi       | 27.53                     | —                                 |
| Hou Po          | 27.65                     | —                                 |
| Ma Huang        | 28.82                     | —                                 |
| Che Qian Zi     | 28.83                     | —                                 |
| Zhu Ling        | 29.59                     | —                                 |
| (Fen) Bi Xie    | 30.17                     | —                                 |
| Dan Shen        | 30.22                     | —                                 |
| Yin Yang Huo    | 30.56                     | —                                 |
| Dan Dou Chi     | 31.57                     | —                                 |
| Ce Bai Ye       | 32.16                     | —                                 |
| Mao Dong Qing   | 32.17                     | —                                 |
| Mang Xiao       | 32.50                     | —                                 |
| Guang Huo Xiang | 33.96                     | —                                 |
| Long Yan Rou    | 35.37                     | —                                 |
| Chai Hu         | 36.26                     | —                                 |
| She Gan         | 36.64                     | —                                 |
| Xie Bai         | 37.43                     | —                                 |
| Hong Jing Tian  | 37.69                     | —                                 |
| Gan Cao         | 38.20                     | —                                 |
| Qiang Huo       | 39.66                     | —                                 |
| Chuang Mu Xiang | 41.60                     | —                                 |
| Sang Zhi        | 42.78                     | —                                 |
| Huang Lian      | 44.53                     | —                                 |
| Qing Pi         | 45.08                     | —                                 |
| Chi Shao (Yao)  | 45.62                     | —                                 |
| Zi Hua Di Ding  | 49.54                     | —                                 |
| Jing Jie        | 50.40                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62275     | 62275               | 0.00                         | 7.10                            |
| 62435     | 62435               | 0.00                         | 8.16                            |
| 62436     | 62436               | 0.00                         | 7.85                            |
| 62601     | 62601               | 0.00                         | 9.83                            |
| 62602     | 62602               | 0.00                         | 10.01                           |
| 62829     | 62829               | 0.00                         | 3.18                            |
| 62830     | 62830               | 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 2.4-2022-02

Validated substance/substance group **Bai Xian Pi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60208-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Bai Xian Pi | G090HS335RP1 | 62286 <sup>†</sup> | 20      |
| PhytoComm | Bai Xian Pi | G090HS335RN1 | 62449 <sup>†</sup> | 20      |
| PhytoComm | Bai Xian Pi | G090HS335RN1 | 62450 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 3              | 152           | 8              | 22 277        |
| <b>Type B</b> | 6              | 80            | 0              | 11 311        |
| <b>Type C</b> | 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         |
|---------------|-------------------------|--------------------------|
| <b>Type A</b> | 99.9888 % (> 99.9725 %) | 95.0000 % (> 93.1250 %)  |
| <b>Type B</b> | 99.9603 % (> 99.9281 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dan Dou Chi     | 3.51                      | —                                 |
| Ye Jiao Teng    | 5.28                      | —                                 |
| Tu Fu Ling      | 6.17                      | —                                 |
| Ling Zhi        | 7.09                      | —                                 |
| Yin Yang Huo    | 7.71                      | —                                 |
| Mao Dong Qing   | 8.55                      | —                                 |
| Ren Dong Teng   | 9.28                      | —                                 |
| Ce Bai Ye       | 9.48                      | —                                 |
| Yu Jin          | 9.72                      | —                                 |
| Hou Po          | 10.45                     | —                                 |
| Jing Jie        | 10.67                     | —                                 |
| Chai Hu         | 11.10                     | —                                 |
| Lian Zi         | 11.44                     | —                                 |
| Shen Qu         | 12.53                     | —                                 |
| Zhu Ling        | 12.58                     | —                                 |
| Fu Zi           | 12.59                     | —                                 |
| Qiang Huo       | 12.93                     | —                                 |
| Che Qian Zi     | 13.05                     | —                                 |
| Guang Huo Xiang | 13.90                     | —                                 |
| Rou Gui         | 14.70                     | —                                 |
| Ji Xue Teng     | 14.78                     | —                                 |
| Zi Hua Di Ding  | 14.88                     | —                                 |
| (Fen) Bi Xie    | 15.07                     | —                                 |
| Dan Shen        | 16.29                     | —                                 |
| He Huan Pi      | 17.55                     | —                                 |
| Sha Ren         | 17.90                     | —                                 |
| Gou Teng        | 18.14                     | —                                 |
| Lu Gen          | 18.27                     | —                                 |
| Suan Zao Ren    | 18.28                     | —                                 |
| Yan Hu Suo      | 19.19                     | —                                 |
| Ma Huang Gen    | 19.31                     | —                                 |
| Du Zhong        | 19.53                     | —                                 |
| Shan Yao        | 19.60                     | —                                 |
| Ji Li           | 19.99                     | —                                 |
| Fu Pen Zi       | 20.21                     | —                                 |
| Gan Cao         | 20.22                     | —                                 |
| Bo He           | 20.23                     | —                                 |
| Pi Pa Ye        | 20.69                     | —                                 |
| Jin Yin Hua     | 20.86                     | —                                 |
| Lian Qiao       | 20.87                     | —                                 |
| Gu Sui Bu       | 21.28                     | —                                 |
| Huang Bai       | 21.40                     | —                                 |
| Ma Huang        | 21.47                     | —                                 |
| Huo Ma Ren      | 21.51                     | —                                 |
| Sheng Jiang     | 21.67                     | —                                 |
| She Gan         | 22.99                     | —                                 |
| Zhi Ke          | 23.08                     | —                                 |
| Bai Shao Yao    | 23.09                     | —                                 |

*continued on the next page*



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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Gui Zhi         | 23.16                     | —                                 |
| Jiao Gu Lan     | 23.21                     | —                                 |
| Qing Pi         | 24.72                     | —                                 |
| Tian Hua Fen    | 24.73                     | —                                 |
| Yi Yi Ren       | 24.75                     | —                                 |
| Hong Jing Tian  | 25.11                     | —                                 |
| Fu Ling         | 25.31                     | —                                 |
| Di Gu Pi        | 25.53                     | —                                 |
| Chuang Mu Xiang | 26.26                     | —                                 |
| Mu Zei          | 26.27                     | —                                 |
| Huang Lian      | 27.03                     | —                                 |
| Tao Ren         | 27.72                     | —                                 |
| Qing Hao        | 28.34                     | —                                 |
| Ban Lan Gen     | 28.61                     | —                                 |
| Zhe Bei Mu      | 29.05                     | —                                 |
| Zhi Gan Cao     | 30.25                     | —                                 |
| Fo Shou         | 30.63                     | —                                 |
| Bai Jiang Cao   | 31.11                     | —                                 |
| Mang Xiao       | 31.96                     | —                                 |
| Ci Wu Jia       | 32.44                     | —                                 |
| Cang Zhu        | 32.81                     | —                                 |
| Ban Zhi Lian    | 33.56                     | —                                 |
| Fu Shen         | 33.82                     | —                                 |
| Fu Xiao Mai     | 34.94                     | —                                 |
| Ban Xia (Jiang) | 35.07                     | —                                 |
| Ren Shen        | 35.28                     | —                                 |
| Bai Zi Ren      | 36.88                     | —                                 |
| Sang Zhi        | 38.06                     | —                                 |
| Zhu Ru          | 39.88                     | —                                 |
| Chi Shao (Yao)  | 40.14                     | —                                 |
| Jie Geng        | 42.31                     | —                                 |
| Huang Qin       | 42.52                     | —                                 |
| Dang Gui        | 43.72                     | —                                 |
| Ze Xie          | 43.97                     | —                                 |
| Pu Gong Ying    | 44.05                     | —                                 |
| Gua Lou         | 44.39                     | —                                 |
| Hong Hua        | 44.78                     | —                                 |
| Ze Lan          | 45.58                     | —                                 |
| San Qi          | 45.87                     | —                                 |
| Xie Bai         | 46.49                     | —                                 |
| Bai Zhu         | 46.95                     | —                                 |
| Cang Er Zi      | 48.43                     | —                                 |
| Long Yan Rou    | 48.47                     | —                                 |
| Lai Fu Zi       | 49.07                     | —                                 |
| Jiang Huang     | 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62285     | 62285               | 0.00                         | 3.51                            |
| 62286     | 62286               | 0.00                         | 3.59                            |
| 62449     | 62449               | 0.00                         | 4.85                            |
| 62450     | 62450               | 0.00                         | 4.62                            |

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 2.4-2022-02

Validated substance/substance group **Bai Zhi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60235-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Bai Zhi; Angelicae dahuricae radix

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bai Zhi                   | 1      | 0      | 1      |

### Second-stage model

For differentiation of the substance/substance group *Bai 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 *Bai Zhi*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Bai Zhi   | G020H0503922 | 62961     | 40      | from supplier |
| PhytoComm | Bai Zhi   | G020H0503922 | 62962     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 | Bai Zhi   | G020H0503922 | 62961 <sup>†</sup> | 20      |
| PhytoComm | Bai Zhi   | G020H0503922 | 62962 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 Zhi*.
- 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 Zhi   | G020H0503421 | 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 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 *Bai 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 1             | 0              | 856           |

The substance/substance group *Bai 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bai 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Chuan Niu Xi        | 13.63                     | —                                 |
| Xiang Fu            | 15.60                     | —                                 |
| (Shi) Chang Pu      | 15.98                     | —                                 |
| Chen Pi             | 16.41                     | —                                 |
| Dang Gui            | 16.92                     | —                                 |
| Wu Yao              | 21.42                     | —                                 |
| Du Huo              | 21.93                     | —                                 |
| Tian Hua Fen        | 22.26                     | —                                 |
| Zhi Gan Cao         | 24.43                     | —                                 |
| Ju Hua              | 25.79                     | —                                 |
| Yan Hu Suo          | 26.04                     | —                                 |
| Shan Yu Rou         | 26.22                     | —                                 |
| Huang Qi            | 26.84                     | —                                 |
| (Huai) Niu Xi       | 27.03                     | —                                 |
| Shan Yao            | 27.14                     | —                                 |
| Chuan Lian Zi       | 27.20                     | —                                 |
| Sha Ren             | 27.22                     | —                                 |
| Xu Duan             | 27.48                     | —                                 |
| Di Gu Pi            | 27.65                     | —                                 |
| Mang Xiao           | 27.69                     | —                                 |
| Ku Shen             | 27.90                     | —                                 |
| Mu Dan Pi           | 28.08                     | —                                 |
| Zi Su Zi            | 28.65                     | —                                 |
| Mi Huan Jun         | 28.74                     | —                                 |
| Bai Hua She She Cao | 29.21                     | —                                 |
| Sang Zhi            | 29.84                     | —                                 |
| Jiang Huang         | 30.71                     | —                                 |
| Gu Sui Bu           | 30.93                     | —                                 |
| Yi Mu Cao           | 30.98                     | —                                 |
| Bing Lang           | 31.15                     | —                                 |
| (Bai) Dou Kou       | 31.30                     | —                                 |
| Wu Zhu Yu           | 31.54                     | —                                 |
| Xiao Hui Xiang      | 32.31                     | —                                 |
| Gan Jiang           | 32.45                     | —                                 |
| Lian Qiao           | 33.22                     | —                                 |
| Fang Feng           | 34.29                     | —                                 |
| Chi Shao (Yao)      | 34.39                     | —                                 |
| Pu Gong Ying        | 34.48                     | —                                 |
| Sang Ye             | 34.58                     | —                                 |
| Xin Yi              | 35.17                     | —                                 |
| Jie Geng            | 35.36                     | —                                 |
| Zhi Ke              | 35.51                     | —                                 |
| Niu Bang Zi         | 35.52                     | —                                 |
| Cang Er Zi          | 35.63                     | —                                 |
| Sang Ji Shend       | 35.73                     | —                                 |
| Ba Ji Tian          | 37.11                     | —                                 |
| Bai Zhu             | 37.74                     | —                                 |
| He Huan Pi          | 39.23                     | —                                 |
| Qin Jiao            | 39.27                     | —                                 |
| E Zhu               | 39.35                     | —                                 |
| Bo He               | 39.94                     | —                                 |
| Ze Lan              | 40.45                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Huang Lian     | 41.44                     | —                                 |
| Chuan Mu Tong  | 41.97                     | —                                 |
| Sha Shen (Bei) | 42.65                     | —                                 |
| Mao Dong Qing  | 42.74                     | —                                 |
| Tu Fu Ling     | 43.09                     | —                                 |
| Gan Cao        | 43.31                     | —                                 |
| He Shou Wu     | 43.45                     | —                                 |
| Ge Gen         | 45.54                     | —                                 |
| Hong Jing Tian | 46.09                     | —                                 |
| Du Zhong       | 46.22                     | —                                 |
| Xi Xian Cao    | 46.70                     | —                                 |
| Yuan Zhi       | 46.79                     | —                                 |
| Jin Yin Hua    | 46.80                     | —                                 |
| Qiang Huo      | 47.08                     | —                                 |
| Zi Hua Di Ding | 47.58                     | —                                 |
| Lai Fu Zi      | 47.67                     | —                                 |
| Hu Zhang       | 48.04                     | —                                 |
| Da Zao         | 49.18                     | —                                 |
| Nü Zhen Zi     | 49.57                     | —                                 |
| Yin Chen Hao   | 49.82                     | —                                 |
| Suan Zao Ren   | 50.16                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Bai 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62961     | 62961                  | 0.00                            | 14.43                              |
| 62962     | 62962                  | 0.00                            | 13.63                              |

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 2.4-2022-02

Validated substance/substance group **Bai Zhu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60015-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bai Zhu                   | 2      | 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   | G041H0501822 | 62385     | 40      | from supplier |
| PhytoComm | Bai Zhu   | G041H0501822 | 62386     | 40      | from supplier |
| PhytoComm | Bai Zhu   | G041H0501922 | 62975     | 40      | from supplier |
| PhytoComm | Bai Zhu   | G041H0501922 | 62976     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Zhu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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   | G041H0501822 | 62385 <sup>†</sup> | 20      |
| PhytoComm | Bai Zhu   | G041H0501822 | 62386 <sup>†</sup> | 20      |
| PhytoComm | Bai Zhu   | G041H0501922 | 62975 <sup>†</sup> | 20      |
| PhytoComm | Bai Zhu   | G041H0501922 | 62976 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | 3       |
| Phytocomm | Bai Zhu   | G041H0501221 | 1       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 79            | 1              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 98.7500 % (> 95.0000 %)  |
| <b>Type C</b> | 99.8140 % (> 99.2266 %)  | n/a (n/a)                |

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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Jie Geng       | 5.96                      | —                                 |
| Mu Gua         | 11.17                     | —                                 |
| Zhi Gan Cao    | 11.84                     | —                                 |
| Huang Qi       | 12.32                     | —                                 |
| Yuan Zhi       | 13.89                     | —                                 |
| (Huai) Niu Xi  | 15.12                     | —                                 |
| Sang Zhi       | 16.53                     | —                                 |
| Chuan Lian Zi  | 16.61                     | —                                 |
| Di Gu Pi       | 16.84                     | —                                 |
| Long Dan (Cao) | 20.19                     | —                                 |
| Tian Hua Fen   | 21.85                     | —                                 |
| Qin Jiao       | 22.23                     | —                                 |
| Bai He         | 22.55                     | —                                 |
| Chi Shao (Yao) | 22.69                     | —                                 |
| Lai Fu Zi      | 23.82                     | —                                 |
| Mang Xiao      | 29.58                     | —                                 |
| Zi Su Zi       | 29.87                     | —                                 |
| Sha Shen (Bei) | 30.17                     | —                                 |
| Lian Qiao      | 30.67                     | —                                 |
| Chuan Mu Tong  | 30.75                     | —                                 |
| Gan Jiang      | 30.89                     | —                                 |
| Dang Gui       | 31.46                     | —                                 |
| Bai Xian Pi    | 32.73                     | —                                 |
| Tu Fu Ling     | 32.95                     | —                                 |
| Shan Yao       | 33.00                     | —                                 |
| Bing Lang      | 33.13                     | —                                 |
| Chuan Niu Xi   | 33.50                     | —                                 |
| E Zhu          | 33.62                     | —                                 |
| Lian Zi        | 35.15                     | —                                 |
| Niu Bang Zi    | 35.67                     | —                                 |
| Bai Shao Yao   | 36.35                     | —                                 |
| Ku Shen        | 36.41                     | —                                 |
| Bai Zhi        | 36.63                     | —                                 |
| Ban Zhi Lian   | 37.16                     | —                                 |
| (Shi) Chang Pu | 38.01                     | —                                 |
| Rou Gui        | 38.62                     | —                                 |
| Du Huo         | 38.62                     | —                                 |
| Cang Er Zi     | 38.90                     | —                                 |
| Ji Li          | 38.90                     | —                                 |
| Chai Hu        | 38.90                     | —                                 |
| Fu Ling        | 40.08                     | —                                 |
| Jin Yin Hua    | 40.24                     | —                                 |
| Mi Huan Jun    | 40.42                     | —                                 |

*continued on the next page*

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| Substanz     | Distance in<br>main model | Distance in<br>second-stage model |
|--------------|---------------------------|-----------------------------------|
| Zhi Ke       | 41.65                     | —                                 |
| Suan Zao Ren | 42.10                     | —                                 |
| Ju Hua       | 42.35                     | —                                 |
| Ye Jiao Teng | 42.67                     | —                                 |
| Cang Zhu     | 43.11                     | —                                 |
| Chen Pi      | 43.22                     | —                                 |
| Gan Cao      | 43.73                     | —                                 |
| Yan Hu Suo   | 44.02                     | —                                 |
| Da Zao       | 45.50                     | —                                 |
| Zhe Bei Mu   | 45.74                     | —                                 |
| Dong Gua Zi  | 45.95                     | —                                 |
| Fo Shou      | 45.97                     | —                                 |
| She Gan      | 47.19                     | —                                 |
| Sheng Jiang  | 47.34                     | —                                 |
| Gou Teng     | 47.55                     | —                                 |
| Fu Zi        | 47.87                     | —                                 |
| Qiang Huo    | 48.13                     | —                                 |
| Jiao Gu Lan  | 48.35                     | —                                 |
| Ce Bai Ye    | 48.37                     | —                                 |
| Dan Dou Chi  | 48.37                     | —                                 |
| Yi Yi Ren    | 48.71                     | —                                 |
| Jiang Huang  | 48.78                     | —                                 |
| Ba Ji Tian   | 48.82                     | —                                 |
| Gui Zhi      | 49.18                     | —                                 |
| Ji Xue Teng  | 49.26                     | —                                 |
| Xiang Fu     | 49.46                     | —                                 |
| Gu Sui Bu    | 49.96                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62385     | 62385                  | 0.00                            | 6.54                               |
| 62386     | 62386                  | 0.00                            | 5.96                               |
| 62975     | 62975                  | 0.00                            | 10.05                              |
| 62976     | 62976                  | 0.00                            | 9.68                               |

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 2.4-2022-02

Validated substance/substance group **Bai Zi Ren**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60197-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Bai Zi Ren | G052HS187SK1 | 62660 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 | G052HS187   | 2       |
| Phytocomm | Bai Zi Ren | g952f110315 | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Lian Zi         | 5.92                      | —                                 |
| Ji Li           | 7.78                      | —                                 |
| Bai Shao Yao    | 9.92                      | —                                 |
| Ling Zhi        | 10.19                     | —                                 |
| Shen Qu         | 10.91                     | —                                 |
| Ze Xie          | 10.95                     | —                                 |
| Huo Ma Ren      | 11.22                     | —                                 |
| He Huan Pi      | 11.27                     | —                                 |
| Sheng Jiang     | 11.97                     | —                                 |
| Di Gu Pi        | 12.76                     | —                                 |
| Zhu Ru          | 12.80                     | —                                 |
| Lai Fu Zi       | 12.81                     | —                                 |
| Zhe Bei Mu      | 14.24                     | —                                 |
| Fu Xiao Mai     | 14.52                     | —                                 |
| Ci Wu Jia       | 14.62                     | —                                 |
| Gui Zhi         | 14.66                     | —                                 |
| Shan Yao        | 14.75                     | —                                 |
| Tian Hua Fen    | 14.94                     | —                                 |
| Pi Pa Ye        | 15.67                     | —                                 |
| Ren Dong Teng   | 16.06                     | —                                 |
| Mu Zei          | 16.06                     | —                                 |
| Tao Ren         | 16.89                     | —                                 |
| Fu Ling         | 17.05                     | —                                 |
| Tu Fu Ling      | 17.52                     | —                                 |
| Ye Jiao Teng    | 17.55                     | —                                 |
| Bai Xian Pi     | 17.63                     | —                                 |
| San Qi          | 18.03                     | —                                 |
| Cang Zhu        | 18.21                     | —                                 |
| Gua Lou         | 18.25                     | —                                 |
| Lian Qiao       | 18.60                     | —                                 |
| Gu Sui Bu       | 18.73                     | —                                 |
| Suan Zao Ren    | 18.81                     | —                                 |
| Yi Yi Ren       | 18.82                     | —                                 |
| Rou Gui         | 20.23                     | —                                 |
| Lu Gen          | 20.53                     | —                                 |
| Gou Teng        | 20.61                     | —                                 |
| Yu Jin          | 21.72                     | —                                 |
| Fo Shou         | 22.71                     | —                                 |
| Mao Dong Qing   | 22.94                     | —                                 |
| Jin Yin Hua     | 23.33                     | —                                 |
| Fu Zi           | 23.79                     | —                                 |
| Ban Xia (Jiang) | 24.27                     | —                                 |
| Ji Xue Teng     | 24.28                     | —                                 |
| Dan Dou Chi     | 24.51                     | —                                 |
| Guang Huo Xiang | 24.62                     | —                                 |
| Jie Geng        | 24.71                     | —                                 |
| Jiao Gu Lan     | 24.72                     | —                                 |
| Ce Bai Ye       | 24.80                     | —                                 |
| Fu Pen Zi       | 24.89                     | —                                 |
| She Gan         | 24.90                     | —                                 |
| Hou Po          | 25.74                     | —                                 |
| Chai Hu         | 25.90                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dan Shen        | 25.91                     | —                                 |
| Ban Lan Gen     | 26.91                     | —                                 |
| Zhi Mu          | 27.31                     | —                                 |
| Che Qian Zi     | 27.67                     | —                                 |
| Ma Huang Gen    | 27.93                     | —                                 |
| Dang Gui        | 28.20                     | —                                 |
| Zhu Ling        | 29.30                     | —                                 |
| (Fen) Bi Xie    | 29.33                     | —                                 |
| Zhi Ke          | 30.29                     | —                                 |
| Mu Gua          | 31.08                     | —                                 |
| Yan Hu Suo      | 31.35                     | —                                 |
| Ren Shen        | 32.87                     | —                                 |
| Ku Shen         | 33.20                     | —                                 |
| Hong Jing Tian  | 33.37                     | —                                 |
| Yuan Zhi        | 33.46                     | —                                 |
| Yin Yang Huo    | 33.48                     | —                                 |
| Xie Bai         | 33.48                     | —                                 |
| Chuang Mu Xiang | 33.54                     | —                                 |
| Mang Xiao       | 34.61                     | —                                 |
| Gan Cao         | 35.43                     | —                                 |
| Qiang Huo       | 36.73                     | —                                 |
| Fu Shen         | 37.37                     | —                                 |
| Gou Qi Zi       | 38.03                     | —                                 |
| Ma Huang        | 38.48                     | —                                 |
| Huang Qin       | 39.67                     | —                                 |
| Long Yan Rou    | 41.33                     | —                                 |
| Zi Hua Di Ding  | 43.59                     | —                                 |
| Qing Pi         | 43.72                     | —                                 |
| Zhi Gan Cao     | 44.48                     | —                                 |
| Jing Jie        | 45.67                     | —                                 |
| Huang Lian      | 45.84                     | —                                 |
| Sang Zhi        | 46.03                     | —                                 |
| Du Zhong        | 46.54                     | —                                 |
| Bo He           | 46.94                     | —                                 |
| Huang Bai       | 49.79                     | —                                 |
| Sha Ren         | 50.39                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62659     | 62659                  | 0.00                            | 6.20                               |
| 62660     | 62660                  | 0.00                            | 5.92                               |

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 2.4-2022-02

Validated substance/substance group **Ban Lan Gen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60230-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Ban Lan Gen; Isatidis radix

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ban Lan Gen               | 1      | 0      | 1      |

### Second-stage model

For differentiation of the substance/substance group *Ban Lan 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 *Ban Lan Gen*:

| Supplier  | Substance   | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-------------|--------------|-----------|---------|---------------|
| PhytoComm | Ban Lan Gen | G128HS165TL1 | 62867     | 40      | from supplier |
| PhytoComm | Ban Lan Gen | G128HS165TL1 | 62868     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Lan Gen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 Lan 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 | Ban Lan Gen | G128HS165TL1 | 62867 <sup>†</sup> | 20      |
| PhytoComm | Ban Lan Gen | G128HS165TL1 | 62868 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Ban Lan 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 | Ban Lan Gen | G128H0816421 | 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 *Ban Lan 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 *Ban Lan 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Ban Lan 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ban Lan 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jin Yin Hua     | 6.82                      | —                                 |
| Ze Xie          | 8.54                      | —                                 |
| Tian Hua Fen    | 10.00                     | —                                 |
| Fu Zi           | 10.55                     | —                                 |
| Hou Po          | 11.73                     | —                                 |
| Hong Jing Tian  | 12.14                     | —                                 |
| Ren Dong Teng   | 12.21                     | —                                 |
| Mu Zei          | 12.29                     | —                                 |
| Pi Pa Ye        | 12.57                     | —                                 |
| Dan Dou Chi     | 12.79                     | —                                 |
| Cang Zhu        | 12.91                     | —                                 |
| Ma Huang        | 14.15                     | —                                 |
| Ku Shen         | 14.21                     | —                                 |
| Lian Qiao       | 14.25                     | —                                 |
| Shan Yao        | 14.26                     | —                                 |
| Fu Pen Zi       | 14.51                     | —                                 |
| Dang Gui        | 14.59                     | —                                 |
| Bai Shao Yao    | 14.74                     | —                                 |
| Guang Huo Xiang | 15.22                     | —                                 |
| Jiao Gu Lan     | 15.24                     | —                                 |
| Ren Shen        | 15.51                     | —                                 |
| Ji Xue Teng     | 15.77                     | —                                 |
| Gua Lou         | 16.04                     | —                                 |
| Yan Hu Suo      | 16.67                     | —                                 |
| Lu Gen          | 16.74                     | —                                 |
| Zhe Bei Mu      | 16.83                     | —                                 |
| Jie Geng        | 17.71                     | —                                 |
| He Huan Pi      | 17.97                     | —                                 |
| Lai Fu Zi       | 18.30                     | —                                 |
| Gu Sui Bu       | 18.48                     | —                                 |
| Zhi Gan Cao     | 18.61                     | —                                 |
| Ye Jiao Teng    | 18.65                     | —                                 |
| Gui Zhi         | 18.77                     | —                                 |
| Ji Li           | 19.06                     | —                                 |
| Zhi Ke          | 19.19                     | —                                 |
| Dan Shen        | 19.35                     | —                                 |
| Tao Ren         | 19.39                     | —                                 |
| Ling Zhi        | 19.70                     | —                                 |
| Zi Hua Di Ding  | 19.88                     | —                                 |
| Yin Yang Huo    | 19.89                     | —                                 |
| San Qi          | 20.20                     | —                                 |
| Shen Qu         | 20.27                     | —                                 |
| Suan Zao Ren    | 20.90                     | —                                 |
| Che Qian Zi     | 20.98                     | —                                 |
| Qiang Huo       | 20.99                     | —                                 |
| Gan Cao         | 21.03                     | —                                 |
| Huo Ma Ren      | 21.26                     | —                                 |
| Zhi Mu          | 21.27                     | —                                 |
| Tu Fu Ling      | 21.38                     | —                                 |
| Bai Zi Ren      | 21.57                     | —                                 |
| Rou Gui         | 21.64                     | —                                 |
| Gou Qi Zi       | 21.79                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Gou Teng        | 22.58                     | —                                 |
| Chai Hu         | 22.59                     | —                                 |
| Huang Qin       | 22.71                     | —                                 |
| Long Yan Rou    | 22.74                     | —                                 |
| Ce Bai Ye       | 23.21                     | —                                 |
| Fu Ling         | 23.42                     | —                                 |
| Lian Zi         | 23.48                     | —                                 |
| Ci Wu Jia       | 23.59                     | —                                 |
| Sheng Jiang     | 23.78                     | —                                 |
| Qing Pi         | 24.20                     | —                                 |
| She Gan         | 24.33                     | —                                 |
| Di Gu Pi        | 24.34                     | —                                 |
| Mao Dong Qing   | 24.58                     | —                                 |
| (Fen) Bi Xie    | 24.64                     | —                                 |
| Xie Bai         | 24.70                     | —                                 |
| Bai Xian Pi     | 24.96                     | —                                 |
| Ban Xia (Jiang) | 26.48                     | —                                 |
| Yu Jin          | 26.83                     | —                                 |
| Zhu Ling        | 26.91                     | —                                 |
| Hong Hua        | 27.12                     | —                                 |
| Zhu Ru          | 28.49                     | —                                 |
| Chuang Mu Xiang | 28.52                     | —                                 |
| Huang Lian      | 28.58                     | —                                 |
| Mu Gua          | 28.91                     | —                                 |
| Bo He           | 29.31                     | —                                 |
| Fo Shou         | 29.88                     | —                                 |
| Mang Xiao       | 31.02                     | —                                 |
| Sha Ren         | 31.17                     | —                                 |
| Jing Jie        | 32.15                     | —                                 |
| Chi Shao (Yao)  | 33.17                     | —                                 |
| Sang Zhi        | 33.27                     | —                                 |
| Du Zhong        | 33.43                     | —                                 |
| Huang Bai       | 33.65                     | —                                 |
| Yi Yi Ren       | 33.83                     | —                                 |
| Yuan Zhi        | 34.77                     | —                                 |
| Ma Huang Gen    | 34.79                     | —                                 |
| Fu Xiao Mai     | 34.88                     | —                                 |
| Sang Ye         | 37.91                     | —                                 |
| Cang Er Zi      | 39.04                     | —                                 |
| Fu Shen         | 41.85                     | —                                 |
| Bai Jiang Cao   | 44.01                     | —                                 |
| Qing Hao        | 47.52                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ban Lan 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62867     | 62867               | 0.00                         | 7.81                            |
| 62868     | 62868               | 0.00                         | 6.82                            |

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 2.4-2022-02

Validated substance/substance group **Ban Xia (Jiang)**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60019-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ban Xia (Jiang) | G191HS090SH1 | 62600 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 79            | 1              | 22 360        |
| <b>Type B</b> | 9              | 39            | 1              | 11 348        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Ban Xia (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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 98.7500 % (> 95.0000 %) |
| <b>Type B</b> | 99.9731 % (> 99.9410 %)  | 97.5000 % (> 90.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| Bai Shao Yao  | 4.40                      | —                                 |
| Di Gu Pi      | 5.85                      | —                                 |
| Gui Zhi       | 7.09                      | —                                 |
| Sheng Jiang   | 7.58                      | —                                 |
| Rou Gui       | 8.48                      | —                                 |
| Zhu Ru        | 8.67                      | —                                 |
| He Huan Pi    | 9.17                      | —                                 |
| Fu Xiao Mai   | 9.30                      | —                                 |
| Shen Qu       | 11.10                     | —                                 |
| Ci Wu Jia     | 11.24                     | —                                 |
| Zhe Bei Mu    | 11.90                     | —                                 |
| Ji Xue Teng   | 12.02                     | —                                 |
| Tao Ren       | 12.11                     | —                                 |
| Yi Yi Ren     | 12.50                     | —                                 |
| Gou Teng      | 13.37                     | —                                 |
| Fu Ling       | 14.10                     | —                                 |
| Tian Hua Fen  | 14.50                     | —                                 |
| Bai Zi Ren    | 14.74                     | —                                 |
| Fo Shou       | 14.82                     | —                                 |
| Ji Li         | 15.11                     | —                                 |
| Ye Jiao Teng  | 15.77                     | —                                 |
| Mu Zei        | 16.54                     | —                                 |
| Lian Zi       | 16.67                     | —                                 |
| Huo Ma Ren    | 17.07                     | —                                 |
| Bai Xian Pi   | 18.65                     | —                                 |
| Ling Zhi      | 18.93                     | —                                 |
| Lai Fu Zi     | 19.09                     | —                                 |
| Ma Huang Gen  | 19.70                     | —                                 |
| Pi Pa Ye      | 20.12                     | —                                 |
| Fu Shen       | 20.47                     | —                                 |
| Gu Sui Bu     | 20.67                     | —                                 |
| Lu Gen        | 20.68                     | —                                 |
| Lian Qiao     | 21.69                     | —                                 |
| Yan Hu Suo    | 24.74                     | —                                 |
| Jin Yin Hua   | 24.97                     | —                                 |
| Shan Yao      | 25.86                     | —                                 |
| Zhu Ling      | 26.60                     | —                                 |
| Ren Dong Teng | 26.78                     | —                                 |
| Tu Fu Ling    | 27.62                     | —                                 |
| Yu Jin        | 27.95                     | —                                 |
| Ze Xie        | 28.07                     | —                                 |
| Ren Shen      | 28.62                     | —                                 |
| (Fen) Bi Xie  | 29.48                     | —                                 |
| Zhi Mu        | 29.56                     | —                                 |
| Dang Gui      | 30.25                     | —                                 |
| Huang Qin     | 30.28                     | —                                 |
| Jie Geng      | 31.10                     | —                                 |
| Fu Zi         | 31.14                     | —                                 |
| Fu Pen Zi     | 31.38                     | —                                 |
| Jiao Gu Lan   | 31.62                     | —                                 |
| Zhi Ke        | 31.87                     | —                                 |
| Gua Lou       | 32.83                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dan Dou Chi     | 33.14                     | —                                 |
| Mang Xiao       | 33.26                     | —                                 |
| Dan Shen        | 33.38                     | —                                 |
| Suan Zao Ren    | 33.45                     | —                                 |
| Ce Bai Ye       | 33.61                     | —                                 |
| Cang Zhu        | 34.14                     | —                                 |
| Yin Yang Huo    | 34.41                     | —                                 |
| Hou Po          | 36.07                     | —                                 |
| Ban Lan Gen     | 36.38                     | —                                 |
| San Qi          | 37.63                     | —                                 |
| Ma Huang        | 37.69                     | —                                 |
| Yuan Zhi        | 38.29                     | —                                 |
| She Gan         | 38.36                     | —                                 |
| Gou Qi Zi       | 39.92                     | —                                 |
| Chai Hu         | 40.27                     | —                                 |
| Ku Shen         | 40.54                     | —                                 |
| Mao Dong Qing   | 40.64                     | —                                 |
| Mu Gua          | 41.35                     | —                                 |
| Che Qian Zi     | 43.15                     | —                                 |
| Guang Huo Xiang | 44.11                     | —                                 |
| Qiang Huo       | 44.19                     | —                                 |
| Long Yan Rou    | 45.64                     | —                                 |
| Huang Lian      | 45.99                     | —                                 |
| Gan Cao         | 46.31                     | —                                 |
| Sang Zhi        | 46.99                     | —                                 |
| Hong Jing Tian  | 47.56                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62599     | 62599                  | 0.00                            | 5.07                               |
| 62600     | 62600                  | 0.00                            | 4.40                               |

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 2.4-2022-02

Validated substance/substance group **Ban Zhi Lian**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60038-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ban Zhi Lian | G224H0528821 | 62754 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 39            | 1              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 97.5000 % (> 90.0000 %)  |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Sang Zhi       | 23.14                     | —                                 |
| Fu Ling        | 25.29                     | —                                 |
| Chuan Mu Tong  | 25.52                     | —                                 |
| Mang Xiao      | 25.57                     | —                                 |
| Rou Gui        | 26.02                     | —                                 |
| Bai He         | 26.34                     | —                                 |
| E Zhu          | 27.75                     | —                                 |
| Tian Hua Fen   | 28.82                     | —                                 |
| Bai Xian Pi    | 28.85                     | —                                 |
| Jiang Huang    | 32.28                     | —                                 |
| Sha Shen (Bei) | 32.40                     | —                                 |
| Ji Xue Teng    | 32.43                     | —                                 |
| Shan Yao       | 32.80                     | —                                 |
| Mi Huan Jun    | 33.19                     | —                                 |
| Di Gu Pi       | 33.23                     | —                                 |
| Chuan Lian Zi  | 33.55                     | —                                 |
| Lian Zi        | 34.09                     | —                                 |
| Ye Jiao Teng   | 35.12                     | —                                 |
| Gou Teng       | 35.21                     | —                                 |
| Dang Gui       | 35.46                     | —                                 |
| Bai Shao Yao   | 35.56                     | —                                 |
| Ling Zhi       | 35.56                     | —                                 |
| Chai Hu        | 35.81                     | —                                 |
| Long Dan (Cao) | 35.82                     | —                                 |
| Yi Yi Ren      | 35.98                     | —                                 |
| Gan Jiang      | 36.23                     | —                                 |
| Dan Dou Chi    | 37.87                     | —                                 |
| (Bai) Dou Kou  | 38.82                     | —                                 |
| Fo Shou        | 38.85                     | —                                 |
| He Huan Pi     | 38.98                     | —                                 |
| Tu Fu Ling     | 39.25                     | —                                 |
| Mao Dong Qing  | 39.42                     | —                                 |
| Jie Geng       | 39.57                     | —                                 |
| Zhi Ke         | 39.67                     | —                                 |
| Du Zhong       | 39.94                     | —                                 |
| Shen Qu        | 40.29                     | —                                 |
| Ma Huang Gen   | 40.79                     | —                                 |
| Ren Dong Teng  | 40.98                     | —                                 |
| Zi Hua Di Ding | 41.22                     | —                                 |
| Bo He          | 41.29                     | —                                 |
| Lai Fu Zi      | 41.46                     | —                                 |
| Ji Li          | 41.93                     | —                                 |
| Huang Lian     | 42.43                     | —                                 |
| Sheng Jiang    | 42.62                     | —                                 |
| Qin Jiao       | 42.62                     | —                                 |
| Yu Jin         | 43.14                     | —                                 |
| Zhu Ling       | 43.29                     | —                                 |
| Qiang Huo      | 43.91                     | —                                 |
| Bai Zhu        | 44.06                     | —                                 |
| Da Zao         | 44.07                     | —                                 |
| Sha Ren        | 44.54                     | —                                 |
| Huang Qi       | 44.85                     | —                                 |

*continued on the next page*

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| Substanz    | Distance in<br>main model | Distance in<br>second-stage model |
|-------------|---------------------------|-----------------------------------|
| Jin Yin Hua | 46.37                     | —                                 |
| Zhu Ru      | 46.57                     | —                                 |
| Cang Er Zi  | 46.73                     | —                                 |
| Gui Zhi     | 48.08                     | —                                 |
| Zi Su Zi    | 48.80                     | —                                 |
| Fu Shen     | 49.24                     | —                                 |
| Yan Hu Suo  | 49.55                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62753     | 62753                  | 0.00                            | 23.14                              |
| 62754     | 62754                  | 0.00                            | 23.54                              |

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



# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Bing Lang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60186-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Bing Lang; Arecae catechu semen

### Special notes

When selecting the *Bing Lang* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bing Lang                 | 1      | 0      | 0      |

### Second-stage model

For differentiation of the substance/substance group *Bing Lang* 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 *Bing Lang*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Bing Lang | G027H1825021 | 63009     | 40      | from supplier |
| PhytoComm | Bing Lang | G027H1825021 | 63010     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Bing Lang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Bing Lang*.
- 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 | Bing Lang | G027H1825021 | 63009 <sup>†</sup> | 20      |
| PhytoComm | Bing Lang | G027H1825021 | 63010 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 *Bing Lang*.
- 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 *Bing Lang* 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 *Bing Lang* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 0              | 857           |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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 *Bing Lang* 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.

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

| Substance      | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Huang Qi       | 22.53                     | —                                 |
| Mang Xiao      | 25.89                     | —                                 |
| Dang Gui       | 27.97                     | —                                 |
| Sang Zhi       | 31.78                     | —                                 |
| Bai Zhi        | 32.36                     | —                                 |
| Chuan Niu Xi   | 32.90                     | —                                 |
| (Huai) Niu Xi  | 33.54                     | —                                 |
| Qin Jiao       | 35.90                     | —                                 |
| Da Zao         | 37.29                     | —                                 |
| Jie Geng       | 38.29                     | —                                 |
| Sha Shen (Bei) | 39.04                     | —                                 |
| Chen Pi        | 39.44                     | —                                 |
| Chi Shao (Yao) | 39.82                     | —                                 |
| Long Dan (Cao) | 39.96                     | —                                 |
| Tian Hua Fen   | 40.75                     | —                                 |
| Shan Yu Rou    | 40.86                     | —                                 |
| Ju Hua         | 41.13                     | —                                 |
| Mu Dan Pi      | 41.35                     | —                                 |
| Bai Zhu        | 41.88                     | —                                 |
| (Shi) Chang Pu | 42.67                     | —                                 |
| Du Huo         | 42.90                     | —                                 |
| Zhi Gan Cao    | 44.24                     | —                                 |
| Zi Su Zi       | 44.29                     | —                                 |
| He Huan Pi     | 44.59                     | —                                 |
| Fang Feng      | 45.11                     | —                                 |
| Di Gu Pi       | 45.64                     | —                                 |
| Chuan Lian Zi  | 45.76                     | —                                 |
| Mu Gua         | 46.92                     | —                                 |
| Lian Qiao      | 47.19                     | —                                 |
| E Zhu          | 49.15                     | —                                 |
| Zhi Ke         | 49.20                     | —                                 |
| Shan Yao       | 49.38                     | —                                 |
| Sha Ren        | 49.45                     | —                                 |
| Gu Sui Bu      | 49.53                     | —                                 |
| Mi Huan Jun    | 50.15                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Bing Lang* 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 63009     | 63009                  | 0.00                            | 22.86                              |
| 63010     | 63010                  | 0.00                            | 22.53                              |

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 2.4-2022-02

Validated substance/substance group **Bo He**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60073-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Bo He; Menthae haplocalysis herba

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bo He                     | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Bo 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 *Bo He*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Bo He     | G158HS332TH1 | 62863     | 40      | from supplier |
| PhytoComm | Bo He     | G158HS332TH1 | 62864     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Bo He*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Bo 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 | Bo He     | G158HS332TH1 | 62863 <sup>†</sup> | 20      |
| PhytoComm | Bo He     | G158HS332TH1 | 62864 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Bo 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 | Bo He     | g158h1712022 | 1       |
| PhytoComm | Bo He     | G158H1712121 | 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 *Bo 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 *Bo 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 34            | 6              | 11 357        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Bo 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 85.0000 % (> 77.5000 %)  |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bo 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Chai Hu         | 5.00                      | —                                 |
| Sha Ren         | 6.03                      | —                                 |
| Fu Zi           | 8.02                      | —                                 |
| Zi Hua Di Ding  | 9.22                      | —                                 |
| Du Zhong        | 9.26                      | —                                 |
| Dan Shen        | 9.73                      | —                                 |
| Qiang Huo       | 9.78                      | —                                 |
| Bai Jiang Cao   | 10.81                     | —                                 |
| Yu Jin          | 10.96                     | —                                 |
| Jing Jie        | 11.02                     | —                                 |
| Mao Dong Qing   | 11.22                     | —                                 |
| Qing Hao        | 11.30                     | —                                 |
| Jiao Gu Lan     | 12.09                     | —                                 |
| Hou Po          | 12.10                     | —                                 |
| Huang Bai       | 12.68                     | —                                 |
| Yin Yang Huo    | 14.07                     | —                                 |
| Bai Xian Pi     | 14.22                     | —                                 |
| Ce Bai Ye       | 14.37                     | —                                 |
| Shan Yao        | 14.56                     | —                                 |
| Dan Dou Chi     | 14.85                     | —                                 |
| Fu Pen Zi       | 14.97                     | —                                 |
| Huang Lian      | 15.95                     | —                                 |
| Ye Jiao Teng    | 15.95                     | —                                 |
| Jin Yin Hua     | 16.52                     | —                                 |
| Che Qian Zi     | 16.61                     | —                                 |
| Qing Pi         | 17.09                     | —                                 |
| Pi Pa Ye        | 17.60                     | —                                 |
| Yan Hu Suo      | 17.72                     | —                                 |
| Zhi Ke          | 17.89                     | —                                 |
| Ji Xue Teng     | 18.26                     | —                                 |
| Ling Zhi        | 18.36                     | —                                 |
| Hong Jing Tian  | 18.43                     | —                                 |
| Pu Gong Ying    | 19.10                     | —                                 |
| Tu Fu Ling      | 19.24                     | —                                 |
| Tian Hua Fen    | 19.31                     | —                                 |
| Shen Qu         | 19.98                     | —                                 |
| Gu Sui Bu       | 20.10                     | —                                 |
| Ma Huang        | 20.35                     | —                                 |
| Guang Huo Xiang | 20.73                     | —                                 |
| Lian Zi         | 20.90                     | —                                 |
| Ren Dong Teng   | 20.99                     | —                                 |
| Bai Shao Yao    | 22.32                     | —                                 |
| Di Gu Pi        | 22.57                     | —                                 |
| Gan Cao         | 23.50                     | —                                 |
| Ji Li           | 23.86                     | —                                 |
| Suan Zao Ren    | 24.35                     | —                                 |
| Ze Lan          | 24.40                     | —                                 |
| (Fen) Bi Xie    | 25.78                     | —                                 |
| Zhu Ling        | 26.05                     | —                                 |
| Ban Lan Gen     | 26.30                     | —                                 |
| He Huan Pi      | 26.63                     | —                                 |
| Ren Shen        | 26.75                     | —                                 |

continued on the next page



continued from previous page

| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Sang Ye             | 27.75                     | —                                 |
| Lian Qiao           | 28.42                     | —                                 |
| Hong Hua            | 28.56                     | —                                 |
| She Gan             | 28.75                     | —                                 |
| Chuang Mu Xiang     | 28.95                     | —                                 |
| Gou Teng            | 29.14                     | —                                 |
| Zhi Gan Cao         | 29.52                     | —                                 |
| Lu Gen              | 29.76                     | —                                 |
| Mu Zei              | 30.52                     | —                                 |
| Xi Xian Cao         | 30.66                     | —                                 |
| Mang Xiao           | 30.71                     | —                                 |
| Ma Huang Gen        | 30.91                     | —                                 |
| Cang Zhu            | 31.09                     | —                                 |
| Rou Gui             | 32.01                     | —                                 |
| Chi Shao (Yao)      | 32.77                     | —                                 |
| Zhe Bei Mu          | 33.67                     | —                                 |
| Cang Er Zi          | 34.32                     | —                                 |
| Sheng Jiang         | 34.48                     | —                                 |
| Huo Ma Ren          | 35.40                     | —                                 |
| Jie Geng            | 36.54                     | —                                 |
| Ban Zhi Lian        | 37.02                     | —                                 |
| Fu Ling             | 37.93                     | —                                 |
| Tao Ren             | 38.09                     | —                                 |
| Nü Zhen Zi          | 38.09                     | —                                 |
| Sang Zhi            | 38.29                     | —                                 |
| Huang Qin           | 38.64                     | —                                 |
| Jiang Huang         | 39.25                     | —                                 |
| E Zhu               | 39.58                     | —                                 |
| Gui Zhi             | 40.14                     | —                                 |
| Zhi Shi             | 40.67                     | —                                 |
| Yi Yi Ren           | 41.11                     | —                                 |
| Xie Bai             | 42.44                     | —                                 |
| Yi Mu Cao           | 43.64                     | —                                 |
| Sha Shen (Bei)      | 43.71                     | —                                 |
| Ze Xie              | 44.51                     | —                                 |
| Zi Su Zi            | 44.58                     | —                                 |
| Dang Gui            | 44.75                     | —                                 |
| Ci Wu Jia           | 44.92                     | —                                 |
| Ban Xia (Jiang)     | 45.32                     | —                                 |
| Xin Yi              | 45.67                     | —                                 |
| Long Yan Rou        | 45.78                     | —                                 |
| Niu Bang Zi         | 46.51                     | —                                 |
| Yin Chen Hao        | 47.03                     | —                                 |
| Bai Zi Ren          | 47.19                     | —                                 |
| Ku Shen             | 47.33                     | —                                 |
| San Qi              | 48.11                     | —                                 |
| Fu Shen             | 48.20                     | —                                 |
| Fo Shou             | 48.58                     | —                                 |
| Zhu Ru              | 49.16                     | —                                 |
| Huang Qi            | 49.56                     | —                                 |
| Gua Lou             | 49.64                     | —                                 |
| Chuan Mu Tong       | 49.91                     | —                                 |
| Bai Hua She She Cao | 50.02                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Bo 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62863     | 62863               | 0.00                         | 5.95                            |
| 62864     | 62864               | 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 2.4-2022-02

Validated substance/substance group **Bu Gu Zhi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60023-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Bu Gu Zhi                 | 2      | 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 |
| PhytoComm | Bu Gu Zhi | G205H1247922 | 62851     | 40      | from supplier |
| PhytoComm | Bu Gu Zhi | G205H1247922 | 62852     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Bu Gu Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Bu Gu Zhi | G205H1247822 | 62488 <sup>†</sup> | 20      |
| PhytoComm | Bu Gu Zhi | G205H1247922 | 62851 <sup>†</sup> | 20      |
| PhytoComm | Bu Gu Zhi | G205H1247922 | 62852 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | 1       |
| Phytocomm | Bu Gu Zhi | G205H1247222 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Tu Si Zi         | 11.52                     | —                                 |
| Gu Sui Bu        | 21.18                     | —                                 |
| Jing Jie         | 21.60                     | —                                 |
| Dan Zhu Ye       | 21.61                     | —                                 |
| Sha Ren          | 22.98                     | —                                 |
| Yu Xing Cao      | 23.50                     | —                                 |
| Wu Yao           | 25.70                     | —                                 |
| Yin Chen Hao     | 25.75                     | —                                 |
| Mang Xiao        | 25.93                     | —                                 |
| Sang Bai Pi      | 26.58                     | —                                 |
| Wu Zhu Yu        | 28.50                     | —                                 |
| Sang Ji Shend    | 28.94                     | —                                 |
| He Huan Pi       | 29.85                     | —                                 |
| He Shou Wu       | 30.23                     | —                                 |
| Xuan Fu Hua      | 33.22                     | —                                 |
| Wu Jia Pi        | 33.36                     | —                                 |
| (Bai) Dou Kou    | 34.17                     | —                                 |
| Xian Mao         | 35.24                     | —                                 |
| Chen Pi          | 35.52                     | —                                 |
| Jiang Huang      | 37.63                     | —                                 |
| Jin Qian Cao     | 39.19                     | —                                 |
| Ge Gen           | 39.91                     | —                                 |
| (Sheng) Di Huang | 43.84                     | —                                 |
| (Shi) Chang Pu   | 44.38                     | —                                 |
| Shan Yao         | 44.85                     | —                                 |
| Du Zhong         | 46.51                     | —                                 |
| E Zhu            | 47.13                     | —                                 |
| Hua Shi          | 47.96                     | —                                 |
| Nü Zhen Zi       | 48.02                     | —                                 |

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                         | 21.61                           |
| 62488     | 62488               | 0.00                         | 21.60                           |
| 62851     | 62851               | 0.00                         | 11.52                           |
| 62852     | 62852               | 0.00                         | 11.83                           |

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





# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Cang Er Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60054-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Cang Er Zi | G251H1401821 | 62504 <sup>†</sup> | 20      |
| PhytoComm | Cang Er Zi | G251H1401921 | 62755 <sup>†</sup> | 20      |
| PhytoComm | Cang Er Zi | G251H1401921 | 62756 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G251H1401322 | 1       |
| Phytocomm | Cang Er Zi | G251H1401521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Zi Su Zi       | 10.30                     | —                                 |
| Shan Yao       | 11.28                     | —                                 |
| Gan Jiang      | 14.77                     | —                                 |
| E Zhu          | 16.42                     | —                                 |
| Suan Zao Ren   | 17.99                     | —                                 |
| Sha Shen (Bei) | 21.14                     | —                                 |
| Niu Bang Zi    | 21.88                     | —                                 |
| Sang Zhi       | 22.10                     | —                                 |
| Zi Hua Di Ding | 23.46                     | —                                 |
| Jiang Huang    | 24.69                     | —                                 |
| Jin Yin Hua    | 24.77                     | —                                 |
| Di Gu Pi       | 25.32                     | —                                 |
| Mang Xiao      | 26.06                     | —                                 |
| Chuan Lian Zi  | 26.18                     | —                                 |
| Qing Pi        | 27.80                     | —                                 |
| Yi Mu Cao      | 28.29                     | —                                 |
| Lai Fu Zi      | 29.26                     | —                                 |
| Jie Geng       | 29.78                     | —                                 |
| (Huai) Niu Xi  | 30.05                     | —                                 |
| Tian Hua Fen   | 30.07                     | —                                 |
| Sha Ren        | 30.29                     | —                                 |
| Zhi Ke         | 30.43                     | —                                 |
| Ku Shen        | 30.61                     | —                                 |
| Chen Pi        | 30.72                     | —                                 |
| Yan Hu Suo     | 30.78                     | —                                 |
| Qiang Huo      | 30.82                     | —                                 |
| Jiao Gu Lan    | 31.20                     | —                                 |
| (Bai) Dou Kou  | 31.95                     | —                                 |
| Sang Ye        | 32.41                     | —                                 |
| Du Zhong       | 32.99                     | —                                 |
| Huang Bai      | 33.08                     | —                                 |
| Hou Po         | 33.40                     | —                                 |
| Lian Qiao      | 33.49                     | —                                 |
| Wu Wei Zi      | 33.85                     | —                                 |
| Ze Lan         | 33.99                     | —                                 |
| Xiang Fu       | 34.03                     | —                                 |
| Huang Lian     | 34.42                     | —                                 |
| Gan Cao        | 34.45                     | —                                 |
| Mao Dong Qing  | 34.85                     | —                                 |
| Pu Gong Ying   | 35.15                     | —                                 |
| Ce Bai Ye      | 35.33                     | —                                 |
| Long Dan (Cao) | 35.62                     | —                                 |
| Dan Dou Chi    | 35.98                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Dang Gui            | 36.25                     | —                                 |
| Fu Zi               | 36.34                     | —                                 |
| Shen Qu             | 37.21                     | —                                 |
| He Huan Pi          | 37.75                     | —                                 |
| Chi Shao (Yao)      | 38.11                     | —                                 |
| Xi Xian Cao         | 38.26                     | —                                 |
| Dong Gua Zi         | 38.58                     | —                                 |
| Chuan Mu Tong       | 39.21                     | —                                 |
| Huang Qi            | 39.52                     | —                                 |
| Dan Shen            | 39.56                     | —                                 |
| Tu Fu Ling          | 39.93                     | —                                 |
| Bo He               | 40.40                     | —                                 |
| Mi Huan Jun         | 40.81                     | —                                 |
| Ji Li               | 41.16                     | —                                 |
| Nü Zhen Zi          | 41.17                     | —                                 |
| Xiao Hui Xiang      | 41.23                     | —                                 |
| Ren Dong Teng       | 42.21                     | —                                 |
| Zhe Bei Mu          | 42.33                     | —                                 |
| Qing Hao            | 42.39                     | —                                 |
| Xin Yi              | 42.44                     | —                                 |
| Hong Jing Tian      | 42.64                     | —                                 |
| Bai Zhu             | 43.00                     | —                                 |
| Ye Jiao Teng        | 43.15                     | —                                 |
| Xie Bai             | 43.30                     | —                                 |
| Jing Jie            | 43.47                     | —                                 |
| Yu Jin              | 43.60                     | —                                 |
| Bai Xian Pi         | 43.71                     | —                                 |
| Fu Ling             | 43.84                     | —                                 |
| Lian Zi             | 44.01                     | —                                 |
| Wang Bu Liu Xing    | 44.16                     | —                                 |
| (Fen) Bi Xie        | 44.64                     | —                                 |
| Chai Hu             | 44.93                     | —                                 |
| Bai Hua She She Cao | 44.96                     | —                                 |
| Yuan Zhi            | 44.99                     | —                                 |
| Chuan Niu Xi        | 45.05                     | —                                 |
| Du Huo              | 45.11                     | —                                 |
| Zhi Shi             | 45.39                     | —                                 |
| Yin Yang Huo        | 45.40                     | —                                 |
| Bai Jiang Cao       | 45.51                     | —                                 |
| Che Qian Zi         | 45.53                     | —                                 |
| Chuang Mu Xiang     | 46.06                     | —                                 |
| (Shi) Chang Pu      | 46.31                     | —                                 |
| Ling Zhi            | 46.33                     | —                                 |
| Da Zao              | 46.36                     | —                                 |
| Hong Hua            | 46.53                     | —                                 |
| Bai He              | 46.70                     | —                                 |
| Zhi Gan Cao         | 47.44                     | —                                 |
| Gou Qi Zi           | 47.56                     | —                                 |
| Fu Pen Zi           | 48.09                     | —                                 |
| Ban Zhi Lian        | 48.89                     | —                                 |
| Ban Lan Gen         | 49.16                     | —                                 |
| Ma Huang            | 49.61                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62503     | 62503               | 0.00                         | 11.28                           |
| 62504     | 62504               | 0.00                         | 11.31                           |
| 62755     | 62755               | 0.00                         | 10.30                           |
| 62756     | 62756               | 0.00                         | 10.44                           |

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 2.4-2022-02

Validated substance/substance group **Cang Zhu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60160-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | G042HS301TG1 | 62977     | 40      | from supplier |
| PhytoComm | Cang Zhu  | G042HS301TG1 | 62978     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G042HS301TG1 | 62977 <sup>†</sup> | 20      |
| PhytoComm | Cang Zhu  | G042HS301TG1 | 62978 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 3              | 40            | 0              | 11 354        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

The substance/substance group *Cang 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9851 % (> 99.9531 %)  | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dang Gui        | 6.00                      | —                                 |
| Jie Geng        | 8.97                      | —                                 |
| Pi Pa Ye        | 12.00                     | —                                 |
| San Qi          | 13.26                     | —                                 |
| Jin Yin Hua     | 13.77                     | —                                 |
| Bai Shao Yao    | 13.96                     | —                                 |
| Gou Qi Zi       | 14.14                     | —                                 |
| Gua Lou         | 14.52                     | —                                 |
| Tian Hua Fen    | 14.79                     | —                                 |
| Zhe Bei Mu      | 14.91                     | —                                 |
| Mu Gua          | 15.18                     | —                                 |
| Long Yan Rou    | 15.52                     | —                                 |
| Zhi Mu          | 15.64                     | —                                 |
| Mu Zei          | 16.07                     | —                                 |
| Chuang Mu Xiang | 16.48                     | —                                 |
| Xie Bai         | 16.48                     | —                                 |
| Ren Dong Teng   | 16.53                     | —                                 |
| Lian Qiao       | 17.08                     | —                                 |
| Ban Lan Gen     | 17.61                     | —                                 |
| Di Gu Pi        | 17.64                     | —                                 |
| Ye Jiao Teng    | 17.83                     | —                                 |
| Ze Xie          | 18.05                     | —                                 |
| Shan Yao        | 18.25                     | —                                 |
| Lai Fu Zi       | 18.27                     | —                                 |
| Dan Dou Chi     | 18.29                     | —                                 |
| Shen Qu         | 18.38                     | —                                 |
| Ren Shen        | 18.51                     | —                                 |
| Ku Shen         | 19.24                     | —                                 |
| Hong Jing Tian  | 19.51                     | —                                 |
| Lian Zi         | 19.59                     | —                                 |
| He Huan Pi      | 19.91                     | —                                 |
| Jiao Gu Lan     | 19.93                     | —                                 |
| Zhi Ke          | 20.04                     | —                                 |
| Fo Shou         | 20.55                     | —                                 |
| Ling Zhi        | 20.56                     | —                                 |
| Yuan Zhi        | 20.93                     | —                                 |
| Bai Zi Ren      | 21.08                     | —                                 |
| Ji Li           | 21.80                     | —                                 |
| Suan Zao Ren    | 22.18                     | —                                 |
| Ci Wu Jia       | 22.55                     | —                                 |
| Tao Ren         | 23.05                     | —                                 |
| Hou Po          | 23.24                     | —                                 |
| Fu Pen Zi       | 23.65                     | —                                 |
| Ma Huang        | 24.14                     | —                                 |
| Lu Gen          | 24.15                     | —                                 |
| Sheng Jiang     | 24.23                     | —                                 |
| Guang Huo Xiang | 24.25                     | —                                 |
| Gu Sui Bu       | 24.42                     | —                                 |
| Gou Teng        | 24.54                     | —                                 |
| Dan Shen        | 24.83                     | —                                 |
| Rou Gui         | 25.19                     | —                                 |
| Fu Zi           | 25.50                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Gan Cao         | 25.90                     | —                                 |
| Huo Ma Ren      | 26.38                     | —                                 |
| Tu Fu Ling      | 26.63                     | —                                 |
| Zhu Ru          | 26.71                     | —                                 |
| Ji Xue Teng     | 26.77                     | —                                 |
| Huang Qin       | 27.88                     | —                                 |
| Gui Zhi         | 27.98                     | —                                 |
| Fu Ling         | 28.37                     | —                                 |
| Bai Xian Pi     | 29.48                     | —                                 |
| Mao Dong Qing   | 29.66                     | —                                 |
| Yin Yang Huo    | 29.88                     | —                                 |
| Chai Hu         | 30.60                     | —                                 |
| Ban Xia (Jiang) | 31.18                     | —                                 |
| Mang Xiao       | 31.47                     | —                                 |
| Che Qian Zi     | 31.74                     | —                                 |
| Yan Hu Suo      | 33.02                     | —                                 |
| She Gan         | 33.48                     | —                                 |
| Zi Hua Di Ding  | 34.03                     | —                                 |
| Fu Xiao Mai     | 34.85                     | —                                 |
| Ce Bai Ye       | 36.12                     | —                                 |
| Yi Yi Ren       | 36.18                     | —                                 |
| Qiang Huo       | 36.34                     | —                                 |
| Sang Zhi        | 36.37                     | —                                 |
| Ma Huang Gen    | 36.53                     | —                                 |
| Zhi Gan Cao     | 36.83                     | —                                 |
| (Fen) Bi Xie    | 37.23                     | —                                 |
| Yu Jin          | 38.74                     | —                                 |
| Chi Shao (Yao)  | 38.80                     | —                                 |
| Hong Hua        | 39.15                     | —                                 |
| Qing Pi         | 40.48                     | —                                 |
| Bo He           | 40.87                     | —                                 |
| Zhu Ling        | 41.69                     | —                                 |
| Fu Shen         | 43.16                     | —                                 |
| Huang Bai       | 44.38                     | —                                 |
| Cang Er Zi      | 44.50                     | —                                 |
| Huang Lian      | 44.91                     | —                                 |
| Sha Ren         | 45.00                     | —                                 |
| Jing Jie        | 45.05                     | —                                 |
| Huang Qi        | 48.94                     | —                                 |
| Chuan Lian Zi   | 49.01                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62977     | 62977               | 0.00                         | 8.29                            |
| 62978     | 62978               | 0.00                         | 6.00                            |

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 2.4-2022-02

Validated substance/substance group **Ce Bai Ye**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60313-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Ce Bai Ye; Biotae orientalis cacumen

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ce Bai Ye                 | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Ce Bai 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 *Ce Bai Ye*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Ce Bai Ye | G050HS245TG1 | 62925     | 40      | from supplier |
| PhytoComm | Ce Bai Ye | G050HS245TG1 | 62926     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Ce Bai Ye*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ce Bai 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 | Ce Bai Ye | G050HS245TG1 | 62925 <sup>†</sup> | 20      |
| PhytoComm | Ce Bai Ye | G050HS245TG1 | 62926 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 3 batches from the substance/substance group *Ce Bai 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 | Ce Bai Ye | g050h0975321 | 2       |
| Phytocomm | Ce Bai Ye | G050H0975321 | 1       |
| Phytocomm | Ce Bai Ye | G050HS245    | 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 *Ce Bai 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 *Ce Bai 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 6              | 79            | 1              | 22 354        |
| <b>Type B</b> | 12             | 36            | 4              | 11 345        |
| <b>Type C</b> | 0              | 0             | 4              | 853           |

The substance/substance group *Ce Bai 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9777 % (> 99.9614 %)  | 98.7500 % (> 95.0000 %) |
| <b>Type B</b> | 99.9107 % (> 99.8787 %)  | 90.0000 % (> 82.5000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ce Bai 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dan Dou Chi     | 2.59                      | —                                 |
| Bai Xian Pi     | 5.26                      | —                                 |
| Guang Huo Xiang | 5.33                      | —                                 |
| Ling Zhi        | 6.25                      | —                                 |
| Ren Dong Teng   | 7.48                      | —                                 |
| Lian Zi         | 7.94                      | —                                 |
| Mao Dong Qing   | 7.98                      | —                                 |
| Tu Fu Ling      | 8.59                      | —                                 |
| Chai Hu         | 8.82                      | —                                 |
| Shen Qu         | 8.92                      | —                                 |
| Zhu Ling        | 10.34                     | —                                 |
| Yin Yang Huo    | 10.47                     | —                                 |
| Hou Po          | 10.57                     | —                                 |
| Yu Jin          | 10.62                     | —                                 |
| (Fen) Bi Xie    | 11.15                     | —                                 |
| Ji Li           | 11.53                     | —                                 |
| Jing Jie        | 11.86                     | —                                 |
| Suan Zao Ren    | 12.14                     | —                                 |
| Gu Sui Bu       | 12.32                     | —                                 |
| Ye Jiao Teng    | 12.38                     | —                                 |
| She Gan         | 12.66                     | —                                 |
| Che Qian Zi     | 12.67                     | —                                 |
| Qiang Huo       | 13.33                     | —                                 |
| Shan Yao        | 13.76                     | —                                 |
| Dan Shen        | 14.01                     | —                                 |
| Bai Shao Yao    | 14.87                     | —                                 |
| Fu Pen Zi       | 15.00                     | —                                 |
| He Huan Pi      | 15.08                     | —                                 |
| Huo Ma Ren      | 15.91                     | —                                 |
| Rou Gui         | 16.00                     | —                                 |
| Pi Pa Ye        | 16.23                     | —                                 |
| Fu Ling         | 16.30                     | —                                 |
| Zi Hua Di Ding  | 16.35                     | —                                 |
| Lian Qiao       | 16.47                     | —                                 |
| Sheng Jiang     | 16.51                     | —                                 |
| Lu Gen          | 16.99                     | —                                 |
| Gou Teng        | 17.00                     | —                                 |
| Fu Zi           | 17.14                     | —                                 |
| Gan Cao         | 17.46                     | —                                 |
| Gui Zhi         | 17.79                     | —                                 |
| Jin Yin Hua     | 18.11                     | —                                 |
| Yan Hu Suo      | 18.20                     | —                                 |
| Ji Xue Teng     | 19.81                     | —                                 |
| Tian Hua Fen    | 19.88                     | —                                 |
| Jiao Gu Lan     | 19.95                     | —                                 |
| Ma Huang Gen    | 20.14                     | —                                 |
| Hong Jing Tian  | 20.33                     | —                                 |
| Sha Ren         | 20.35                     | —                                 |
| Ban Lan Gen     | 20.38                     | —                                 |
| Yi Yi Ren       | 20.79                     | —                                 |
| Zhe Bei Mu      | 20.91                     | —                                 |
| Bo He           | 21.32                     | —                                 |

*continued on the next page*



continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mu Zei          | 21.42                     | —                                 |
| Tao Ren         | 21.99                     | —                                 |
| Di Gu Pi        | 22.61                     | —                                 |
| Ma Huang        | 22.85                     | —                                 |
| Qing Pi         | 24.55                     | —                                 |
| Ci Wu Jia       | 24.62                     | —                                 |
| Zhi Gan Cao     | 24.65                     | —                                 |
| Fo Shou         | 24.95                     | —                                 |
| Du Zhong        | 25.06                     | —                                 |
| Huang Bai       | 25.20                     | —                                 |
| Fu Xiao Mai     | 25.51                     | —                                 |
| Bai Zi Ren      | 26.13                     | —                                 |
| Chuang Mu Xiang | 26.68                     | —                                 |
| Zhu Ru          | 27.26                     | —                                 |
| Ban Xia (Jiang) | 27.88                     | —                                 |
| Zhi Ke          | 28.02                     | —                                 |
| Huang Lian      | 28.68                     | —                                 |
| Cang Zhu        | 28.68                     | —                                 |
| Ze Xie          | 28.70                     | —                                 |
| Ren Shen        | 29.52                     | —                                 |
| Mang Xiao       | 32.78                     | —                                 |
| Sang Zhi        | 33.40                     | —                                 |
| San Qi          | 34.56                     | —                                 |
| Dang Gui        | 34.90                     | —                                 |
| Bai Jiang Cao   | 35.54                     | —                                 |
| Gua Lou         | 35.69                     | —                                 |
| Xie Bai         | 36.18                     | —                                 |
| Fu Shen         | 36.38                     | —                                 |
| Jie Geng        | 36.44                     | —                                 |
| Chi Shao (Yao)  | 36.60                     | —                                 |
| Lai Fu Zi       | 36.73                     | —                                 |
| Long Yan Rou    | 38.08                     | —                                 |
| Qing Hao        | 38.31                     | —                                 |
| Huang Qin       | 38.83                     | —                                 |
| Hong Hua        | 41.81                     | —                                 |
| Bai Zhu         | 44.34                     | —                                 |
| Ban Zhi Lian    | 44.81                     | —                                 |
| Cang Er Zi      | 45.25                     | —                                 |
| Ku Shen         | 46.37                     | —                                 |
| Gou Qi Zi       | 46.50                     | —                                 |
| Pu Gong Ying    | 47.14                     | —                                 |
| Zhi Mu          | 48.93                     | —                                 |
| Ze Lan          | 50.09                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ce Bai 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62925     | 62925               | 0.00                         | 2.59                            |
| 62926     | 62926               | 0.00                         | 2.64                            |

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 2.4-2022-02

Validated substance/substance group **Chai Hu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60010-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Chai Hu                   | 2      | 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 |
| PhytoComm | Chai Hu   | G055HS233TG1 | 62905     | 40      | from supplier |
| PhytoComm | Chai Hu   | G055HS233TG1 | 62906     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Chai Hu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Chai Hu   | G055HS233SK1 | 62662 <sup>†</sup> | 20      |
| PhytoComm | Chai Hu   | G055HS233TG1 | 62905 <sup>†</sup> | 20      |
| PhytoComm | Chai Hu   | G055HS233TG1 | 62906 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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   | G055H1055322 | 1       |
| Phytocomm | Chai Hu   | G055H1055422 | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 159           | 1              | 22 279        |
| <b>Type B</b> | 5              | 76            | 4              | 11 312        |
| <b>Type C</b> | 0              | 0             | 8              | 849           |

The substance/substance group *Chai Hu* 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9975 % (> 99.9812 %)  | 99.3750 % (> 97.5000 %) |
| <b>Type B</b> | 99.9256 % (> 99.8934 %)  | 95.0000 % (> 91.2500 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jing Jie        | 4.82                      | —                                 |
| Ji Li           | 5.68                      | —                                 |
| Bo He           | 6.05                      | —                                 |
| Mao Dong Qing   | 6.41                      | —                                 |
| Qiang Huo       | 6.64                      | —                                 |
| Zi Hua Di Ding  | 7.04                      | —                                 |
| Sha Ren         | 7.28                      | —                                 |
| Ling Zhi        | 7.47                      | —                                 |
| Hou Po          | 7.68                      | —                                 |
| Yin Yang Huo    | 7.77                      | —                                 |
| Yu Jin          | 7.80                      | —                                 |
| Bai Xian Pi     | 8.11                      | —                                 |
| Shen Qu         | 8.53                      | —                                 |
| Fu Zi           | 8.74                      | —                                 |
| Dan Dou Chi     | 8.78                      | —                                 |
| Ce Bai Ye       | 9.34                      | —                                 |
| Lian Zi         | 9.76                      | —                                 |
| Du Zhong        | 9.88                      | —                                 |
| Guang Huo Xiang | 9.91                      | —                                 |
| Lian Qiao       | 11.49                     | —                                 |
| Shan Yao        | 11.57                     | —                                 |
| Tu Fu Ling      | 11.85                     | —                                 |
| Che Qian Zi     | 12.04                     | —                                 |
| Ye Jiao Teng    | 12.28                     | —                                 |
| Ren Dong Teng   | 12.77                     | —                                 |
| Fu Pen Zi       | 13.32                     | —                                 |
| Dan Shen        | 13.36                     | —                                 |
| Huang Bai       | 13.48                     | —                                 |
| Pi Pa Ye        | 13.65                     | —                                 |
| Yan Hu Suo      | 14.27                     | —                                 |
| Gu Sui Bu       | 14.41                     | —                                 |
| Qing Hao        | 14.68                     | —                                 |
| Jiao Gu Lan     | 15.26                     | —                                 |
| Tian Hua Fen    | 15.29                     | —                                 |
| Suan Zao Ren    | 15.46                     | —                                 |
| Bai Shao Yao    | 15.47                     | —                                 |
| Zhu Ling        | 15.65                     | —                                 |
| Fu Ling         | 15.88                     | —                                 |
| Qing Pi         | 15.98                     | —                                 |
| Bai Jiang Cao   | 16.16                     | —                                 |
| Hong Jing Tian  | 16.59                     | —                                 |
| He Huan Pi      | 16.70                     | —                                 |
| Jin Yin Hua     | 16.97                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| She Gan         | 17.14                             | —                                         |
| Sheng Jiang     | 17.71                             | —                                         |
| Ban Lan Gen     | 17.89                             | —                                         |
| Ji Xue Teng     | 18.20                             | —                                         |
| Ma Huang        | 18.22                             | —                                         |
| (Fen) Bi Xie    | 18.61                             | —                                         |
| Gan Cao         | 18.90                             | —                                         |
| Zhe Bei Mu      | 19.02                             | —                                         |
| Huang Lian      | 19.70                             | —                                         |
| Gui Zhi         | 20.65                             | —                                         |
| Huo Ma Ren      | 21.22                             | —                                         |
| Rou Gui         | 22.06                             | —                                         |
| Yi Yi Ren       | 22.08                             | —                                         |
| Gou Teng        | 22.37                             | —                                         |
| Zhi Ke          | 22.47                             | —                                         |
| Di Gu Pi        | 22.86                             | —                                         |
| Lu Gen          | 23.00                             | —                                         |
| Bai Zi Ren      | 23.11                             | —                                         |
| Zhi Gan Cao     | 23.49                             | —                                         |
| Mu Zei          | 23.74                             | —                                         |
| Ma Huang Gen    | 24.01                             | —                                         |
| Zhu Ru          | 25.37                             | —                                         |
| Pu Gong Ying    | 26.21                             | —                                         |
| Ze Xie          | 26.32                             | —                                         |
| Ren Shen        | 26.68                             | —                                         |
| Chuang Mu Xiang | 26.80                             | —                                         |
| Tao Ren         | 27.06                             | —                                         |
| Fu Xiao Mai     | 27.74                             | —                                         |
| Xie Bai         | 28.28                             | —                                         |
| Ci Wu Jia       | 29.22                             | —                                         |
| Cang Zhu        | 29.75                             | —                                         |
| San Qi          | 30.72                             | —                                         |
| Ze Lan          | 31.13                             | —                                         |
| Mang Xiao       | 31.59                             | —                                         |
| Hong Hua        | 31.83                             | —                                         |
| Fo Shou         | 32.56                             | —                                         |
| Gua Lou         | 32.90                             | —                                         |
| Ban Xia (Jiang) | 33.39                             | —                                         |
| Chi Shao (Yao)  | 33.43                             | —                                         |
| Dang Gui        | 33.70                             | —                                         |
| Sang Zhi        | 33.97                             | —                                         |
| Ban Zhi Lian    | 35.67                             | —                                         |
| Long Yan Rou    | 36.01                             | —                                         |
| Jie Geng        | 36.01                             | —                                         |
| Sang Ye         | 36.19                             | —                                         |
| Xi Xian Cao     | 36.74                             | —                                         |
| Cang Er Zi      | 37.18                             | —                                         |
| Ku Shen         | 38.59                             | —                                         |
| Huang Qin       | 39.29                             | —                                         |
| Lai Fu Zi       | 39.53                             | —                                         |
| E Zhu           | 40.38                             | —                                         |
| Jiang Huang     | 42.13                             | —                                         |
| Fu Shen         | 42.83                             | —                                         |
| Nü Zhen Zi      | 44.07                             | —                                         |
| Gou Qi Zi       | 44.32                             | —                                         |
| Bai Zhu         | 47.33                             | —                                         |
| Zhi Mu          | 48.41                             | —                                         |
| Yi Mu Cao       | 50.26                             | —                                         |

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                         | 6.58                            |
| 62662     | 62662               | 0.00                         | 5.68                            |
| 62905     | 62905               | 0.00                         | 4.82                            |
| 62906     | 62906               | 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 2.4-2022-02

Validated substance/substance group **Che Qian Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60255-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Che Qian Zi               | 2      | 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 |
| PhytoComm | Che Qian Zi | G192HS120SR1 | 62841     | 40      | from supplier |
| PhytoComm | Che Qian Zi | G192HS120SR1 | 62842     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Che Qian Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Che Qian Zi | G192HS120SH1 | 62608 <sup>†</sup> | 20      |
| PhytoComm | Che Qian Zi | G192HS120SR1 | 62841 <sup>†</sup> | 20      |
| PhytoComm | Che Qian Zi | G192HS120SR1 | 62842 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G192H0723321 | 2       |
| Phytocomm | Che Qian Zi | G192H0723421 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Hou Po          | 5.52                      | —                                 |
| Yu Jin          | 6.82                      | —                                 |
| Mao Dong Qing   | 7.48                      | —                                 |
| Ling Zhi        | 7.68                      | —                                 |
| Ren Dong Teng   | 8.22                      | —                                 |
| Bai Xian Pi     | 9.06                      | —                                 |
| Yin Yang Huo    | 9.27                      | —                                 |
| Chai Hu         | 9.44                      | —                                 |
| Dan Dou Chi     | 10.14                     | —                                 |
| Du Zhong        | 10.37                     | —                                 |
| Yan Hu Suo      | 10.81                     | —                                 |
| Zhu Ling        | 11.34                     | —                                 |
| Guang Huo Xiang | 11.45                     | —                                 |
| Shen Qu         | 11.57                     | —                                 |
| Ji Li           | 11.66                     | —                                 |
| Sha Ren         | 11.98                     | —                                 |
| Ce Bai Ye       | 12.13                     | —                                 |
| Jing Jie        | 12.90                     | —                                 |
| Qiang Huo       | 13.28                     | —                                 |
| Ye Jiao Teng    | 13.61                     | —                                 |
| Pi Pa Ye        | 13.94                     | —                                 |
| Fu Zi           | 13.97                     | —                                 |
| Shan Yao        | 14.51                     | —                                 |
| Fu Pen Zi       | 14.53                     | —                                 |
| Tu Fu Ling      | 14.69                     | —                                 |
| Zi Hua Di Ding  | 16.18                     | —                                 |
| Dan Shen        | 16.31                     | —                                 |
| Lian Qiao       | 16.43                     | —                                 |
| Bo He           | 16.54                     | —                                 |
| Ji Xue Teng     | 16.58                     | —                                 |
| Lian Zi         | 17.03                     | —                                 |
| Bai Jiang Cao   | 17.64                     | —                                 |
| Gu Sui Bu       | 17.95                     | —                                 |
| She Gan         | 18.17                     | —                                 |
| He Huan Pi      | 18.45                     | —                                 |
| Qing Pi         | 19.80                     | —                                 |
| Ma Huang Gen    | 20.08                     | —                                 |
| Gou Teng        | 20.25                     | —                                 |
| Qing Hao        | 20.42                     | —                                 |
| Tian Hua Fen    | 20.46                     | —                                 |
| Hong Jing Tian  | 20.56                     | —                                 |
| Zhe Bei Mu      | 20.87                     | —                                 |
| Jiao Gu Lan     | 20.98                     | —                                 |
| Zhi Ke          | 21.64                     | —                                 |
| Rou Gui         | 21.68                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Fu Ling         | 21.71                     | —                                 |
| Sheng Jiang     | 21.93                     | —                                 |
| Jin Yin Hua     | 22.04                     | —                                 |
| Ma Huang        | 22.20                     | —                                 |
| Suan Zao Ren    | 22.20                     | —                                 |
| Huang Lian      | 22.34                     | —                                 |
| Mu Zei          | 22.35                     | —                                 |
| Yi Yi Ren       | 22.38                     | —                                 |
| Huo Ma Ren      | 22.46                     | —                                 |
| (Fen) Bi Xie    | 22.60                     | —                                 |
| Bai Shao Yao    | 22.76                     | —                                 |
| Huang Bai       | 23.72                     | —                                 |
| Gui Zhi         | 24.01                     | —                                 |
| Lu Gen          | 24.66                     | —                                 |
| Gan Cao         | 25.87                     | —                                 |
| Ren Shen        | 26.37                     | —                                 |
| Pu Gong Ying    | 26.80                     | —                                 |
| Ban Lan Gen     | 27.50                     | —                                 |
| Tao Ren         | 28.36                     | —                                 |
| Ze Lan          | 29.04                     | —                                 |
| Di Gu Pi        | 29.27                     | —                                 |
| Bai Zi Ren      | 29.97                     | —                                 |
| Mang Xiao       | 30.64                     | —                                 |
| Fu Xiao Mai     | 30.96                     | —                                 |
| Zhu Ru          | 31.78                     | —                                 |
| Ze Xie          | 31.91                     | —                                 |
| Zhi Gan Cao     | 32.01                     | —                                 |
| Ban Zhi Lian    | 33.03                     | —                                 |
| Ban Xia (Jiang) | 34.23                     | —                                 |
| Ci Wu Jia       | 34.70                     | —                                 |
| Xi Xian Cao     | 35.23                     | —                                 |
| E Zhu           | 36.35                     | —                                 |
| Fu Shen         | 37.05                     | —                                 |
| Lai Fu Zi       | 37.08                     | —                                 |
| Fo Shou         | 37.29                     | —                                 |
| Cang Zhu        | 38.00                     | —                                 |
| Chi Shao (Yao)  | 38.36                     | —                                 |
| Jiang Huang     | 38.71                     | —                                 |
| Sang Zhi        | 38.94                     | —                                 |
| Gua Lou         | 39.07                     | —                                 |
| San Qi          | 39.97                     | —                                 |
| Chuang Mu Xiang | 40.17                     | —                                 |
| Jie Geng        | 40.32                     | —                                 |
| Xie Bai         | 40.91                     | —                                 |
| Huang Qin       | 40.93                     | —                                 |
| Sang Ye         | 42.46                     | —                                 |
| Dang Gui        | 42.80                     | —                                 |
| Nü Zhen Zi      | 42.83                     | —                                 |
| Ku Shen         | 42.84                     | —                                 |
| Hong Hua        | 43.48                     | —                                 |
| Cang Er Zi      | 45.43                     | —                                 |
| Sha Shen (Bei)  | 45.64                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62607     | 62607               | 0.00                         | 5.67                            |
| 62608     | 62608               | 0.00                         | 5.52                            |
| 62841     | 62841               | 0.00                         | 8.66                            |
| 62842     | 62842               | 0.00                         | 7.48                            |

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 2.4-2022-02

Validated substance/substance group **Chen Pi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60009-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Chen Pi                   | 2      | 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   | G073H1128022 | 62909     | 40      | from supplier |
| PhytoComm | Chen Pi   | G073H1128022 | 62910     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Chen Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Chen Pi   | G073H1128821 | 62378 <sup>†</sup> | 20      |
| PhytoComm | Chen Pi   | G073H1128022 | 62909 <sup>†</sup> | 20      |
| PhytoComm | Chen Pi   | G073H1128022 | 62910 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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   | G073H1128222 | 1       |
| PhytoComm | Chen Pi   | G073H1128222 | 1       |
| Phytocomm | Chen Pi   | g07h1128221  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 1              | 1             | 3              | 852           |

The substance/substance group *Chen 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 99.9225 % (> 99.3359 %)  | n/a (n/a)                |

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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| (Shi) Chang Pu      | 8.29                      | —                                 |
| Ju Hua              | 11.60                     | —                                 |
| Mu Dan Pi           | 12.87                     | —                                 |
| Shan Yu Rou         | 13.13                     | —                                 |
| Wu Yao              | 13.18                     | —                                 |
| Gu Sui Bu           | 14.20                     | —                                 |
| Dang Gui            | 18.16                     | —                                 |
| Fang Feng           | 18.53                     | —                                 |
| Sang Bai Pi         | 19.00                     | —                                 |
| Sang Ji Shend       | 19.50                     | —                                 |
| Chuan Niu Xi        | 19.54                     | —                                 |
| Sha Ren             | 19.90                     | —                                 |
| Hong Jing Tian      | 19.98                     | —                                 |
| He Huan Pi          | 20.05                     | —                                 |
| Xiang Fu            | 20.27                     | —                                 |
| Wu Zhu Yu           | 24.30                     | —                                 |
| Chuan Lian Zi       | 24.37                     | —                                 |
| Jiang Huang         | 24.48                     | —                                 |
| Yin Chen Hao        | 24.88                     | —                                 |
| He Shou Wu          | 26.40                     | —                                 |
| Mang Xiao           | 26.76                     | —                                 |
| Ba Ji Tian          | 28.59                     | —                                 |
| Yi Mu Cao           | 29.16                     | —                                 |
| Xiao Hui Xiang      | 29.31                     | —                                 |
| Huang Qi            | 30.26                     | —                                 |
| Xu Duan             | 30.92                     | —                                 |
| Ku Shen             | 30.95                     | —                                 |
| Zhi Gan Cao         | 32.22                     | —                                 |
| Shan Yao            | 33.24                     | —                                 |
| Tu Si Zi            | 33.28                     | —                                 |
| Ge Gen              | 34.86                     | —                                 |
| Tian Hua Fen        | 34.96                     | —                                 |
| Bai Zhi             | 35.10                     | —                                 |
| (Bai) Dou Kou       | 36.33                     | —                                 |
| Nü Zhen Zi          | 36.71                     | —                                 |
| Di Gu Pi            | 36.82                     | —                                 |
| Bing Lang           | 37.05                     | —                                 |
| Bu Gu Zhi           | 37.78                     | —                                 |
| Bai Hua She She Cao | 37.91                     | —                                 |
| Xin Yi              | 38.25                     | —                                 |
| Cang Er Zi          | 38.72                     | —                                 |
| E Zhu               | 39.06                     | —                                 |
| (Huai) Niu Xi       | 39.52                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Sang Zhi       | 39.68                     | —                                 |
| Niu Bang Zi    | 39.83                     | —                                 |
| Zhi Ke         | 39.94                     | —                                 |
| Hu Zhang       | 40.19                     | —                                 |
| Xuan Fu Hua    | 40.29                     | —                                 |
| Yan Hu Suo     | 40.33                     | —                                 |
| Zi Su Zi       | 41.64                     | —                                 |
| Bai Zhu        | 43.19                     | —                                 |
| Chi Shao (Yao) | 44.90                     | —                                 |
| Du Huo         | 45.58                     | —                                 |
| Sang Ye        | 45.61                     | —                                 |
| Jie Geng       | 45.64                     | —                                 |
| Lian Qiao      | 45.89                     | —                                 |
| Mi Huan Jun    | 46.03                     | —                                 |
| Pu Gong Ying   | 46.18                     | —                                 |
| Huang Lian     | 47.08                     | —                                 |
| Dan Zhu Ye     | 47.60                     | —                                 |
| Ze Lan         | 47.98                     | —                                 |
| Suan Zao Ren   | 49.64                     | —                                 |
| Jing Jie       | 49.78                     | —                                 |
| Du Zhong       | 49.86                     | —                                 |
| Mao Dong Qing  | 50.41                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62377     | 62377                  | 0.00                            | 12.87                              |
| 62378     | 62378                  | 0.00                            | 13.73                              |
| 62909     | 62909                  | 0.00                            | 8.63                               |
| 62910     | 62910                  | 0.00                            | 8.29                               |

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 2.4-2022-02

Validated substance/substance group **Chi Shao (Yao)**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60014-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Chi Shao (Yao)            | 3      | 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 |
| PhytoComm | Chi Shao (Yao) | G180H0705922 | 62831     | 40      | from supplier |
| PhytoComm | Chi Shao (Yao) | G180H0705922 | 62832     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Chi Shao (Yao)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Chi Shao (Yao) | G180H0705821 | 62364 <sup>†</sup> | 20      |
| PhytoComm | Chi Shao (Yao) | G180H0705822 | 62481 <sup>†</sup> | 20      |
| PhytoComm | Chi Shao (Yao) | G180H0705822 | 62482 <sup>†</sup> | 20      |
| PhytoComm | Chi Shao (Yao) | G180H0705922 | 62831 <sup>†</sup> | 20      |
| PhytoComm | Chi Shao (Yao) | G180H0705922 | 62832 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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) | G180H0705422 | 1       |
| Phytocomm | Chi Shao (Yao) | G189H0705321 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8269 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Huang Qi       | 11.31                     | —                                 |
| Zhi Gan Cao    | 19.97                     | —                                 |
| Mu Gua         | 22.52                     | —                                 |
| Bing Lang      | 24.20                     | —                                 |
| Gan Cao        | 25.04                     | —                                 |
| Yuan Zhi       | 25.24                     | —                                 |
| Mang Xiao      | 26.19                     | —                                 |
| (Huai) Niu Xi  | 28.26                     | —                                 |
| Bai Zhu        | 29.04                     | —                                 |
| Lian Qiao      | 29.27                     | —                                 |
| Zhi Ke         | 30.25                     | —                                 |
| Xiang Fu       | 30.56                     | —                                 |
| Chuan Lian Zi  | 30.66                     | —                                 |
| Sang Zhi       | 32.10                     | —                                 |
| Jie Geng       | 33.08                     | —                                 |
| Di Gu Pi       | 34.86                     | —                                 |
| Ma Huang       | 34.91                     | —                                 |
| Zi Su Zi       | 35.96                     | —                                 |
| Shan Yao       | 37.87                     | —                                 |
| Ban Zhi Lian   | 38.10                     | —                                 |
| Dang Gui       | 38.48                     | —                                 |
| Huang Qin      | 38.58                     | —                                 |
| Chuan Niu Xi   | 39.10                     | —                                 |
| Ju Hua         | 40.70                     | —                                 |
| Du Huo         | 40.89                     | —                                 |
| Bai Zhi        | 40.95                     | —                                 |
| Jiao Gu Lan    | 42.16                     | —                                 |
| Jin Yin Hua    | 42.23                     | —                                 |
| Fu Zi          | 42.25                     | —                                 |
| Tian Hua Fen   | 42.43                     | —                                 |
| Huang Bai      | 42.71                     | —                                 |
| Niu Bang Zi    | 43.23                     | —                                 |
| Suan Zao Ren   | 43.26                     | —                                 |
| Chuan Mu Tong  | 43.33                     | —                                 |
| Dan Shen       | 43.44                     | —                                 |
| Cang Zhu       | 43.89                     | —                                 |
| Chai Hu        | 44.56                     | —                                 |
| Huang Lian     | 44.71                     | —                                 |
| Mao Dong Qing  | 44.99                     | —                                 |
| Hong Hua       | 45.11                     | —                                 |
| (Shi) Chang Pu | 45.31                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Zi Hua Di Ding | 45.77                     | —                                 |
| Long Dan (Cao) | 46.03                     | —                                 |
| Bo He          | 46.27                     | —                                 |
| Cang Er Zi     | 46.83                     | —                                 |
| Zhe Bei Mu     | 47.59                     | —                                 |
| Sha Shen (Bei) | 47.59                     | —                                 |
| Tu Fu Ling     | 47.68                     | —                                 |
| Qin Jiao       | 47.79                     | —                                 |
| Pu Gong Ying   | 48.45                     | —                                 |
| E Zhu          | 48.61                     | —                                 |
| Ku Shen        | 48.69                     | —                                 |
| Yan Hu Suo     | 48.75                     | —                                 |
| Gou Teng       | 49.38                     | —                                 |
| Lian Zi        | 49.41                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62363     | 62363                  | 0.00                            | 11.71                              |
| 62364     | 62364                  | 0.00                            | 11.31                              |
| 62481     | 62481                  | 0.00                            | 16.82                              |
| 62482     | 62482                  | 0.00                            | 16.56                              |
| 62831     | 62831                  | 0.00                            | 16.12                              |
| 62832     | 62832                  | 0.00                            | 16.21                              |

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 2.4-2022-02

Validated substance/substance group **Chuan Lian Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60078-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Chuan Lian Zi             | 2      | 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 | G157H0306921 | 62893     | 40      | from supplier |
| PhytoComm | Chuan Lian Zi | G157H0306921 | 62894     | 40      | from supplier |
| PhytoComm | Chuan Lian Zi | G157H0306021 | 62995     | 40      | from supplier |
| PhytoComm | Chuan Lian Zi | G157H0306021 | 62996     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Lian Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 | G157H0306921 | 62893 <sup>†</sup> | 20      |
| PhytoComm | Chuan Lian Zi | G157H0306921 | 62894 <sup>†</sup> | 20      |
| PhytoComm | Chuan Lian Zi | G157H0306021 | 62995 <sup>†</sup> | 20      |
| PhytoComm | Chuan Lian Zi | G157H0306021 | 62996 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 4              | 0             | 3              | 850           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 99.4961 % (> 98.9101 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Sang Zhi       | 6.91                      | —                                 |
| Tian Hua Fen   | 9.07                      | —                                 |
| Di Gu Pi       | 10.07                     | —                                 |
| Jie Geng       | 10.71                     | —                                 |
| Bai He         | 11.60                     | —                                 |
| Sha Shen (Bei) | 11.75                     | —                                 |
| Gan Jiang      | 12.88                     | —                                 |
| Long Dan (Cao) | 14.36                     | —                                 |
| Chuan Mu Tong  | 15.35                     | —                                 |
| Bai Zhu        | 16.29                     | —                                 |
| Lai Fu Zi      | 17.20                     | —                                 |
| Zi Su Zi       | 17.23                     | —                                 |
| E Zhu          | 17.30                     | —                                 |
| Mi Huan Jun    | 17.37                     | —                                 |
| Qin Jiao       | 18.18                     | —                                 |
| Dang Gui       | 19.97                     | —                                 |
| Zhi Gan Cao    | 20.12                     | —                                 |
| Huang Qi       | 20.26                     | —                                 |
| (Huai) Niu Xi  | 20.92                     | —                                 |
| Cang Er Zi     | 22.05                     | —                                 |
| Da Zao         | 22.85                     | —                                 |
| Mang Xiao      | 22.94                     | —                                 |
| Shan Yao       | 26.37                     | —                                 |
| Jiang Huang    | 28.72                     | —                                 |
| Niu Bang Zi    | 28.81                     | —                                 |
| Bai Zhi        | 28.98                     | —                                 |
| Lian Qiao      | 29.67                     | —                                 |
| Chuan Niu Xi   | 31.63                     | —                                 |
| Ban Zhi Lian   | 31.68                     | —                                 |
| Chi Shao (Yao) | 32.24                     | —                                 |
| Yan Hu Suo     | 33.17                     | —                                 |
| Mu Gua         | 34.87                     | —                                 |
| Yuan Zhi       | 35.10                     | —                                 |
| Lian Zi        | 35.73                     | —                                 |
| Ku Shen        | 35.77                     | —                                 |
| Xiao Hui Xiang | 36.94                     | —                                 |
| (Bai) Dou Kou  | 36.99                     | —                                 |
| Suan Zao Ren   | 37.35                     | —                                 |
| Chen Pi        | 37.49                     | —                                 |
| Fu Ling        | 37.68                     | —                                 |
| Sha Ren        | 37.95                     | —                                 |
| Bai Xian Pi    | 38.32                     | —                                 |
| (Shi) Chang Pu | 39.07                     | —                                 |
| Ji Li          | 39.09                     | —                                 |
| Tu Fu Ling     | 40.01                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Bai Shao Yao   | 40.21                     | —                                 |
| Chai Hu        | 40.43                     | —                                 |
| Jin Yin Hua    | 41.25                     | —                                 |
| He Huan Pi     | 41.30                     | —                                 |
| Qiang Huo      | 42.11                     | —                                 |
| Pu Gong Ying   | 42.36                     | —                                 |
| Bo He          | 43.34                     | —                                 |
| Bing Lang      | 43.62                     | —                                 |
| Rou Gui        | 43.94                     | —                                 |
| Ren Dong Teng  | 43.96                     | —                                 |
| Zhi Ke         | 44.72                     | —                                 |
| Huang Lian     | 45.53                     | —                                 |
| Zi Hua Di Ding | 45.91                     | —                                 |
| Ye Jiao Teng   | 46.20                     | —                                 |
| Gou Teng       | 46.26                     | —                                 |
| Yi Yi Ren      | 46.53                     | —                                 |
| Ce Bai Ye      | 46.55                     | —                                 |
| Xiang Fu       | 46.76                     | —                                 |
| Gan Cao        | 47.05                     | —                                 |
| Shen Qu        | 47.37                     | —                                 |
| Du Huo         | 47.43                     | —                                 |
| Dan Dou Chi    | 47.46                     | —                                 |
| Fang Feng      | 48.60                     | —                                 |
| Yu Jin         | 48.62                     | —                                 |
| Shan Yu Rou    | 48.76                     | —                                 |
| Fo Shou        | 48.79                     | —                                 |
| Dong Gua Zi    | 49.04                     | —                                 |
| Zhu Ling       | 49.15                     | —                                 |
| Sheng Jiang    | 50.37                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62893     | 62893                  | 0.00                            | 8.81                               |
| 62894     | 62894                  | 0.00                            | 8.19                               |
| 62995     | 62995                  | 0.00                            | 7.03                               |
| 62996     | 62996                  | 0.00                            | 6.91                               |

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 2.4-2022-02

Validated substance/substance group **Chuan Mu Tong**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60173-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Chuan Mu Tong; Clematidis armandii caulis

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Chuan Mu Tong             | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Chuan Mu Tong* 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 Mu Tong*:

| Supplier  | Substance     | Batch        | Sample ID | Spectra | Certificate   |
|-----------|---------------|--------------|-----------|---------|---------------|
| PhytoComm | Chuan Mu Tong | G009H0310921 | 62947     | 40      | from supplier |
| PhytoComm | Chuan Mu Tong | G009H0310921 | 62948     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Mu Tong*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 Mu Tong*.
- 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 Mu Tong | G009H0310921 | 62947 <sup>†</sup> | 20      |
| PhytoComm | Chuan Mu Tong | G009H0310921 | 62948 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Chuan Mu Tong*.
- 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 | Chuan Mu Tong | g009h0310321 | 1       |
| Phytocomm | Chuan Mu Tong | G009H0310321 | 1       |
| PhytoComm | Chuan Mu Tong | G009H0310521 | 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 *Chuan Mu Tong* 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 Mu Tong* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 80            | 0              | 22 359        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 1              | 0             | 3              | 853           |

The substance/substance group *Chuan Mu Tong* 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 99.9926 % (> 99.9763 %)  | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.)

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

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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chuan Mu Tong* 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Mi Huan Jun    | 4.91                      | —                                 |
| Sang Zhi       | 11.11                     | —                                 |
| Dang Gui       | 11.70                     | —                                 |
| Di Gu Pi       | 12.35                     | —                                 |
| Chuan Lian Zi  | 13.43                     | —                                 |
| Bai He         | 13.49                     | —                                 |
| Sha Shen (Bei) | 18.18                     | —                                 |
| Gan Jiang      | 18.25                     | —                                 |
| Tian Hua Fen   | 19.28                     | —                                 |
| E Zhu          | 19.35                     | —                                 |
| Qin Jiao       | 19.36                     | —                                 |
| Long Dan (Cao) | 19.46                     | —                                 |
| Ban Zhi Lian   | 22.38                     | —                                 |
| (Huai) Niu Xi  | 24.21                     | —                                 |
| Mang Xiao      | 24.72                     | —                                 |
| Lai Fu Zi      | 25.50                     | —                                 |
| Chuan Niu Xi   | 27.64                     | —                                 |
| Huang Qi       | 27.70                     | —                                 |
| Bai Zhi        | 29.43                     | —                                 |
| Da Zao         | 29.67                     | —                                 |
| Zi Su Zi       | 29.70                     | —                                 |
| Zhi Gan Cao    | 29.70                     | —                                 |
| Jie Geng       | 29.72                     | —                                 |
| Jiang Huang    | 29.89                     | —                                 |
| Bai Zhu        | 31.12                     | —                                 |
| Shan Yao       | 31.83                     | —                                 |
| Cang Er Zi     | 32.27                     | —                                 |
| Yan Hu Suo     | 32.54                     | —                                 |
| (Bai) Dou Kou  | 34.88                     | —                                 |
| Sha Ren        | 36.55                     | —                                 |
| Niu Bang Zi    | 37.50                     | —                                 |
| Bing Lang      | 38.10                     | —                                 |
| Lian Qiao      | 38.13                     | —                                 |
| Chen Pi        | 38.42                     | —                                 |
| He Huan Pi     | 38.50                     | —                                 |
| Fu Ling        | 39.56                     | —                                 |
| Rou Gui        | 39.67                     | —                                 |
| Lian Zi        | 40.21                     | —                                 |
| (Shi) Chang Pu | 41.36                     | —                                 |
| Bai Xian Pi    | 42.29                     | —                                 |
| Bai Shao Yao   | 43.70                     | —                                 |
| Chi Shao (Yao) | 43.80                     | —                                 |
| Mu Dan Pi      | 43.97                     | —                                 |
| Yi Yi Ren      | 44.39                     | —                                 |
| Ji Li          | 44.61                     | —                                 |
| Xiang Fu       | 45.69                     | —                                 |
| Xiao Hui Xiang | 45.74                     | —                                 |
| Suan Zao Ren   | 46.04                     | —                                 |
| Tu Fu Ling     | 46.15                     | —                                 |
| Ku Shen        | 46.76                     | —                                 |
| Mu Gua         | 47.18                     | —                                 |
| Chai Hu        | 47.71                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Huang Lian          | 47.96                     | —                                 |
| Zhi Ke              | 48.18                     | —                                 |
| Shan Yu Rou         | 48.37                     | —                                 |
| Ji Xue Teng         | 48.61                     | —                                 |
| Jin Yin Hua         | 48.89                     | —                                 |
| Yuan Zhi            | 48.94                     | —                                 |
| Ye Jiao Teng        | 49.04                     | —                                 |
| Fang Feng           | 49.08                     | —                                 |
| Bai Hua She She Cao | 50.27                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chuan Mu Tong* 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62947     | 62947                  | 0.00                            | 4.91                               |
| 62948     | 62948                  | 0.00                            | 7.37                               |

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 2.4-2022-02

Validated substance/substance group **Chuan Niu Xi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60122-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Chuan Niu Xi; Cyathulae radix

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Chuan Niu Xi              | 1      | 0      | 1      |

### Second-stage model

For differentiation of the substance/substance group *Chuan 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 *Chuan Niu Xi*:

| Supplier  | Substance    | Batch        | Sample ID | Spectra | Certificate   |
|-----------|--------------|--------------|-----------|---------|---------------|
| PhytoComm | Chuan Niu Xi | G318H0431923 | 62817     | 40      | from supplier |
| PhytoComm | Chuan Niu Xi | G318H0431923 | 62818     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Niu Xi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 | Chuan Niu Xi | G318H0431923 | 62817 <sup>†</sup> | 20      |
| PhytoComm | Chuan Niu Xi | G318H0431923 | 62818 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 *Chuan Niu Xi*.
- 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 Niu Xi | g318h0431321 | 1       |
| PhytoComm | Chuan Niu Xi | G318H0431321 | 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 *Chuan 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 *Chuan 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 4              | 2             | 0              | 851           |

The substance/substance group *Chuan 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 99.5194 % (> 98.9345 %)  | n/a (n/a)                |

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

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

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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chuan 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Dang Gui            | 12.82                     | —                                 |
| Du Huo              | 13.58                     | —                                 |
| Sang Zhi            | 14.64                     | —                                 |
| Chuan Lian Zi       | 14.67                     | —                                 |
| (Huai) Niu Xi       | 17.22                     | —                                 |
| Shan Yu Rou         | 17.85                     | —                                 |
| Ba Ji Tian          | 18.51                     | —                                 |
| Chen Pi             | 19.46                     | —                                 |
| (Shi) Chang Pu      | 22.48                     | —                                 |
| Xiang Fu            | 22.55                     | —                                 |
| Huang Qi            | 23.56                     | —                                 |
| Long Dan (Cao)      | 23.97                     | —                                 |
| Fang Feng           | 24.00                     | —                                 |
| Zhi Gan Cao         | 24.26                     | —                                 |
| E Zhu               | 24.53                     | —                                 |
| Da Zao              | 25.46                     | —                                 |
| Mang Xiao           | 26.12                     | —                                 |
| Bing Lang           | 26.12                     | —                                 |
| Lai Fu Zi           | 26.98                     | —                                 |
| Bai Zhu             | 27.73                     | —                                 |
| Ju Hua              | 27.83                     | —                                 |
| Mu Dan Pi           | 29.31                     | —                                 |
| Jie Geng            | 29.63                     | —                                 |
| Zi Su Zi            | 29.66                     | —                                 |
| Tian Hua Fen        | 29.71                     | —                                 |
| He Huan Pi          | 29.72                     | —                                 |
| Yan Hu Suo          | 30.18                     | —                                 |
| Mi Huan Jun         | 30.50                     | —                                 |
| Jiang Huang         | 30.83                     | —                                 |
| Yuan Zhi            | 33.18                     | —                                 |
| Qin Jiao            | 34.37                     | —                                 |
| Lian Qiao           | 34.47                     | —                                 |
| Shan Yao            | 34.48                     | —                                 |
| Wu Yao              | 35.20                     | —                                 |
| Sha Shen (Bei)      | 35.69                     | —                                 |
| Di Gu Pi            | 35.75                     | —                                 |
| Sha Ren             | 36.99                     | —                                 |
| Niu Bang Zi         | 37.13                     | —                                 |
| Chuan Mu Tong       | 40.00                     | —                                 |
| Bai Zhi             | 40.09                     | —                                 |
| Bai He              | 40.50                     | —                                 |
| (Bai) Dou Kou       | 40.96                     | —                                 |
| Xiao Hui Xiang      | 41.65                     | —                                 |
| Bai Hua She She Cao | 42.02                     | —                                 |
| Ku Shen             | 42.06                     | —                                 |
| Gan Jiang           | 42.18                     | —                                 |
| Gu Sui Bu           | 42.54                     | —                                 |
| Chi Shao (Yao)      | 43.37                     | —                                 |
| Zhi Ke              | 43.49                     | —                                 |
| Dong Gua Zi         | 44.53                     | —                                 |
| Xu Duan             | 44.79                     | —                                 |
| Cang Er Zi          | 45.73                     | —                                 |

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| Substanz     | Distance in<br>main model | Distance in<br>second-stage model |
|--------------|---------------------------|-----------------------------------|
| Suan Zao Ren | 47.08                     | —                                 |
| Lian Zi      | 47.66                     | —                                 |
| Jin Yin Hua  | 47.78                     | —                                 |
| Bai Xian Pi  | 49.64                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chuan 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62817     | 62817                  | 0.00                            | 12.82                              |
| 62818     | 62818                  | 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 2.4-2022-02

Validated substance/substance group **Chuang Mu Xiang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50323-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G219HS046SR1 | 62861     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Chuang Mu Xiang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 400 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G219HS046SR1 | 62861 <sup>†</sup> | 20      |
| PhytoComm | Chuang Mu Xiang | G219HS046SR1 | 62862              | 59      |

- 11 318 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | g219h0309321 | 1       |
| Phytocomm | Chuang Mu Xiang | g219h0309322 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 40            | 0              | 22 400        |
| <b>Type B</b> | 0              | 79            | 0              | 11 318        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9677 %) | 100.0000 % (> 85.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.4051 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Hong Jing Tian  | 12.08                     | —                                 |
| Jin Yin Hua     | 13.61                     | —                                 |
| Cang Zhu        | 13.85                     | —                                 |
| Jiao Gu Lan     | 15.95                     | —                                 |
| Long Yan Rou    | 16.65                     | —                                 |
| Gou Qi Zi       | 17.60                     | —                                 |
| Dan Shen        | 17.61                     | —                                 |
| Pi Pa Ye        | 18.44                     | —                                 |
| Shan Yao        | 18.46                     | —                                 |
| Dan Dou Chi     | 18.54                     | —                                 |
| Dang Gui        | 18.70                     | —                                 |
| Tian Hua Fen    | 19.07                     | —                                 |
| Ma Huang        | 19.32                     | —                                 |
| Zhi Ke          | 19.87                     | —                                 |
| Lian Zi         | 20.04                     | —                                 |
| Xie Bai         | 20.18                     | —                                 |
| Zi Hua Di Ding  | 20.74                     | —                                 |
| Gu Sui Bu       | 20.79                     | —                                 |
| Ren Dong Teng   | 21.21                     | —                                 |
| Di Gu Pi        | 21.54                     | —                                 |
| Hong Hua        | 21.62                     | —                                 |
| Suan Zao Ren    | 22.09                     | —                                 |
| Fu Pen Zi       | 22.26                     | —                                 |
| Gan Cao         | 22.26                     | —                                 |
| Lian Qiao       | 22.59                     | —                                 |
| Jie Geng        | 22.87                     | —                                 |
| Zhi Gan Cao     | 22.98                     | —                                 |
| Hou Po          | 23.02                     | —                                 |
| Shen Qu         | 23.42                     | —                                 |
| Zhe Bei Mu      | 23.49                     | —                                 |
| Ren Shen        | 23.79                     | —                                 |
| Ze Xie          | 23.83                     | —                                 |
| Bai Shao Yao    | 23.91                     | —                                 |
| She Gan         | 24.26                     | —                                 |
| Chai Hu         | 24.27                     | —                                 |
| Mu Zei          | 24.28                     | —                                 |
| Lu Gen          | 24.85                     | —                                 |
| Guang Huo Xiang | 25.04                     | —                                 |
| Ji Li           | 25.62                     | —                                 |
| Ye Jiao Teng    | 25.96                     | —                                 |
| Ban Lan Gen     | 26.43                     | —                                 |
| Yin Yang Huo    | 26.81                     | —                                 |
| Ku Shen         | 26.83                     | —                                 |
| Mu Gua          | 27.15                     | —                                 |
| Tao Ren         | 27.30                     | —                                 |
| Bai Xian Pi     | 27.45                     | —                                 |
| He Huan Pi      | 27.56                     | —                                 |
| Fu Zi           | 27.64                     | —                                 |
| Ling Zhi        | 27.74                     | —                                 |
| Ji Xue Teng     | 27.92                     | —                                 |
| San Qi          | 28.01                     | —                                 |
| Gou Teng        | 28.64                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Tu Fu Ling      | 28.99                     | —                                 |
| Mao Dong Qing   | 29.37                     | —                                 |
| Zhi Mu          | 29.86                     | —                                 |
| Bai Zi Ren      | 30.60                     | —                                 |
| Mang Xiao       | 30.63                     | —                                 |
| Gui Zhi         | 30.68                     | —                                 |
| Sheng Jiang     | 30.80                     | —                                 |
| Huang Qin       | 30.99                     | —                                 |
| Rou Gui         | 31.01                     | —                                 |
| Yan Hu Suo      | 31.17                     | —                                 |
| Ci Wu Jia       | 31.50                     | —                                 |
| Qiang Huo       | 31.62                     | —                                 |
| Bo He           | 31.73                     | —                                 |
| Sang Zhi        | 31.80                     | —                                 |
| Huang Bai       | 32.24                     | —                                 |
| Fo Shou         | 32.24                     | —                                 |
| Che Qian Zi     | 32.56                     | —                                 |
| Ce Bai Ye       | 33.56                     | —                                 |
| Chi Shao (Yao)  | 33.74                     | —                                 |
| Lai Fu Zi       | 33.78                     | —                                 |
| Sha Ren         | 33.97                     | —                                 |
| Cang Er Zi      | 34.30                     | —                                 |
| Qing Pi         | 34.37                     | —                                 |
| Jing Jie        | 34.40                     | —                                 |
| Yu Jin          | 34.43                     | —                                 |
| Gua Lou         | 34.76                     | —                                 |
| Huo Ma Ren      | 35.24                     | —                                 |
| Yuan Zhi        | 35.42                     | —                                 |
| (Fen) Bi Xie    | 35.54                     | —                                 |
| Fu Ling         | 35.62                     | —                                 |
| Ma Huang Gen    | 36.57                     | —                                 |
| Huang Lian      | 39.12                     | —                                 |
| Zhu Ling        | 39.67                     | —                                 |
| Du Zhong        | 41.60                     | —                                 |
| Ban Xia (Jiang) | 42.14                     | —                                 |
| Huang Qi        | 42.32                     | —                                 |
| Zhu Ru          | 42.67                     | —                                 |
| Niu Bang Zi     | 43.52                     | —                                 |
| Bai Jiang Cao   | 44.50                     | —                                 |
| Fu Xiao Mai     | 46.11                     | —                                 |
| Yi Yi Ren       | 47.34                     | —                                 |
| Chuan Lian Zi   | 47.47                     | —                                 |
| Qing Hao        | 49.46                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62861     | 62861               | 0.00                         | 12.08                           |

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 2.4-2022-02

Validated substance/substance group **Ci Wu Jia**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60354-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ci Wu Jia | G302HS422SH1 | 62624 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 3              | 72            | 8              | 22 357        |
| <b>Type B</b> | 1              | 29            | 11             | 11 356        |
| <b>Type C</b> | 0              | 0             | 0              | 857           |

The substance/substance group *Ci Wu Jia* 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9888 % (> 99.9726 %)  | 90.0000 % (> 86.2500 %) |
| <b>Type B</b> | 99.9963 % (> 99.9642 %)  | 72.5000 % (> 65.0000 %) |
| <b>Type C</b> | 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.

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

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Sheng Jiang     | 2.71                      | —                                 |
| He Huan Pi      | 3.49                      | —                                 |
| Fu Xiao Mai     | 4.27                      | —                                 |
| Tao Ren         | 4.64                      | —                                 |
| Gui Zhi         | 4.97                      | —                                 |
| Lai Fu Zi       | 5.78                      | —                                 |
| Di Gu Pi        | 7.41                      | —                                 |
| Zhu Ru          | 8.11                      | —                                 |
| Fu Ling         | 8.22                      | —                                 |
| Ban Xia (Jiang) | 8.78                      | —                                 |
| Bai Zi Ren      | 8.96                      | —                                 |
| Yi Yi Ren       | 9.27                      | —                                 |
| Lian Zi         | 9.63                      | —                                 |
| Rou Gui         | 10.17                     | —                                 |
| Ji Li           | 10.39                     | —                                 |
| Gou Teng        | 10.46                     | —                                 |
| Mu Zei          | 10.65                     | —                                 |
| Huo Ma Ren      | 10.82                     | —                                 |
| Ling Zhi        | 11.75                     | —                                 |
| Bai Shao Yao    | 12.14                     | —                                 |
| Shen Qu         | 13.26                     | —                                 |
| Bai Xian Pi     | 13.70                     | —                                 |
| Zhe Bei Mu      | 13.73                     | —                                 |
| Gu Sui Bu       | 15.36                     | —                                 |
| Ji Xue Teng     | 16.00                     | —                                 |
| Fo Shou         | 16.63                     | —                                 |
| Lu Gen          | 16.81                     | —                                 |
| Tian Hua Fen    | 16.86                     | —                                 |
| Ye Jiao Teng    | 16.90                     | —                                 |
| Ma Huang Gen    | 17.13                     | —                                 |
| Ren Dong Teng   | 19.83                     | —                                 |
| Ze Xie          | 20.02                     | —                                 |
| Suan Zao Ren    | 20.90                     | —                                 |
| Tu Fu Ling      | 21.36                     | —                                 |
| Zhu Ling        | 21.41                     | —                                 |
| Yu Jin          | 21.67                     | —                                 |
| Fu Shen         | 22.41                     | —                                 |
| (Fen) Bi Xie    | 22.89                     | —                                 |
| Shan Yao        | 23.04                     | —                                 |
| Pi Pa Ye        | 23.87                     | —                                 |
| Lian Qiao       | 24.38                     | —                                 |
| She Gan         | 25.34                     | —                                 |
| Ce Bai Ye       | 26.43                     | —                                 |
| Dan Dou Chi     | 27.57                     | —                                 |
| Yan Hu Suo      | 28.47                     | —                                 |
| Jin Yin Hua     | 28.64                     | —                                 |
| Dan Shen        | 29.49                     | —                                 |
| Gua Lou         | 29.53                     | —                                 |
| Mao Dong Qing   | 30.18                     | —                                 |
| Cang Zhu        | 31.20                     | —                                 |
| Fu Pen Zi       | 31.31                     | —                                 |
| Jiao Gu Lan     | 31.50                     | —                                 |
| Chai Hu         | 31.84                     | —                                 |
| Fu Zi           | 32.15                     | —                                 |
| Jie Geng        | 32.21                     | —                                 |
| Zhi Mu          | 33.54                     | —                                 |
| San Qi          | 33.68                     | —                                 |
| Yin Yang Huo    | 33.77                     | —                                 |
| Ren Shen        | 33.96                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mang Xiao       | 34.23                     | —                                 |
| Dang Gui        | 34.86                     | —                                 |
| Zhi Ke          | 35.33                     | —                                 |
| Ban Lan Gen     | 35.66                     | —                                 |
| Hong Jing Tian  | 36.81                     | —                                 |
| Hou Po          | 36.91                     | —                                 |
| Guang Huo Xiang | 37.77                     | —                                 |
| Che Qian Zi     | 38.55                     | —                                 |
| Yuan Zhi        | 39.66                     | —                                 |
| Huang Qin       | 39.70                     | —                                 |
| Ma Huang        | 40.47                     | —                                 |
| Gan Cao         | 40.56                     | —                                 |
| Qiang Huo       | 40.90                     | —                                 |
| Mu Gua          | 41.51                     | —                                 |
| Gou Qi Zi       | 45.15                     | —                                 |
| Huang Lian      | 46.25                     | —                                 |
| Chuang Mu Xiang | 47.74                     | —                                 |
| Jing Jie        | 48.11                     | —                                 |
| Sang Zhi        | 48.21                     | —                                 |
| Long Yan Rou    | 48.45                     | —                                 |
| Zi Hua Di Ding  | 49.34                     | —                                 |
| Ku Shen         | 50.47                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62623     | 62623                  | 0.00                            | 2.71                               |
| 62624     | 62624                  | 0.00                            | 2.84                               |

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 2.4-2022-02

Validated substance/substance group **Da Huang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60140-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Da Huang  | G212H0320822 | 62496 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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  | g212h0320023 | 1       |
| Phytocomm | Da Huang  | G212H0320321 | 2       |
| PhytoComm | Da Huang  | G212H0320321 | 1       |
| Phytocomm | Da Huang  | G212H0320521 | 3       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------|---------------------------|-----------------------------------|
| Hua Shi   | 36.02                     | —                                 |
| Mang Xiao | 36.66                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62495     | 62495                  | 0.00                            | 36.05                              |
| 62496     | 62496                  | 0.00                            | 36.02                              |

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 2.4-2022-02

Validated substance/substance group **Da Zao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60055-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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    | G129H0316821 | 62539     | 40      | from supplier |
| PhytoComm | Da Zao    | G129H0316821 | 62540     | 40      | from supplier |
| PhytoComm | Da Zao    | G129H0316921 | 63007     | 40      | from supplier |
| PhytoComm | Da Zao    | G129H0316921 | 63008     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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    | G129H0316821 | 62539 <sup>†</sup> | 20      |
| PhytoComm | Da Zao    | G129H0316821 | 62540 <sup>†</sup> | 20      |
| PhytoComm | Da Zao    | G129H0316921 | 63007 <sup>†</sup> | 20      |
| PhytoComm | Da Zao    | G129H0316921 | 63008 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Dang Gui       | 15.69                     | —                                 |
| Long Dan (Cao) | 20.76                     | —                                 |
| Bing Lang      | 23.30                     | —                                 |
| Mang Xiao      | 24.57                     | —                                 |
| Chuan Niu Xi   | 26.75                     | —                                 |
| Qin Jiao       | 27.13                     | —                                 |
| Sang Zhi       | 27.40                     | —                                 |
| Huang Qi       | 28.05                     | —                                 |
| (Shi) Chang Pu | 28.07                     | —                                 |
| Shan Yu Rou    | 28.43                     | —                                 |
| Chen Pi        | 29.54                     | —                                 |
| Chuan Mu Tong  | 30.74                     | —                                 |
| He Huan Pi     | 32.47                     | —                                 |
| Zhi Gan Cao    | 33.02                     | —                                 |
| (Huai) Niu Xi  | 33.30                     | —                                 |
| Mu Dan Pi      | 34.02                     | —                                 |
| Mi Huan Jun    | 34.64                     | —                                 |
| Jie Geng       | 34.87                     | —                                 |
| Ba Ji Tian     | 35.55                     | —                                 |
| E Zhu          | 35.85                     | —                                 |
| Sha Shen (Bei) | 37.17                     | —                                 |
| Bai He         | 37.62                     | —                                 |
| Lai Fu Zi      | 39.62                     | —                                 |
| Tian Hua Fen   | 39.99                     | —                                 |
| Fang Feng      | 40.13                     | —                                 |
| Chuan Lian Zi  | 40.52                     | —                                 |
| Zi Su Zi       | 40.75                     | —                                 |
| Ju Hua         | 40.86                     | —                                 |
| Yuan Zhi       | 41.75                     | —                                 |
| Xiang Fu       | 42.24                     | —                                 |
| Bai Zhi        | 43.63                     | —                                 |
| Bai Zhu        | 44.05                     | —                                 |
| Jiang Huang    | 48.21                     | —                                 |
| Shan Yao       | 49.20                     | —                                 |
| Sha Ren        | 49.78                     | —                                 |

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                         | 15.93                           |
| 62540     | 62540               | 0.00                         | 15.69                           |
| 63007     | 63007               | 0.00                         | 19.12                           |
| 63008     | 63008               | 0.00                         | 19.12                           |

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 2.4-2022-02

Validated substance/substance group **Dan Dou Chi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60794-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Dan Dou Chi               | 2      | 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 |
| PhytoComm | Dan Dou Chi | G232HS239TK1 | 62793     | 40      | from supplier |
| PhytoComm | Dan Dou Chi | G232HS239TK1 | 62794     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Dou Chi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Dan Dou Chi | G232HS239SK1 | 62714 <sup>†</sup> | 20      |
| PhytoComm | Dan Dou Chi | G232HS239TK1 | 62793 <sup>†</sup> | 20      |
| PhytoComm | Dan Dou Chi | G232HS239TK1 | 62794 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 6              | 151           | 9              | 22 274        |
| <b>Type B</b> | 5              | 68            | 12             | 11 312        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9740 % (> 99.9576 %)  | 94.3750 % (> 92.5000 %) |
| <b>Type B</b> | 99.9405 % (> 99.9083 %)  | 85.0000 % (> 81.2500 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bai Xian Pi     | 3.34                      | —                                 |
| Ce Bai Ye       | 3.98                      | —                                 |
| Guang Huo Xiang | 4.70                      | —                                 |
| Ren Dong Teng   | 6.04                      | —                                 |
| Ling Zhi        | 6.09                      | —                                 |
| Lian Zi         | 8.09                      | —                                 |
| Ye Jiao Teng    | 8.40                      | —                                 |
| Shen Qu         | 8.58                      | —                                 |
| Mao Dong Qing   | 9.35                      | —                                 |
| Tu Fu Ling      | 9.39                      | —                                 |
| She Gan         | 9.54                      | —                                 |
| Yin Yang Huo    | 9.71                      | —                                 |
| Zhu Ling        | 10.08                     | —                                 |
| Hou Po          | 10.30                     | —                                 |
| (Fen) Bi Xie    | 10.49                     | —                                 |
| Jing Jie        | 10.52                     | —                                 |
| Gu Sui Bu       | 10.74                     | —                                 |
| Suan Zao Ren    | 10.93                     | —                                 |
| Yu Jin          | 11.08                     | —                                 |
| Chai Hu         | 11.30                     | —                                 |
| Fu Pen Zi       | 11.94                     | —                                 |
| Dan Shen        | 12.25                     | —                                 |
| Ji Li           | 13.44                     | —                                 |
| Che Qian Zi     | 13.45                     | —                                 |
| He Huan Pi      | 13.55                     | —                                 |
| Shan Yao        | 13.61                     | —                                 |
| Fu Zi           | 13.62                     | —                                 |
| Rou Gui         | 13.62                     | —                                 |
| Gan Cao         | 14.03                     | —                                 |
| Pi Pa Ye        | 14.07                     | —                                 |
| Lu Gen          | 14.35                     | —                                 |
| Qiang Huo       | 14.41                     | —                                 |
| Huo Ma Ren      | 15.61                     | —                                 |
| Gou Teng        | 15.77                     | —                                 |
| Zi Hua Di Ding  | 15.79                     | —                                 |
| Bai Shao Yao    | 15.81                     | —                                 |
| Yan Hu Suo      | 15.82                     | —                                 |
| Fu Ling         | 16.17                     | —                                 |
| Sheng Jiang     | 16.26                     | —                                 |
| Lian Qiao       | 16.43                     | —                                 |
| Ji Xue Teng     | 16.76                     | —                                 |
| Jin Yin Hua     | 17.09                     | —                                 |
| Tian Hua Fen    | 17.49                     | —                                 |
| Gui Zhi         | 17.54                     | —                                 |
| Ma Huang Gen    | 17.61                     | —                                 |
| Mu Zei          | 18.26                     | —                                 |
| Ma Huang        | 19.08                     | —                                 |
| Ban Lan Gen     | 19.19                     | —                                 |

*continued on the next page*

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Hong Jing Tian  | 19.42                     | —                                 |
| Zhe Bei Mu      | 20.18                     | —                                 |
| Jiao Gu Lan     | 20.42                     | —                                 |
| Sha Ren         | 20.54                     | —                                 |
| Tao Ren         | 21.02                     | —                                 |
| Yi Yi Ren       | 21.23                     | —                                 |
| Huang Bai       | 21.89                     | —                                 |
| Bo He           | 21.90                     | —                                 |
| Zhi Gan Cao     | 22.20                     | —                                 |
| Di Gu Pi        | 22.67                     | —                                 |
| Du Zhong        | 23.46                     | —                                 |
| Bai Zi Ren      | 24.18                     | —                                 |
| Ci Wu Jia       | 25.11                     | —                                 |
| Chuang Mu Xiang | 25.17                     | —                                 |
| Zhi Ke          | 25.26                     | —                                 |
| Qing Pi         | 25.54                     | —                                 |
| Ze Xie          | 25.87                     | —                                 |
| Fo Shou         | 26.74                     | —                                 |
| Fu Xiao Mai     | 26.80                     | —                                 |
| Cang Zhu        | 27.32                     | —                                 |
| Huang Lian      | 28.26                     | —                                 |
| Ban Xia (Jiang) | 28.73                     | —                                 |
| Ren Shen        | 29.86                     | —                                 |
| Zhu Ru          | 29.93                     | —                                 |
| Gua Lou         | 32.08                     | —                                 |
| Qing Hao        | 32.35                     | —                                 |
| Mang Xiao       | 32.51                     | —                                 |
| Dang Gui        | 32.57                     | —                                 |
| Bai Jiang Cao   | 34.36                     | —                                 |
| Fu Shen         | 34.44                     | —                                 |
| San Qi          | 34.99                     | —                                 |
| Sang Zhi        | 35.43                     | —                                 |
| Jie Geng        | 35.57                     | —                                 |
| Lai Fu Zi       | 36.45                     | —                                 |
| Long Yan Rou    | 36.95                     | —                                 |
| Xie Bai         | 36.96                     | —                                 |
| Huang Qin       | 37.06                     | —                                 |
| Chi Shao (Yao)  | 38.24                     | —                                 |
| Ban Zhi Lian    | 39.46                     | —                                 |
| Hong Hua        | 41.18                     | —                                 |
| Ku Shen         | 44.34                     | —                                 |
| Gou Qi Zi       | 45.21                     | —                                 |
| Cang Er Zi      | 45.42                     | —                                 |
| Zhi Mu          | 45.78                     | —                                 |
| Bai Zhu         | 47.25                     | —                                 |
| Pu Gong Ying    | 47.52                     | —                                 |
| Mu Gua          | 48.91                     | —                                 |
| Ze Lan          | 49.95                     | —                                 |

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                         | 3.34                            |
| 62714     | 62714               | 0.00                         | 4.15                            |
| 62793     | 62793               | 0.00                         | 3.98                            |
| 62794     | 62794               | 0.00                         | 4.25                            |

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 2.4-2022-02

Validated substance/substance group **Dan Shen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60030-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Dan Shen  | G214HS059SG1 | 62574 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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  | G214H0441121 | 1       |
| Phytocomm | Dan Shen  | G214H0441221 | 1       |
| PhytoComm | Dan Shen  | G214H0441221 | 2       |
| Phytocomm | Dan Shen  | G214H0441322 | 1       |
| PhytoComm | Dan Shen  | G214H0441322 | 1       |
| Phytocomm | Dan Shen  | G214H0441522 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 9              | 848           |

The substance/substance group *Dan 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zi Hua Di Ding  | 4.78                      | —                                 |
| Fu Zi           | 8.81                      | —                                 |
| Huang Bai       | 8.84                      | —                                 |
| Bo He           | 9.23                      | —                                 |
| Gan Cao         | 10.34                     | —                                 |
| Jin Yin Hua     | 10.61                     | —                                 |
| Hou Po          | 10.62                     | —                                 |
| Hong Jing Tian  | 11.14                     | —                                 |
| Yin Yang Huo    | 11.54                     | —                                 |
| Qiang Huo       | 11.58                     | —                                 |
| Chai Hu         | 11.76                     | —                                 |
| Fu Pen Zi       | 11.82                     | —                                 |
| Zhi Ke          | 11.93                     | —                                 |
| Ye Jiao Teng    | 12.42                     | —                                 |
| Jing Jie        | 12.47                     | —                                 |
| Jiao Gu Lan     | 13.01                     | —                                 |
| Sha Ren         | 13.37                     | —                                 |
| Dan Dou Chi     | 14.10                     | —                                 |
| Ce Bai Ye       | 14.81                     | —                                 |
| Ma Huang        | 15.54                     | —                                 |
| Yu Jin          | 16.85                     | —                                 |
| Shan Yao        | 17.16                     | —                                 |
| Bai Xian Pi     | 17.59                     | —                                 |
| Zhi Gan Cao     | 17.63                     | —                                 |
| Mao Dong Qing   | 17.64                     | —                                 |
| Ren Dong Teng   | 18.07                     | —                                 |
| Pi Pa Ye        | 18.27                     | —                                 |
| Ji Xue Teng     | 18.53                     | —                                 |
| Du Zhong        | 18.54                     | —                                 |
| Huang Lian      | 18.58                     | —                                 |
| Guang Huo Xiang | 18.60                     | —                                 |
| Suan Zao Ren    | 18.72                     | —                                 |
| Qing Pi         | 19.14                     | —                                 |
| Tu Fu Ling      | 19.21                     | —                                 |
| Chuang Mu Xiang | 19.27                     | —                                 |
| Tian Hua Fen    | 19.46                     | —                                 |
| Bai Shao Yao    | 20.11                     | —                                 |
| Lian Zi         | 20.33                     | —                                 |
| Bai Jiang Cao   | 20.53                     | —                                 |
| Gu Sui Bu       | 21.48                     | —                                 |
| Che Qian Zi     | 21.65                     | —                                 |
| She Gan         | 21.68                     | —                                 |
| Yan Hu Suo      | 21.70                     | —                                 |
| Di Gu Pi        | 22.02                     | —                                 |
| Qing Hao        | 22.53                     | —                                 |
| Hong Hua        | 22.54                     | —                                 |
| Lu Gen          | 22.63                     | —                                 |
| Ban Lan Gen     | 22.96                     | —                                 |

*continued on the next page*

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Shen Qu         | 23.96                     | —                                 |
| (Fen) Bi Xie    | 24.52                     | —                                 |
| Lian Qiao       | 24.58                     | —                                 |
| Cang Zhu        | 24.82                     | —                                 |
| He Huan Pi      | 25.17                     | —                                 |
| Ji Li           | 25.49                     | —                                 |
| Ling Zhi        | 26.00                     | —                                 |
| Mu Zei          | 26.93                     | —                                 |
| Ren Shen        | 27.19                     | —                                 |
| Chi Shao (Yao)  | 27.51                     | —                                 |
| Gou Teng        | 28.13                     | —                                 |
| Zhu Ling        | 28.86                     | —                                 |
| Pu Gong Ying    | 29.84                     | —                                 |
| Rou Gui         | 29.96                     | —                                 |
| Mang Xiao       | 30.15                     | —                                 |
| Tao Ren         | 31.49                     | —                                 |
| Cang Er Zi      | 31.76                     | —                                 |
| Sang Ye         | 31.89                     | —                                 |
| Huang Qin       | 32.04                     | —                                 |
| Zhe Bei Mu      | 32.14                     | —                                 |
| Huo Ma Ren      | 32.85                     | —                                 |
| Sheng Jiang     | 32.92                     | —                                 |
| Jie Geng        | 33.08                     | —                                 |
| Ze Lan          | 33.20                     | —                                 |
| Ban Zhi Lian    | 33.25                     | —                                 |
| Ma Huang Gen    | 34.24                     | —                                 |
| Fu Ling         | 35.78                     | —                                 |
| Dang Gui        | 36.85                     | —                                 |
| Xie Bai         | 36.86                     | —                                 |
| Sang Zhi        | 37.37                     | —                                 |
| Gui Zhi         | 37.90                     | —                                 |
| Ze Xie          | 38.03                     | —                                 |
| Ku Shen         | 39.12                     | —                                 |
| Long Yan Rou    | 39.24                     | —                                 |
| Gou Qi Zi       | 40.99                     | —                                 |
| San Qi          | 41.15                     | —                                 |
| Ci Wu Jia       | 41.77                     | —                                 |
| Gua Lou         | 41.90                     | —                                 |
| Ban Xia (Jiang) | 43.24                     | —                                 |
| Bai Zi Ren      | 43.25                     | —                                 |
| Xi Xian Cao     | 43.92                     | —                                 |
| Yi Yi Ren       | 44.27                     | —                                 |
| Fo Shou         | 45.83                     | —                                 |
| E Zhu           | 46.00                     | —                                 |
| Niu Bang Zi     | 46.58                     | —                                 |
| Jiang Huang     | 46.85                     | —                                 |
| Zi Su Zi        | 47.07                     | —                                 |
| Fu Shen         | 47.64                     | —                                 |
| Yi Mu Cao       | 48.82                     | —                                 |
| Lai Fu Zi       | 48.84                     | —                                 |
| Nü Zhen Zi      | 49.35                     | —                                 |
| Zhu Ru          | 49.63                     | —                                 |
| Huang Qi        | 49.68                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62573     | 62573               | 0.00                         | 4.78                            |
| 62574     | 62574               | 0.00                         | 8.35                            |

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 2.4-2022-02

Validated substance/substance group **Dan Zhu Ye**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60147-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Dan Zhu Ye                | 1      | 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 | G046H1105921 | 62903     | 40      | from supplier |
| PhytoComm | Dan Zhu Ye | G046H1105921 | 62904     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Zhu Ye*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 | G046H1105921 | 62903 <sup>†</sup> | 20      |
| PhytoComm | Dan Zhu Ye | G046H1105921 | 62904 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Dan Zhu 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Jing Jie         | 15.41                     | —                                 |
| Bu Gu Zhi        | 18.79                     | —                                 |
| Mang Xiao        | 24.15                     | —                                 |
| Sang Ji Shend    | 24.24                     | —                                 |
| Xian Mao         | 25.93                     | —                                 |
| Wu Jia Pi        | 26.12                     | —                                 |
| Yu Xing Cao      | 26.64                     | —                                 |
| Gu Sui Bu        | 28.69                     | —                                 |
| (Sheng) Di Huang | 33.16                     | —                                 |
| Yin Chen Hao     | 34.59                     | —                                 |
| Ge Gen           | 35.70                     | —                                 |
| Sha Ren          | 39.47                     | —                                 |
| Jin Qian Cao     | 39.77                     | —                                 |
| He Shou Wu       | 41.62                     | —                                 |
| Ding Xiang       | 41.68                     | —                                 |
| Tu Si Zi         | 41.74                     | —                                 |
| Wu Zhu Yu        | 43.55                     | —                                 |
| Xuan Fu Hua      | 44.96                     | —                                 |
| He Huan Pi       | 46.51                     | —                                 |
| Hua Shi          | 47.32                     | —                                 |
| Du Zhong         | 52.46                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62903     | 62903                  | 0.00                            | 15.57                              |
| 62904     | 62904                  | 0.00                            | 15.41                              |

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 2.4-2022-02

Validated substance/substance group **Dang Gui**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60003-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Dang Gui                  | 3      | 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  | G022H1306921 | 62963     | 40      | from supplier |
| PhytoComm | Dang Gui  | G022H1306921 | 62964     | 40      | from supplier |
| PhytoComm | Dang Gui  | G022HS290TH1 | 62965     | 40      | from supplier |
| PhytoComm | Dang Gui  | G022HS290TH1 | 62966     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Dang Gui*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Dang Gui  | G022H1306822 | 62414 <sup>†</sup> | 20      |
| PhytoComm | Dang Gui  | G022H1306921 | 62963 <sup>†</sup> | 20      |
| PhytoComm | Dang Gui  | G022H1306921 | 62964 <sup>†</sup> | 20      |
| PhytoComm | Dang Gui  | G022HS290TH1 | 62965 <sup>†</sup> | 20      |
| PhytoComm | Dang Gui  | G022HS290TH1 | 62966 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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  | G022H1306121 | 1       |
| Phytocomm | Dang Gui  | G022H1306422 | 3       |
| PhytoComm | Dang Gui  | G022H1306621 | 4       |
| PhytoComm | Dang Gui  | G13-0784     | 1       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 115           | 5              | 11 277        |
| <b>Type C</b> | 2              | 5             | 7              | 843           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 95.8333 % (> 93.3333 %)  |
| <b>Type C</b> | 99.8450 % (> 99.2573 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Cang Zhu       | 5.06                      | —                                 |
| Jie Geng       | 7.14                      | —                                 |
| Sang Zhi       | 10.92                     | —                                 |
| Chuan Niu Xi   | 11.15                     | —                                 |
| Long Yan Rou   | 11.75                     | —                                 |
| Du Huo         | 11.79                     | —                                 |
| Gou Qi Zi      | 13.27                     | —                                 |
| Ban Lan Gen    | 13.91                     | —                                 |
| Zhi Mu         | 14.60                     | —                                 |
| San Qi         | 14.69                     | —                                 |
| Tian Hua Fen   | 14.74                     | —                                 |
| Bai Shao Yao   | 14.80                     | —                                 |
| Gua Lou        | 14.96                     | —                                 |
| Jin Yin Hua    | 15.12                     | —                                 |
| Mu Zei         | 15.73                     | —                                 |
| Zhe Bei Mu     | 16.27                     | —                                 |
| Ren Dong Teng  | 16.29                     | —                                 |
| Ye Jiao Teng   | 16.45                     | —                                 |
| Ze Xie         | 16.50                     | —                                 |
| Pi Pa Ye       | 16.68                     | —                                 |
| Ren Shen       | 16.69                     | —                                 |
| Hong Jing Tian | 16.95                     | —                                 |
| Lian Qiao      | 17.10                     | —                                 |
| Ju Hua         | 17.27                     | —                                 |
| Shan Yu Rou    | 17.47                     | —                                 |
| Mu Gua         | 18.29                     | —                                 |
| Di Gu Pi       | 18.48                     | —                                 |
| Dan Dou Chi    | 18.49                     | —                                 |
| Fo Shou        | 18.86                     | —                                 |
| Bing Lang      | 18.89                     | —                                 |
| Chuan Lian Zi  | 18.97                     | —                                 |
| He Huan Pi     | 19.51                     | —                                 |
| Xiang Fu       | 19.62                     | —                                 |
| Mu Dan Pi      | 19.65                     | —                                 |
| (Shi) Chang Pu | 19.69                     | —                                 |
| Chen Pi        | 19.73                     | —                                 |
| Zhi Ke         | 19.75                     | —                                 |
| Huang Qi       | 19.82                     | —                                 |
| Jiao Gu Lan    | 19.97                     | —                                 |
| Ma Huang       | 20.12                     | —                                 |
| Shen Qu        | 20.17                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Ku Shen         | 20.31                             | —                                         |
| Chuang Mu Xiang | 20.76                             | —                                         |
| Ling Zhi        | 20.94                             | —                                         |
| (Huai) Niu Xi   | 21.05                             | —                                         |
| Lai Fu Zi       | 21.10                             | —                                         |
| Shan Yao        | 21.13                             | —                                         |
| Suan Zao Ren    | 21.23                             | —                                         |
| Tao Ren         | 21.56                             | —                                         |
| Yuan Zhi        | 21.57                             | —                                         |
| Ci Wu Jia       | 21.61                             | —                                         |
| Ba Ji Tian      | 21.75                             | —                                         |
| Fu Pen Zi       | 22.02                             | —                                         |
| Xie Bai         | 22.40                             | —                                         |
| Hou Po          | 22.42                             | —                                         |
| Ji Li           | 22.57                             | —                                         |
| Bai Zi Ren      | 22.71                             | —                                         |
| Qin Jiao        | 22.79                             | —                                         |
| Bai Zhi         | 22.87                             | —                                         |
| Lian Zi         | 23.08                             | —                                         |
| Lu Gen          | 23.09                             | —                                         |
| Gou Teng        | 23.40                             | —                                         |
| Gan Cao         | 23.66                             | —                                         |
| Long Dan (Cao)  | 24.03                             | —                                         |
| Fu Zi           | 24.09                             | —                                         |
| E Zhu           | 24.30                             | —                                         |
| Fang Feng       | 24.59                             | —                                         |
| Sha Shen (Bei)  | 24.59                             | —                                         |
| Rou Gui         | 24.73                             | —                                         |
| Huang Qin       | 25.19                             | —                                         |
| Zhi Gan Cao     | 25.24                             | —                                         |
| Dan Shen        | 25.38                             | —                                         |
| Mi Huan Jun     | 25.76                             | —                                         |
| Guang Huo Xiang | 25.80                             | —                                         |
| Wu Yao          | 25.87                             | —                                         |
| Gui Zhi         | 26.05                             | —                                         |
| Gu Sui Bu       | 26.29                             | —                                         |
| Sheng Jiang     | 26.30                             | —                                         |
| Ji Xue Teng     | 26.35                             | —                                         |
| Da Zao          | 26.38                             | —                                         |
| Ban Xia (Jiang) | 26.50                             | —                                         |
| Chuan Mu Tong   | 26.69                             | —                                         |
| Mang Xiao       | 26.76                             | —                                         |
| Huo Ma Ren      | 27.10                             | —                                         |
| Tu Fu Ling      | 27.17                             | —                                         |
| Yin Yang Huo    | 27.27                             | —                                         |
| Zhu Ru          | 27.50                             | —                                         |
| Fu Ling         | 28.49                             | —                                         |
| Bai Zhu         | 28.87                             | —                                         |
| Bai He          | 29.42                             | —                                         |
| Sha Ren         | 30.40                             | —                                         |
| Che Qian Zi     | 30.79                             | —                                         |
| Yan Hu Suo      | 30.92                             | —                                         |
| Jiang Huang     | 31.02                             | —                                         |
| Zi Hua Di Ding  | 31.18                             | —                                         |
| Bai Xian Pi     | 31.41                             | —                                         |
| Zi Su Zi        | 31.49                             | —                                         |
| Mao Dong Qing   | 32.00                             | —                                         |
| Chai Hu         | 32.61                             | —                                         |
| Fu Xiao Mai     | 33.12                             | —                                         |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Qiang Huo           | 34.29                     | —                                 |
| (Fen) Bi Xie        | 34.89                     | —                                 |
| She Gan             | 35.38                     | —                                 |
| Ce Bai Ye           | 35.46                     | —                                 |
| Yi Yi Ren           | 35.92                     | —                                 |
| Chi Shao (Yao)      | 36.27                     | —                                 |
| Ma Huang Gen        | 36.42                     | —                                 |
| Hong Hua            | 36.55                     | —                                 |
| Yu Jin              | 38.08                     | —                                 |
| Bai Hua She She Cao | 38.12                     | —                                 |
| He Shou Wu          | 38.41                     | —                                 |
| (Bai) Dou Kou       | 39.58                     | —                                 |
| Ban Zhi Lian        | 39.91                     | —                                 |
| Bo He               | 40.16                     | —                                 |
| Gan Jiang           | 40.32                     | —                                 |
| Qing Pi             | 40.42                     | —                                 |
| Fu Shen             | 41.39                     | —                                 |
| Zhu Ling            | 41.47                     | —                                 |
| Huang Lian          | 42.42                     | —                                 |
| Jing Jie            | 43.04                     | —                                 |
| Xu Duan             | 43.36                     | —                                 |
| Sang Ji Shend       | 43.59                     | —                                 |
| Xiao Hui Xiang      | 44.12                     | —                                 |
| Huang Bai           | 44.38                     | —                                 |
| Niu Bang Zi         | 45.63                     | —                                 |
| Xin Yi              | 45.77                     | —                                 |
| Cang Er Zi          | 46.24                     | —                                 |
| Ge Gen              | 47.52                     | —                                 |
| Du Zhong            | 48.16                     | —                                 |
| Wu Zhu Yu           | 49.94                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62413     | 62413                  | 0.00                            | 10.92                              |
| 62414     | 62414                  | 0.00                            | 11.19                              |
| 62963     | 62963                  | 0.00                            | 11.93                              |
| 62964     | 62964                  | 0.00                            | 11.15                              |
| 62965     | 62965                  | 0.00                            | 5.06                               |
| 62966     | 62966                  | 0.00                            | 5.37                               |

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 2.4-2022-02

Validated substance/substance group **Di Fu Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002264-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Di Fu Zi  | G131H0605921 | 62738 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mang Xiao       | 23.52                     | —                                 |
| Guang Huo Xiang | 32.49                     | —                                 |
| Hua Shi         | 46.07                     | —                                 |
| Wu Mei          | 53.65                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62737     | 62737                  | 0.00                            | 23.54                              |
| 62738     | 62738                  | 0.00                            | 23.52                              |

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 2.4-2022-02

Validated substance/substance group **Di Gu Pi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60036-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | 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 |
| PhytoComm | Di Gu Pi  | G149H0601922 | 62997     | 40      | from supplier |
| PhytoComm | Di Gu Pi  | G149H0601922 | 62998     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G149H0601821 | 62347 <sup>†</sup> | 20      |
| PhytoComm | Di Gu Pi  | G149H0601821 | 62348 <sup>†</sup> | 20      |
| PhytoComm | Di Gu Pi  | G149HS101SK1 | 62691 <sup>†</sup> | 20      |
| PhytoComm | Di Gu Pi  | G149HS101SK1 | 62692 <sup>†</sup> | 20      |
| PhytoComm | Di Gu Pi  | G149H0601922 | 62997 <sup>†</sup> | 20      |
| PhytoComm | Di Gu Pi  | G149H0601922 | 62998 <sup>†</sup> | 20      |



- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 238           | 2              | 22 200        |
| <b>Type B</b> | 7              | 118           | 2              | 11 270        |
| <b>Type C</b> | 3              | 1             | 3              | 850           |

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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 99.1667 % (> 97.9167 %) |
| <b>Type B</b> | 99.9405 % (> 99.9082 %)  | 98.3333 % (> 95.8333 %) |
| <b>Type C</b> | 99.6589 % (> 99.0724 %)  | n/a (n/a)               |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| He Huan Pi      | 4.72                      | —                                 |
| Sheng Jiang     | 4.76                      | —                                 |
| Gui Zhi         | 5.58                      | —                                 |
| Ci Wu Jia       | 5.85                      | —                                 |
| Sha Shen (Bei)  | 5.86                      | —                                 |
| Zhu Ru          | 6.94                      | —                                 |
| Bai Shao Yao    | 7.60                      | —                                 |
| Ban Xia (Jiang) | 8.00                      | —                                 |
| Fu Xiao Mai     | 9.11                      | —                                 |
| Sang Zhi        | 9.35                      | —                                 |
| Lai Fu Zi       | 9.52                      | —                                 |
| Tao Ren         | 9.69                      | —                                 |
| Bai Zi Ren      | 10.45                     | —                                 |
| Yi Yi Ren       | 10.64                     | —                                 |
| Rou Gui         | 10.93                     | —                                 |
| Shen Qu         | 11.00                     | —                                 |
| Zhe Bei Mu      | 11.03                     | —                                 |
| Lian Zi         | 11.76                     | —                                 |
| Gan Jiang       | 11.89                     | —                                 |
| Fu Ling         | 12.88                     | —                                 |
| Ji Li           | 13.06                     | —                                 |
| Chuan Lian Zi   | 13.90                     | —                                 |
| Gou Teng        | 14.05                     | —                                 |
| E Zhu           | 14.42                     | —                                 |
| Mi Huan Jun     | 14.48                     | —                                 |
| Ye Jiao Teng    | 14.53                     | —                                 |
| Huo Ma Ren      | 14.66                     | —                                 |
| Fo Shou         | 15.01                     | —                                 |
| Ling Zhi        | 15.16                     | —                                 |
| Mu Zei          | 15.18                     | —                                 |
| Tian Hua Fen    | 15.24                     | —                                 |
| Bai Xian Pi     | 15.89                     | —                                 |
| Ji Xue Teng     | 16.79                     | —                                 |
| Jie Geng        | 17.42                     | —                                 |
| Dang Gui        | 17.65                     | —                                 |
| Chuan Mu Tong   | 17.67                     | —                                 |
| Zi Su Zi        | 17.91                     | —                                 |
| Pi Pa Ye        | 19.39                     | —                                 |
| Shan Yao        | 19.59                     | —                                 |
| Gu Sui Bu       | 19.78                     | —                                 |
| Jiang Huang     | 20.20                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| (Huai) Niu Xi   | 21.02                             | —                                         |
| Ze Xie          | 21.15                             | —                                         |
| Lu Gen          | 21.16                             | —                                         |
| Ma Huang Gen    | 21.19                             | —                                         |
| Cang Er Zi      | 22.11                             | —                                         |
| Lian Qiao       | 22.14                             | —                                         |
| Ren Dong Teng   | 22.63                             | —                                         |
| Long Dan (Cao)  | 22.74                             | —                                         |
| Tu Fu Ling      | 23.29                             | —                                         |
| Yan Hu Suo      | 23.92                             | —                                         |
| (Bai) Dou Kou   | 23.97                             | —                                         |
| Suan Zao Ren    | 23.99                             | —                                         |
| Yu Jin          | 24.00                             | —                                         |
| Mang Xiao       | 24.01                             | —                                         |
| Chi Shao (Yao)  | 24.29                             | —                                         |
| Fu Shen         | 24.70                             | —                                         |
| Bai Zhu         | 24.72                             | —                                         |
| Jin Yin Hua     | 25.27                             | —                                         |
| Sha Ren         | 25.89                             | —                                         |
| Qiang Huo       | 25.93                             | —                                         |
| Niu Bang Zi     | 25.98                             | —                                         |
| Huang Qi        | 26.47                             | —                                         |
| Zhu Ling        | 26.57                             | —                                         |
| Zhi Gan Cao     | 26.68                             | —                                         |
| Bai He          | 27.27                             | —                                         |
| Zhi Mu          | 27.50                             | —                                         |
| Mu Gua          | 28.12                             | —                                         |
| Cang Zhu        | 29.41                             | —                                         |
| Fu Zi           | 29.52                             | —                                         |
| Gua Lou         | 29.85                             | —                                         |
| (Fen) Bi Xie    | 29.98                             | —                                         |
| Chuan Niu Xi    | 30.02                             | —                                         |
| Fu Pen Zi       | 30.14                             | —                                         |
| Ce Bai Ye       | 30.59                             | —                                         |
| Chai Hu         | 31.21                             | —                                         |
| Jiao Gu Lan     | 31.33                             | —                                         |
| Ren Shen        | 31.52                             | —                                         |
| Dan Dou Chi     | 31.64                             | —                                         |
| Qin Jiao        | 31.86                             | —                                         |
| Ban Zhi Lian    | 32.24                             | —                                         |
| Dan Shen        | 32.33                             | —                                         |
| Zhi Ke          | 32.62                             | —                                         |
| Ku Shen         | 32.66                             | —                                         |
| San Qi          | 32.68                             | —                                         |
| Yuan Zhi        | 32.89                             | —                                         |
| Chen Pi         | 32.90                             | —                                         |
| Bo He           | 33.02                             | —                                         |
| She Gan         | 33.78                             | —                                         |
| Bai Zhi         | 34.01                             | —                                         |
| Gan Cao         | 34.58                             | —                                         |
| Hou Po          | 34.60                             | —                                         |
| Da Zao          | 35.06                             | —                                         |
| Huang Qin       | 35.30                             | —                                         |
| Xiang Fu        | 35.49                             | —                                         |
| Zi Hua Di Ding  | 35.53                             | —                                         |
| Mao Dong Qing   | 35.65                             | —                                         |
| Yin Yang Huo    | 35.68                             | —                                         |
| Ban Lan Gen     | 36.11                             | —                                         |
| (Shi) Chang Pu  | 36.99                             | —                                         |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Che Qian Zi         | 38.30                     | —                                 |
| Xiao Hui Xiang      | 38.30                     | —                                 |
| Pu Gong Ying        | 38.36                     | —                                 |
| Chuang Mu Xiang     | 38.66                     | —                                 |
| Xie Bai             | 39.78                     | —                                 |
| Gou Qi Zi           | 39.79                     | —                                 |
| Guang Huo Xiang     | 40.26                     | —                                 |
| Bai Hua She She Cao | 40.47                     | —                                 |
| Shan Yu Rou         | 41.05                     | —                                 |
| Huang Lian          | 41.14                     | —                                 |
| Ma Huang            | 41.54                     | —                                 |
| Jing Jie            | 42.98                     | —                                 |
| Huang Bai           | 43.07                     | —                                 |
| Du Huo              | 43.11                     | —                                 |
| Du Zhong            | 43.43                     | —                                 |
| Qing Pi             | 44.10                     | —                                 |
| Hong Jing Tian      | 44.82                     | —                                 |
| Yi Mu Cao           | 45.26                     | —                                 |
| Dong Gua Zi         | 46.00                     | —                                 |
| Mu Dan Pi           | 46.76                     | —                                 |
| Sang Ji Shend       | 47.32                     | —                                 |
| Ba Ji Tian          | 47.46                     | —                                 |
| Long Yan Rou        | 48.74                     | —                                 |
| Wu Yao              | 49.35                     | —                                 |
| Ju Hua              | 49.85                     | —                                 |
| Ze Lan              | 49.91                     | —                                 |
| Sang Ye             | 50.01                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62347     | 62347                  | 0.00                            | 9.35                               |
| 62348     | 62348                  | 0.00                            | 9.73                               |
| 62691     | 62691                  | 0.00                            | 5.12                               |
| 62692     | 62692                  | 0.00                            | 4.72                               |
| 62997     | 62997                  | 0.00                            | 5.86                               |
| 62998     | 62998                  | 0.00                            | 6.51                               |

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 2.4-2022-02

Validated substance/substance group **Ding Xiang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50309-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Ding Xiang; Caryophylli flos

### Special notes

When selecting the *Ding Xiang* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ding Xiang                | 1      | 0      | 0      |

### Second-stage model

For differentiation of the substance/substance group *Ding 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 *Ding Xiang*:

| Supplier  | Substance  | Batch        | Sample ID | Spectra | Certificate   |
|-----------|------------|--------------|-----------|---------|---------------|
| PhytoComm | Ding Xiang | G058H0210021 | 63013     | 40      | from supplier |
| PhytoComm | Ding Xiang | G058H0210021 | 63014     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Ding Xiang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ding 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 | Ding Xiang | G058H0210021 | 63013 <sup>†</sup> | 20      |
| PhytoComm | Ding Xiang | G058H0210021 | 63014 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 *Ding Xiang*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier  | Substance  | Batch        | Spectra |
|-----------|------------|--------------|---------|
| Phytocomm | Ding Xiang | G058H0210021 | 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 *Ding 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 *Ding 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

The substance/substance group *Ding 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ding 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Mang Xiao        | 18.87                     | —                                 |
| (Sheng) Di Huang | 24.66                     | —                                 |
| Yu Xing Cao      | 25.20                     | —                                 |
| Xian Mao         | 25.26                     | —                                 |
| Jin Qian Cao     | 27.49                     | —                                 |
| Jing Jie         | 30.61                     | —                                 |
| Du Zhong         | 34.31                     | —                                 |
| Sang Ye          | 34.62                     | —                                 |
| Ge Gen           | 35.86                     | —                                 |
| Shu Di (Huang)   | 38.48                     | —                                 |
| Wu Jia Pi        | 39.59                     | —                                 |
| Dan Zhu Ye       | 39.62                     | —                                 |
| Sang Ji Shend    | 41.87                     | —                                 |
| Guang Huo Xiang  | 46.18                     | —                                 |
| Hua Shi          | 47.02                     | —                                 |
| Gou Teng         | 50.01                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ding 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 63013     | 63013                  | 0.00                            | 18.98                              |
| 63014     | 63014                  | 0.00                            | 18.87                              |

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 2.4-2022-02

Validated substance/substance group **Dong Gua Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60202-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Dong Gua Zi | G049H0551822 | 62514 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Ku Shen        | 29.84                     | —                                 |
| Shan Yao       | 30.83                     | —                                 |
| Shen Qu        | 34.58                     | —                                 |
| Mang Xiao      | 37.27                     | —                                 |
| Di Gu Pi       | 47.16                     | —                                 |
| Cang Er Zi     | 48.60                     | —                                 |
| Bai Shao Yao   | 49.33                     | —                                 |
| Chi Shao (Yao) | 49.62                     | —                                 |
| Sang Zhi       | 50.01                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62513     | 62513                  | 0.00                            | 29.84                              |
| 62514     | 62514                  | 0.00                            | 30.03                              |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Du Huo**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10005053-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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    | G021H1610921 | 63021     | 40      | from supplier |
| PhytoComm | Du Huo    | G021H1610921 | 63022     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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    | G021H1610921 | 63021 <sup>†</sup> | 20      |
| PhytoComm | Du Huo    | G021H1610921 | 63022 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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    | G021H1610421 | 2       |
| Phytocomm | Du Huo    | g021h610221  | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 3              | 854           |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Dang Gui            | 8.95                      | —                                 |
| Chuan Niu Xi        | 10.47                     | —                                 |
| Chuan Lian Zi       | 18.75                     | —                                 |
| Bing Lang           | 18.81                     | —                                 |
| Sang Zhi            | 19.76                     | —                                 |
| Huang Qi            | 20.05                     | —                                 |
| Shan Yu Rou         | 20.39                     | —                                 |
| Ju Hua              | 21.37                     | —                                 |
| (Shi) Chang Pu      | 21.40                     | —                                 |
| Bai Zhi             | 21.61                     | —                                 |
| Chen Pi             | 21.93                     | —                                 |
| Xiang Fu            | 23.05                     | —                                 |
| Zhi Gan Cao         | 25.08                     | —                                 |
| Tian Hua Fen        | 25.83                     | —                                 |
| (Huai) Niu Xi       | 26.21                     | —                                 |
| Mu Dan Pi           | 26.42                     | —                                 |
| Mang Xiao           | 27.35                     | —                                 |
| Fang Feng           | 27.51                     | —                                 |
| Ba Ji Tian          | 27.66                     | —                                 |
| E Zhu               | 28.06                     | —                                 |
| Jie Geng            | 28.60                     | —                                 |
| Zi Su Zi            | 30.83                     | —                                 |
| Bai Zhu             | 31.35                     | —                                 |
| Di Gu Pi            | 31.51                     | —                                 |
| Mi Huan Jun         | 31.53                     | —                                 |
| Wu Yao              | 32.29                     | —                                 |
| He Huan Pi          | 32.84                     | —                                 |
| Sha Ren             | 32.87                     | —                                 |
| Jiang Huang         | 33.19                     | —                                 |
| Shan Yao            | 33.22                     | —                                 |
| Qin Jiao            | 33.69                     | —                                 |
| Lian Qiao           | 33.90                     | —                                 |
| Da Zao              | 34.42                     | —                                 |
| Yan Hu Suo          | 35.60                     | —                                 |
| Zhi Ke              | 36.21                     | —                                 |
| Lai Fu Zi           | 36.49                     | —                                 |
| Sha Shen (Bei)      | 36.69                     | —                                 |
| Chi Shao (Yao)      | 37.93                     | —                                 |
| Bai Hua She She Cao | 38.01                     | —                                 |
| Gu Sui Bu           | 38.43                     | —                                 |
| (Bai) Dou Kou       | 38.93                     | —                                 |
| Long Dan (Cao)      | 39.50                     | —                                 |
| Ku Shen             | 40.12                     | —                                 |
| Yuan Zhi            | 42.09                     | —                                 |
| Gan Jiang           | 42.50                     | —                                 |
| Xu Duan             | 43.27                     | —                                 |
| Niu Bang Zi         | 44.31                     | —                                 |
| Xiao Hui Xiang      | 44.59                     | —                                 |
| Chuan Mu Tong       | 44.60                     | —                                 |
| Sang Ji Shend       | 45.24                     | —                                 |
| He Shou Wu          | 45.47                     | —                                 |
| Bai He              | 46.81                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Hong Jing Tian | 47.03                     | —                                 |
| Huang Lian     | 47.76                     | —                                 |
| Xin Yi         | 48.24                     | —                                 |
| Cang Er Zi     | 48.68                     | —                                 |
| Pu Gong Ying   | 48.73                     | —                                 |
| Jin Yin Hua    | 49.06                     | —                                 |
| Mao Dong Qing  | 49.09                     | —                                 |
| Du Zhong       | 49.22                     | —                                 |
| Tu Fu Ling     | 49.34                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 63021     | 63021                  | 0.00                            | 8.95                               |
| 63022     | 63022                  | 0.00                            | 8.98                               |

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 2.4-2022-02

Validated substance/substance group **Du Zhong**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60214-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Du Zhong  | G101H0736821 | 62336 <sup>†</sup> | 20      |
| PhytoComm | Du Zhong  | G101HS133SH1 | 62579 <sup>†</sup> | 20      |
| PhytoComm | Du Zhong  | G101HS133SH1 | 62580 <sup>†</sup> | 20      |
| PhytoComm | Du Zhong  | G101HS133SP1 | 62729 <sup>†</sup> | 20      |
| PhytoComm | Du Zhong  | G101HS133SP1 | 62730 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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  | G101H0736522 | 5       |
| Phytocomm | Du Zhong  | g101h076521  | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 1              | 118           | 2              | 11 276        |
| <b>Type C</b> | 0              | 1             | 7              | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 99.9926 % (> 99.9603 %)  | 98.3333 % (> 95.8333 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8253 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Qing Hao        | 4.21                      | —                                 |
| Mao Dong Qing   | 4.82                      | —                                 |
| Yu Jin          | 5.12                      | —                                 |
| Qiang Huo       | 7.50                      | —                                 |
| Chai Hu         | 7.77                      | —                                 |
| Sha Ren         | 7.82                      | —                                 |
| Ling Zhi        | 8.18                      | —                                 |
| Bo He           | 8.29                      | —                                 |
| Hou Po          | 9.16                      | —                                 |
| Jing Jie        | 9.22                      | —                                 |
| Bai Jiang Cao   | 9.93                      | —                                 |
| Zi Hua Di Ding  | 10.06                     | —                                 |
| Yin Yang Huo    | 11.27                     | —                                 |
| Bai Xian Pi     | 11.29                     | —                                 |
| Fu Zi           | 11.54                     | —                                 |
| Dan Dou Chi     | 12.61                     | —                                 |
| Qing Pi         | 13.50                     | —                                 |
| Yan Hu Suo      | 13.85                     | —                                 |
| Jiao Gu Lan     | 14.25                     | —                                 |
| Ye Jiao Teng    | 14.84                     | —                                 |
| Shen Qu         | 15.07                     | —                                 |
| Shan Yao        | 15.63                     | —                                 |
| Ce Bai Ye       | 15.71                     | —                                 |
| Che Qian Zi     | 16.59                     | —                                 |
| Dan Shen        | 16.85                     | —                                 |
| Fu Pen Zi       | 16.92                     | —                                 |
| Pi Pa Ye        | 17.08                     | —                                 |
| Ji Li           | 17.39                     | —                                 |
| Tu Fu Ling      | 18.14                     | —                                 |
| Ren Dong Teng   | 18.39                     | —                                 |
| Yin Chen Hao    | 18.79                     | —                                 |
| Hong Jing Tian  | 18.87                     | —                                 |
| Tian Hua Fen    | 19.05                     | —                                 |
| Zhu Ling        | 19.21                     | —                                 |
| Wu Jia Pi       | 19.38                     | —                                 |
| Huang Bai       | 19.56                     | —                                 |
| Lian Zi         | 19.65                     | —                                 |
| Guang Huo Xiang | 19.95                     | —                                 |
| Huang Lian      | 21.59                     | —                                 |
| Ma Huang        | 21.71                     | —                                 |
| Ji Xue Teng     | 22.06                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Pu Gong Ying    | 22.11                             | —                                         |
| Gu Sui Bu       | 22.27                             | —                                         |
| Zhi Ke          | 22.44                             | —                                         |
| Jin Yin Hua     | 23.64                             | —                                         |
| Ze Lan          | 24.03                             | —                                         |
| Xi Xian Cao     | 24.11                             | —                                         |
| Lian Qiao       | 24.18                             | —                                         |
| Mang Xiao       | 24.70                             | —                                         |
| Di Gu Pi        | 25.71                             | —                                         |
| Ban Lan Gen     | 26.00                             | —                                         |
| He Huan Pi      | 26.14                             | —                                         |
| Bu Gu Zhi       | 26.24                             | —                                         |
| Bai Shao Yao    | 26.48                             | —                                         |
| Sang Ji Shend   | 26.67                             | —                                         |
| Ren Shen        | 27.38                             | —                                         |
| Suan Zao Ren    | 27.76                             | —                                         |
| Gou Teng        | 28.20                             | —                                         |
| Nü Zhen Zi      | 28.29                             | —                                         |
| Ma Huang Gen    | 28.97                             | —                                         |
| He Shou Wu      | 29.50                             | —                                         |
| (Fen) Bi Xie    | 30.10                             | —                                         |
| Dan Zhu Ye      | 30.38                             | —                                         |
| Sheng Jiang     | 30.41                             | —                                         |
| Zhe Bei Mu      | 30.42                             | —                                         |
| Xuan Fu Hua     | 30.58                             | —                                         |
| Rou Gui         | 30.94                             | —                                         |
| Jin Qian Cao    | 31.22                             | —                                         |
| Gan Cao         | 31.55                             | —                                         |
| Sang Ye         | 31.70                             | —                                         |
| Mu Zei          | 32.79                             | —                                         |
| Chuang Mu Xiang | 32.80                             | —                                         |
| She Gan         | 32.90                             | —                                         |
| Yi Mu Cao       | 33.00                             | —                                         |
| Fu Ling         | 33.03                             | —                                         |
| Ding Xiang      | 33.30                             | —                                         |
| Lu Gen          | 33.33                             | —                                         |
| Sang Bai Pi     | 33.43                             | —                                         |
| Wu Zhu Yu       | 35.16                             | —                                         |
| Yi Yi Ren       | 35.20                             | —                                         |
| E Zhu           | 35.48                             | —                                         |
| Hong Hua        | 35.50                             | —                                         |
| Zhi Gan Cao     | 35.66                             | —                                         |
| Huo Ma Ren      | 35.80                             | —                                         |
| Cang Er Zi      | 35.89                             | —                                         |
| Gui Zhi         | 36.39                             | —                                         |
| Jiang Huang     | 37.12                             | —                                         |
| Zhi Shi         | 38.41                             | —                                         |
| Ban Zhi Lian    | 39.29                             | —                                         |
| Yu Xing Cao     | 39.39                             | —                                         |
| Cang Zhu        | 39.39                             | —                                         |
| Tao Ren         | 39.78                             | —                                         |
| Chi Shao (Yao)  | 39.86                             | —                                         |
| Sang Zhi        | 40.30                             | —                                         |
| Xin Yi          | 40.82                             | —                                         |
| Ge Gen          | 41.98                             | —                                         |
| Jie Geng        | 42.41                             | —                                         |
| Xie Bai         | 43.00                             | —                                         |
| Bai Zi Ren      | 43.41                             | —                                         |
| Huang Qin       | 44.48                             | —                                         |

*continued on the next page*

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ze Xie          | 44.70                     | —                                 |
| Xuan Shen       | 44.74                     | —                                 |
| Zhu Ru          | 44.93                     | —                                 |
| Niu Bang Zi     | 45.70                     | —                                 |
| Ban Xia (Jiang) | 46.19                     | —                                 |
| Ci Wu Jia       | 46.63                     | —                                 |
| Wu Wei Zi       | 47.81                     | —                                 |
| Xia Ku Cao      | 48.56                     | —                                 |
| Gua Lou         | 48.69                     | —                                 |
| Sha Shen (Bei)  | 49.21                     | —                                 |
| Fu Xiao Mai     | 49.32                     | —                                 |
| Hua Shi         | 49.36                     | —                                 |
| Dang Gui        | 49.44                     | —                                 |
| San Qi          | 49.54                     | —                                 |
| Fu Shen         | 49.61                     | —                                 |
| Han Lian Cao    | 51.41                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62335     | 62335                  | 0.00                            | 12.92                              |
| 62336     | 62336                  | 0.00                            | 13.29                              |
| 62579     | 62579                  | 0.00                            | 4.82                               |
| 62580     | 62580                  | 0.00                            | 5.01                               |
| 62729     | 62729                  | 0.00                            | 4.21                               |
| 62730     | 62730                  | 0.00                            | 5.01                               |

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 2.4-2022-02

Validated substance/substance group **E Zhu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50344-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | E Zhu     | G083H1110821 | 62516 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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     | G083H1110222 | 2       |
| Phytocomm | E Zhu     | h1110021     | 1       |
| Phytocomm | E Zhu     | H1110021     | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 2              | 0             | 4              | 851           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 99.8062 % (> 99.2197 %)  | n/a (n/a)                |

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

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

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

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Jiang Huang         | 17.34                     | —                                 |
| Cang Er Zi          | 17.40                     | —                                 |
| Sha Shen (Bei)      | 17.71                     | —                                 |
| Gan Jiang           | 19.16                     | —                                 |
| (Bai) Dou Kou       | 22.03                     | —                                 |
| Di Gu Pi            | 22.09                     | —                                 |
| Mang Xiao           | 23.19                     | —                                 |
| Sha Ren             | 23.72                     | —                                 |
| He Huan Pi          | 24.53                     | —                                 |
| Zi Su Zi            | 24.55                     | —                                 |
| Niu Bang Zi         | 26.51                     | —                                 |
| Lai Fu Zi           | 27.93                     | —                                 |
| Chuan Lian Zi       | 27.98                     | —                                 |
| Sang Zhi            | 29.22                     | —                                 |
| Yan Hu Suo          | 31.46                     | —                                 |
| Shan Yao            | 32.52                     | —                                 |
| Chen Pi             | 33.04                     | —                                 |
| Mi Huan Jun         | 35.30                     | —                                 |
| Suan Zao Ren        | 38.77                     | —                                 |
| Chuan Mu Tong       | 39.25                     | —                                 |
| Dang Gui            | 39.56                     | —                                 |
| Bai Hua She She Cao | 39.81                     | —                                 |
| (Huai) Niu Xi       | 40.43                     | —                                 |
| Huang Lian          | 40.86                     | —                                 |
| Fu Ling             | 40.99                     | —                                 |
| Rou Gui             | 41.34                     | —                                 |
| Long Dan (Cao)      | 41.71                     | —                                 |
| Du Huo              | 42.75                     | —                                 |
| Wang Bu Liu Xing    | 42.98                     | —                                 |
| Ban Zhi Lian        | 43.30                     | —                                 |
| Tian Hua Fen        | 44.17                     | —                                 |
| Lian Qiao           | 44.46                     | —                                 |
| Da Zao              | 44.72                     | —                                 |
| Du Zhong            | 44.89                     | —                                 |
| Chuan Niu Xi        | 46.63                     | —                                 |
| Xi Xian Cao         | 47.40                     | —                                 |
| Zhi Ke              | 47.76                     | —                                 |
| Huang Qi            | 47.94                     | —                                 |
| Qiang Huo           | 48.09                     | —                                 |
| Xiang Fu            | 48.23                     | —                                 |
| Xin Yi              | 48.67                     | —                                 |
| Lian Zi             | 49.26                     | —                                 |

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                         | 17.34                           |
| 62516     | 62516               | 0.00                         | 17.42                           |

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 2.4-2022-02

Validated substance/substance group **Fang Feng**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50261-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Fang Feng; Saposhnikoviae radix

### Special notes

When selecting the *Fang Feng* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G217H0728922 | 62859     | 40      | from supplier |
| PhytoComm | Fang Feng | G217H0728922 | 62860     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G217H0728922 | 62859 <sup>†</sup> | 20      |
| PhytoComm | Fang Feng | G217H0728922 | 62860 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | g217h0728221 | 1       |
| Phytocomm | Fang Feng | G217H0728521 | 3       |
| PhytoComm | Fang Feng | G217H0728521 | 2       |
| Phytocomm | Fang Feng | g217h0728923 | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 1              | 0             | 7              | 849           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Chen Pi        | 15.74                     | —                                 |
| Ju Hua         | 19.74                     | —                                 |
| Hong Jing Tian | 20.45                     | —                                 |
| Mang Xiao      | 25.92                     | —                                 |
| Chuan Lian Zi  | 28.01                     | —                                 |
| Shan Yu Rou    | 28.61                     | —                                 |
| Chuan Niu Xi   | 28.65                     | —                                 |
| Gu Sui Bu      | 28.67                     | —                                 |
| Sang Bai Pi    | 29.58                     | —                                 |
| Sha Ren        | 30.23                     | —                                 |
| Dang Gui       | 31.08                     | —                                 |
| (Shi) Chang Pu | 31.87                     | —                                 |
| Xiang Fu       | 32.03                     | —                                 |
| Yi Mu Cao      | 32.53                     | —                                 |
| Wu Zhu Yu      | 33.32                     | —                                 |
| He Huan Pi     | 34.22                     | —                                 |
| Sang Ji Shend  | 34.72                     | —                                 |
| Huang Qi       | 35.13                     | —                                 |
| Ku Shen        | 36.08                     | —                                 |
| Jiang Huang    | 36.42                     | —                                 |
| Ba Ji Tian     | 36.58                     | —                                 |
| Wu Yao         | 36.99                     | —                                 |
| Mu Dan Pi      | 37.42                     | —                                 |
| Bing Lang      | 38.63                     | —                                 |
| Zhi Gan Cao    | 40.61                     | —                                 |
| Ge Gen         | 41.50                     | —                                 |
| Yin Chen Hao   | 41.93                     | —                                 |
| Sang Zhi       | 44.22                     | —                                 |
| Xu Duan        | 44.43                     | —                                 |
| He Shou Wu     | 44.57                     | —                                 |
| Shan Yao       | 44.79                     | —                                 |
| Nü Zhen Zi     | 45.28                     | —                                 |
| Chi Shao (Yao) | 45.29                     | —                                 |
| Xiao Hui Xiang | 45.82                     | —                                 |
| Cang Er Zi     | 46.00                     | —                                 |
| Xin Yi         | 47.18                     | —                                 |
| Hu Zhang       | 48.14                     | —                                 |
| E Zhu          | 48.68                     | —                                 |
| Bu Gu Zhi      | 49.48                     | —                                 |
| Tian Hua Fen   | 49.51                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62859     | 62859               | 0.00                         | 15.74                           |
| 62860     | 62860               | 0.00                         | 15.96                           |

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



# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Fo Shou**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60119-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Fo Shou   | G307HS159RQ1 | 62420 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 0              | 857           |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ye Jiao Teng    | 9.41                      | —                                 |
| Gua Lou         | 9.65                      | —                                 |
| Mu Zei          | 10.79                     | —                                 |
| Bai Shao Yao    | 11.53                     | —                                 |
| Tao Ren         | 11.83                     | —                                 |
| Rou Gui         | 12.87                     | —                                 |
| He Huan Pi      | 13.08                     | —                                 |
| Ze Xie          | 13.78                     | —                                 |
| Di Gu Pi        | 14.08                     | —                                 |
| Shen Qu         | 14.37                     | —                                 |
| Jin Yin Hua     | 14.81                     | —                                 |
| Lai Fu Zi       | 15.02                     | —                                 |
| Lian Zi         | 15.10                     | —                                 |
| Ci Wu Jia       | 15.32                     | —                                 |
| Ban Xia (Jiang) | 15.49                     | —                                 |
| Gui Zhi         | 15.85                     | —                                 |
| Zhe Bei Mu      | 15.88                     | —                                 |
| Cang Zhu        | 16.65                     | —                                 |
| Pi Pa Ye        | 16.67                     | —                                 |
| Bai Zi Ren      | 16.70                     | —                                 |
| Ling Zhi        | 16.70                     | —                                 |
| Jie Geng        | 16.75                     | —                                 |
| Zhi Mu          | 16.86                     | —                                 |
| Ji Li           | 17.05                     | —                                 |
| Sheng Jiang     | 17.09                     | —                                 |
| Tian Hua Fen    | 17.12                     | —                                 |
| Bai Xian Pi     | 18.07                     | —                                 |
| Fu Xiao Mai     | 18.41                     | —                                 |
| Lu Gen          | 18.50                     | —                                 |
| Fu Ling         | 18.78                     | —                                 |
| Gou Teng        | 18.91                     | —                                 |
| Gu Sui Bu       | 19.18                     | —                                 |
| Ren Dong Teng   | 19.48                     | —                                 |
| Tu Fu Ling      | 19.61                     | —                                 |
| Dang Gui        | 19.74                     | —                                 |
| Zhu Ru          | 20.53                     | —                                 |
| Suan Zao Ren    | 20.63                     | —                                 |
| San Qi          | 20.71                     | —                                 |
| Ban Lan Gen     | 20.82                     | —                                 |
| Huo Ma Ren      | 21.37                     | —                                 |
| Ji Xue Teng     | 22.68                     | —                                 |
| Shan Yao        | 23.16                     | —                                 |
| Ma Huang Gen    | 23.33                     | —                                 |
| Mu Gua          | 24.04                     | —                                 |
| Lian Qiao       | 24.21                     | —                                 |
| Ren Shen        | 24.28                     | —                                 |
| Long Yan Rou    | 25.81                     | —                                 |
| Yi Yi Ren       | 25.94                     | —                                 |
| Fu Pen Zi       | 26.00                     | —                                 |
| Ma Huang        | 26.01                     | —                                 |
| Yuan Zhi        | 27.00                     | —                                 |
| Fu Shen         | 27.65                     | —                                 |
| Jiao Gu Lan     | 27.80                     | —                                 |
| Dan Shen        | 27.93                     | —                                 |
| (Fen) Bi Xie    | 27.94                     | —                                 |
| Zhi Ke          | 28.26                     | —                                 |
| Dan Dou Chi     | 28.81                     | —                                 |
| Fu Zi           | 28.90                     | —                                 |
| Hong Jing Tian  | 29.09                     | —                                 |

*continued on the next page*

continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| She Gan         | 29.90                     | —                                 |
| Huang Qin       | 30.79                     | —                                 |
| Gou Qi Zi       | 30.99                     | —                                 |
| Yin Yang Huo    | 31.51                     | —                                 |
| Ku Shen         | 31.56                     | —                                 |
| Yu Jin          | 31.85                     | —                                 |
| Mang Xiao       | 32.09                     | —                                 |
| Ce Bai Ye       | 32.67                     | —                                 |
| Xie Bai         | 32.87                     | —                                 |
| Mao Dong Qing   | 32.95                     | —                                 |
| Chai Hu         | 33.24                     | —                                 |
| Chuang Mu Xiang | 33.28                     | —                                 |
| Hou Po          | 34.49                     | —                                 |
| Guang Huo Xiang | 35.00                     | —                                 |
| Yan Hu Suo      | 35.79                     | —                                 |
| Zhu Ling        | 36.37                     | —                                 |
| Sang Zhi        | 38.61                     | —                                 |
| Gan Cao         | 38.96                     | —                                 |
| Che Qian Zi     | 38.98                     | —                                 |
| Qiang Huo       | 39.59                     | —                                 |
| Jing Jie        | 43.13                     | —                                 |
| Chi Shao (Yao)  | 44.28                     | —                                 |
| Chuan Lian Zi   | 45.29                     | —                                 |
| Zi Hua Di Ding  | 46.45                     | —                                 |
| Huang Lian      | 46.62                     | —                                 |
| Bai Zhu         | 48.84                     | —                                 |
| Bo He           | 48.95                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62419     | 62419                  | 0.00                            | 9.92                               |
| 62420     | 62420                  | 0.00                            | 9.41                               |

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 2.4-2022-02

Validated substance/substance group **Fu Ling**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50260-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Fu Ling                   | 3      | 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 |
| PhytoComm | Fu Ling   | G200HS211TK1 | 62849     | 40      | from supplier |
| PhytoComm | Fu Ling   | G200HS211TK1 | 62850     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Fu Ling*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Fu Ling   | G200HS211RT1 | 62430 <sup>†</sup> | 20      |
| PhytoComm | Fu Ling   | G200HS211SH1 | 62597 <sup>†</sup> | 20      |
| PhytoComm | Fu Ling   | G200HS211SH1 | 62598 <sup>†</sup> | 20      |
| PhytoComm | Fu Ling   | G200HS211TK1 | 62849 <sup>†</sup> | 20      |
| PhytoComm | Fu Ling   | G200HS211TK1 | 62850 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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   | G200H1019221 | 1       |
| Phytocomm  | Fu Ling   | g200h1019321 | 3       |
| Phytocomm  | Fu Ling   | G200H1019321 | 1       |
| PhytoComm  | Fu Ling   | G200H1019321 | 1       |
| Phytocomm  | Fu Ling   | G200H1019522 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 119           | 1              | 11 277        |
| <b>Type C</b> | 1              | 0             | 12             | 844           |

The substance/substance group *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:

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

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 99.1667 % (> 96.6667 %)  |
| <b>Type C</b> | 99.7674 % (> 99.1798 %)  | n/a (n/a)                |

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

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

| <b>Substance</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|------------------|-----------------------------------|-------------------------------------------|
| Yi Yi Ren        | 4.56                              | —                                         |
| Gui Zhi          | 6.76                              | —                                         |
| Fu Shen          | 7.03                              | —                                         |
| Rou Gui          | 8.38                              | —                                         |
| Sheng Jiang      | 8.86                              | —                                         |
| Ma Huang Gen     | 8.94                              | —                                         |
| He Huan Pi       | 9.17                              | —                                         |
| Fu Xiao Mai      | 10.08                             | —                                         |
| Gou Teng         | 10.55                             | —                                         |
| Ji Xue Teng      | 12.53                             | —                                         |
| Mu Zei           | 12.88                             | —                                         |
| Lai Fu Zi        | 13.35                             | —                                         |
| Zhu Ru           | 14.16                             | —                                         |
| Ling Zhi         | 14.32                             | —                                         |
| Ban Xia (Jiang)  | 15.03                             | —                                         |
| Di Gu Pi         | 15.16                             | —                                         |
| Lian Zi          | 15.79                             | —                                         |
| Bai Xian Pi      | 15.80                             | —                                         |
| Ci Wu Jia        | 16.52                             | —                                         |
| Ji Li            | 16.67                             | —                                         |
| Tao Ren          | 16.80                             | —                                         |
| Ren Dong Teng    | 18.62                             | —                                         |
| Huo Ma Ren       | 19.42                             | —                                         |
| Zhu Ling         | 19.76                             | —                                         |
| Gu Sui Bu        | 19.78                             | —                                         |
| Lu Gen           | 20.35                             | —                                         |
| She Gan          | 20.87                             | —                                         |
| Bai Zi Ren       | 20.88                             | —                                         |
| (Fen) Bi Xie     | 21.83                             | —                                         |
| Bai Shao Yao     | 22.34                             | —                                         |
| Fo Shou          | 22.49                             | —                                         |
| Ye Jiao Teng     | 22.63                             | —                                         |
| Ce Bai Ye        | 23.19                             | —                                         |
| Shen Qu          | 23.84                             | —                                         |
| Yu Jin           | 26.38                             | —                                         |
| Suan Zao Ren     | 26.57                             | —                                         |

*continued on the next page*



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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dan Dou Chi     | 26.60                     | —                                 |
| Zhe Bei Mu      | 26.62                     | —                                 |
| Tu Fu Ling      | 28.47                     | —                                 |
| Mao Dong Qing   | 30.97                     | —                                 |
| Shan Yao        | 31.16                     | —                                 |
| Chai Hu         | 31.77                     | —                                 |
| Tian Hua Fen    | 32.19                     | —                                 |
| Ze Xie          | 32.22                     | —                                 |
| Mang Xiao       | 32.96                     | —                                 |
| Dan Shen        | 34.54                     | —                                 |
| Lian Qiao       | 35.33                     | —                                 |
| Pi Pa Ye        | 36.16                     | —                                 |
| Yan Hu Suo      | 36.22                     | —                                 |
| Yin Yang Huo    | 36.70                     | —                                 |
| Jiao Gu Lan     | 37.41                     | —                                 |
| Ren Shen        | 39.39                     | —                                 |
| Hong Jing Tian  | 39.96                     | —                                 |
| Zhi Mu          | 40.55                     | —                                 |
| Gua Lou         | 40.89                     | —                                 |
| Guang Huo Xiang | 40.94                     | —                                 |
| Zhi Ke          | 41.37                     | —                                 |
| San Qi          | 42.04                     | —                                 |
| Che Qian Zi     | 42.70                     | —                                 |
| Qiang Huo       | 43.05                     | —                                 |
| Jie Geng        | 43.24                     | —                                 |
| Cang Zhu        | 43.47                     | —                                 |
| Dang Gui        | 43.49                     | —                                 |
| Jin Yin Hua     | 43.59                     | —                                 |
| Ban Lan Gen     | 43.64                     | —                                 |
| Gan Cao         | 44.38                     | —                                 |
| Huang Qin       | 44.62                     | —                                 |
| Fu Zi           | 45.04                     | —                                 |
| Sang Zhi        | 45.87                     | —                                 |
| Zi Hua Di Ding  | 46.21                     | —                                 |
| Yuan Zhi        | 46.39                     | —                                 |
| Huang Lian      | 47.41                     | —                                 |
| Jing Jie        | 47.45                     | —                                 |
| Hou Po          | 48.04                     | —                                 |
| Ma Huang        | 48.20                     | —                                 |
| Fu Pen Zi       | 48.39                     | —                                 |
| Sha Ren         | 48.56                     | —                                 |
| Bai Zhu         | 50.01                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62429     | 62429               | 0.00                         | 9.50                            |
| 62430     | 62430               | 0.00                         | 8.73                            |
| 62597     | 62597               | 0.00                         | 9.46                            |
| 62598     | 62598               | 0.00                         | 9.13                            |
| 62849     | 62849               | 0.00                         | 4.56                            |
| 62850     | 62850               | 0.00                         | 5.34                            |

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 2.4-2022-02

Validated substance/substance group **Fu Pen Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60044-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Fu Pen Zi; Rubi chingii fructus

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Fu Pen Zi                 | 1      | 0      | 1      |

### Second-stage model

For differentiation of the substance/substance group *Fu Pen 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 Pen Zi*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Fu Pen Zi | G213HS343TH1 | 62855     | 40      | from supplier |
| PhytoComm | Fu Pen Zi | G213HS343TH1 | 62856     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Pen Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 Pen 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 Pen Zi | G213HS343TH1 | 62855 <sup>†</sup> | 20      |
| PhytoComm | Fu Pen Zi | G213HS343TH1 | 62856 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Fu Pen 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 | Fu Pen Zi | g213h1813122 | 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 *Fu Pen 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 Pen 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

The substance/substance group *Fu Pen 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fu Pen 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Fu Zi           | 6.12                      | —                                 |
| Hou Po          | 7.60                      | —                                 |
| Guang Huo Xiang | 8.21                      | —                                 |
| Yan Hu Suo      | 8.21                      | —                                 |
| Gan Cao         | 8.25                      | —                                 |
| She Gan         | 9.02                      | —                                 |
| Dan Dou Chi     | 10.43                     | —                                 |
| Gu Sui Bu       | 10.68                     | —                                 |
| Zi Hua Di Ding  | 11.05                     | —                                 |
| Ma Huang        | 11.81                     | —                                 |
| Jin Yin Hua     | 12.20                     | —                                 |
| Hong Jing Tian  | 12.33                     | —                                 |
| Pi Pa Ye        | 12.60                     | —                                 |
| Qiang Huo       | 12.78                     | —                                 |
| Dan Shen        | 12.96                     | —                                 |
| Yin Yang Huo    | 13.19                     | —                                 |
| Ce Bai Ye       | 13.72                     | —                                 |
| Shan Yao        | 13.79                     | —                                 |
| Tian Hua Fen    | 14.21                     | —                                 |
| Ye Jiao Teng    | 14.32                     | —                                 |
| Mu Zei          | 14.52                     | —                                 |
| Chai Hu         | 14.59                     | —                                 |
| Ren Dong Teng   | 14.64                     | —                                 |
| Jing Jie        | 15.80                     | —                                 |
| Lu Gen          | 16.16                     | —                                 |
| Che Qian Zi     | 16.17                     | —                                 |
| Bai Shao Yao    | 16.68                     | —                                 |
| Zhi Ke          | 16.88                     | —                                 |
| Ban Lan Gen     | 17.01                     | —                                 |
| Yu Jin          | 17.10                     | —                                 |
| Zhi Gan Cao     | 17.80                     | —                                 |
| Bai Xian Pi     | 17.98                     | —                                 |
| Qing Pi         | 18.02                     | —                                 |
| Zhu Ling        | 18.26                     | —                                 |
| Huang Lian      | 18.73                     | —                                 |
| (Fen) Bi Xie    | 18.74                     | —                                 |
| Suan Zao Ren    | 19.38                     | —                                 |
| Ji Xue Teng     | 19.92                     | —                                 |
| He Huan Pi      | 19.97                     | —                                 |
| Jiao Gu Lan     | 20.00                     | —                                 |
| Ze Xie          | 20.05                     | —                                 |
| Lian Qiao       | 20.36                     | —                                 |
| Sha Ren         | 20.49                     | —                                 |
| Tu Fu Ling      | 20.54                     | —                                 |
| Ren Shen        | 21.26                     | —                                 |
| Mao Dong Qing   | 21.46                     | —                                 |
| Bo He           | 21.52                     | —                                 |
| Du Zhong        | 21.68                     | —                                 |
| Shen Qu         | 22.13                     | —                                 |
| Huang Bai       | 22.58                     | —                                 |
| Zhe Bei Mu      | 22.58                     | —                                 |
| Ji Li           | 22.59                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Tao Ren         | 22.63                     | —                                 |
| Lian Zi         | 22.96                     | —                                 |
| Cang Zhu        | 24.53                     | —                                 |
| Ling Zhi        | 24.98                     | —                                 |
| Sheng Jiang     | 25.22                     | —                                 |
| Huo Ma Ren      | 26.01                     | —                                 |
| Di Gu Pi        | 27.20                     | —                                 |
| Gou Teng        | 27.20                     | —                                 |
| Hong Hua        | 27.33                     | —                                 |
| Jie Geng        | 27.34                     | —                                 |
| Gui Zhi         | 27.66                     | —                                 |
| Fu Ling         | 27.70                     | —                                 |
| Gua Lou         | 27.76                     | —                                 |
| Huang Qin       | 28.33                     | —                                 |
| Qing Hao        | 29.10                     | —                                 |
| Rou Gui         | 29.58                     | —                                 |
| Bai Jiang Cao   | 30.02                     | —                                 |
| Sang Ye         | 30.35                     | —                                 |
| Bai Zi Ren      | 30.66                     | —                                 |
| Mang Xiao       | 31.30                     | —                                 |
| Chuang Mu Xiang | 31.62                     | —                                 |
| Ku Shen         | 31.62                     | —                                 |
| Dang Gui        | 32.18                     | —                                 |
| Lai Fu Zi       | 32.76                     | —                                 |
| Ban Xia (Jiang) | 33.32                     | —                                 |
| San Qi          | 33.58                     | —                                 |
| Chi Shao (Yao)  | 33.80                     | —                                 |
| Ma Huang Gen    | 35.07                     | —                                 |
| Gou Qi Zi       | 35.16                     | —                                 |
| Ci Wu Jia       | 35.46                     | —                                 |
| Xie Bai         | 35.46                     | —                                 |
| Zhu Ru          | 37.80                     | —                                 |
| Pu Gong Ying    | 38.06                     | —                                 |
| Cang Er Zi      | 38.75                     | —                                 |
| Sang Zhi        | 39.58                     | —                                 |
| Yi Yi Ren       | 39.90                     | —                                 |
| Ze Lan          | 40.05                     | —                                 |
| Fu Xiao Mai     | 42.82                     | —                                 |
| Zhi Mu          | 43.35                     | —                                 |
| Long Yan Rou    | 43.56                     | —                                 |
| Fu Shen         | 44.49                     | —                                 |
| Ban Zhi Lian    | 45.56                     | —                                 |
| Fo Shou         | 45.56                     | —                                 |
| Xi Xian Cao     | 46.49                     | —                                 |
| Mu Gua          | 46.81                     | —                                 |
| Wu Wei Zi       | 50.38                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Fu Pen 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62855     | 62855               | 0.00                         | 6.86                            |
| 62856     | 62856               | 0.00                         | 6.12                            |

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 2.4-2022-02

Validated substance/substance group **Fu Shen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60004-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Fu Shen   | G201HS212SH1 | 62618 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 1              | 40            | 0              | 11 356        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9950 % (> 99.9630 %)  | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Rou Gui         | 6.60                      | —                                 |
| Yi Yi Ren       | 6.81                      | —                                 |
| Ma Huang Gen    | 7.63                      | —                                 |
| Fu Ling         | 8.94                      | —                                 |
| Gui Zhi         | 13.15                     | —                                 |
| Fu Xiao Mai     | 13.65                     | —                                 |
| Sheng Jiang     | 13.97                     | —                                 |
| He Huan Pi      | 16.31                     | —                                 |
| Ji Xue Teng     | 17.16                     | —                                 |
| Gou Teng        | 19.05                     | —                                 |
| Ban Xia (Jiang) | 19.18                     | —                                 |
| Zhu Ru          | 19.93                     | —                                 |
| Bai Shao Yao    | 20.24                     | —                                 |
| Mu Zei          | 21.65                     | —                                 |
| Di Gu Pi        | 23.27                     | —                                 |
| Bai Xian Pi     | 26.08                     | —                                 |
| Bai Zi Ren      | 26.10                     | —                                 |
| Lian Zi         | 26.93                     | —                                 |
| Fo Shou         | 27.19                     | —                                 |
| Ji Li           | 27.19                     | —                                 |
| Ling Zhi        | 28.13                     | —                                 |
| Tao Ren         | 29.22                     | —                                 |
| Gu Sui Bu       | 30.26                     | —                                 |
| Ye Jiao Teng    | 30.80                     | —                                 |
| Ci Wu Jia       | 31.18                     | —                                 |
| Huo Ma Ren      | 31.57                     | —                                 |
| Shen Qu         | 32.00                     | —                                 |
| Lai Fu Zi       | 32.02                     | —                                 |
| Lu Gen          | 32.45                     | —                                 |
| Mang Xiao       | 32.85                     | —                                 |
| Zhu Ling        | 36.20                     | —                                 |
| Ren Dong Teng   | 36.78                     | —                                 |
| Tian Hua Fen    | 37.03                     | —                                 |
| Zhe Bei Mu      | 38.41                     | —                                 |
| Tu Fu Ling      | 38.97                     | —                                 |
| Ze Xie          | 39.08                     | —                                 |
| Dan Dou Chi     | 40.60                     | —                                 |
| Yu Jin          | 41.06                     | —                                 |
| Pi Pa Ye        | 41.13                     | —                                 |
| Zhi Mu          | 41.23                     | —                                 |
| Ren Shen        | 41.72                     | —                                 |
| Suan Zao Ren    | 42.04                     | —                                 |
| Shan Yao        | 42.82                     | —                                 |
| Lian Qiao       | 43.41                     | —                                 |
| She Gan         | 43.76                     | —                                 |
| (Fen) Bi Xie    | 43.82                     | —                                 |
| Dan Shen        | 44.23                     | —                                 |
| Yan Hu Suo      | 44.99                     | —                                 |
| Jiao Gu Lan     | 46.80                     | —                                 |
| Zhi Ke          | 47.78                     | —                                 |
| Dang Gui        | 48.08                     | —                                 |
| Huang Qin       | 48.42                     | —                                 |

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| Substanz | Distance in<br>main model | Distance in<br>second-stage model |
|----------|---------------------------|-----------------------------------|
| Jie Geng | 49.09                     | —                                 |
| Cang Zhu | 49.64                     | —                                 |
| Gua Lou  | 49.78                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62617     | 62617                  | 0.00                            | 6.60                               |
| 62618     | 62618                  | 0.00                            | 6.62                               |

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 2.4-2022-02

Validated substance/substance group **Fu Xiao Mai**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60081-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Fu Xiao Mai               | 3      | 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 |
| PhytoComm | Fu Xiao Mai | G244HS021SW1 | 62801     | 40      | from supplier |
| PhytoComm | Fu Xiao Mai | G244HS021SW1 | 62802     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Fu Xiao Mai*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Fu Xiao Mai | G244HS021RT1 | 62424 <sup>†</sup> | 20      |
| PhytoComm | Fu Xiao Mai | G244HS021SK1 | 62631 <sup>†</sup> | 20      |
| PhytoComm | Fu Xiao Mai | G244HS021SK1 | 62632 <sup>†</sup> | 20      |
| PhytoComm | Fu Xiao Mai | G244HS021SW1 | 62801 <sup>†</sup> | 20      |
| PhytoComm | Fu Xiao Mai | G244HS021SW1 | 62802 <sup>†</sup> | 20      |



- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 8              | 230           | 10             | 22 192        |
| <b>Type B</b> | 20             | 102           | 18             | 11 257        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9789 % (> 99.9625 %)  | 95.8333 % (> 94.5833 %) |
| <b>Type B</b> | 99.8611 % (> 99.8289 %)  | 85.0000 % (> 82.5000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Yi Yi Ren       | 2.58                      | —                                 |
| Zhu Ru          | 3.32                      | —                                 |
| Sheng Jiang     | 3.76                      | —                                 |
| Rou Gui         | 5.73                      | —                                 |
| Gui Zhi         | 7.23                      | —                                 |
| Di Gu Pi        | 7.24                      | —                                 |
| Fu Ling         | 7.47                      | —                                 |
| Bai Shao Yao    | 8.76                      | —                                 |
| Ci Wu Jia       | 9.43                      | —                                 |
| He Huan Pi      | 9.59                      | —                                 |
| Ban Xia (Jiang) | 10.24                     | —                                 |
| Ji Li           | 11.05                     | —                                 |
| Lian Zi         | 11.74                     | —                                 |
| Fu Shen         | 12.06                     | —                                 |
| Shen Qu         | 12.52                     | —                                 |
| Bai Zi Ren      | 13.37                     | —                                 |
| Tao Ren         | 13.75                     | —                                 |
| Ma Huang Gen    | 14.35                     | —                                 |
| Ling Zhi        | 14.81                     | —                                 |
| Lai Fu Zi       | 14.90                     | —                                 |
| Gou Teng        | 16.16                     | —                                 |
| Ji Xue Teng     | 16.30                     | —                                 |
| Mu Zei          | 16.74                     | —                                 |
| Zhe Bei Mu      | 17.01                     | —                                 |
| Bai Xian Pi     | 18.20                     | —                                 |
| Ye Jiao Teng    | 19.80                     | —                                 |
| Huo Ma Ren      | 19.80                     | —                                 |
| Shan Yao        | 19.95                     | —                                 |
| Tian Hua Fen    | 20.28                     | —                                 |
| Fo Shou         | 20.41                     | —                                 |
| Gu Sui Bu       | 21.90                     | —                                 |
| Pi Pa Ye        | 22.49                     | —                                 |
| Yu Jin          | 23.41                     | —                                 |
| Tu Fu Ling      | 25.54                     | —                                 |
| Ren Dong Teng   | 25.71                     | —                                 |
| Lu Gen          | 26.17                     | —                                 |
| Ze Xie          | 27.02                     | —                                 |
| Lian Qiao       | 27.71                     | —                                 |
| Suan Zao Ren    | 28.72                     | —                                 |
| Zhu Ling        | 29.99                     | —                                 |
| Zhi Mu          | 31.17                     | —                                 |
| Yan Hu Suo      | 32.64                     | —                                 |
| (Fen) Bi Xie    | 33.15                     | —                                 |
| Ren Shen        | 33.21                     | —                                 |
| San Qi          | 33.49                     | —                                 |
| Jin Yin Hua     | 33.72                     | —                                 |
| Mang Xiao       | 34.27                     | —                                 |
| Cang Zhu        | 34.34                     | —                                 |
| Fu Zi           | 34.50                     | —                                 |
| Ce Bai Ye       | 34.72                     | —                                 |
| Jie Geng        | 34.91                     | —                                 |
| Fu Pen Zi       | 35.94                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jiao Gu Lan     | 36.18                     | —                                 |
| Mao Dong Qing   | 37.15                     | —                                 |
| Dan Dou Chi     | 37.69                     | —                                 |
| Zhi Ke          | 37.79                     | —                                 |
| Yuan Zhi        | 38.03                     | —                                 |
| Dan Shen        | 38.36                     | —                                 |
| Gua Lou         | 38.52                     | —                                 |
| Chai Hu         | 38.79                     | —                                 |
| Dang Gui        | 38.96                     | —                                 |
| Huang Qin       | 39.14                     | —                                 |
| She Gan         | 39.71                     | —                                 |
| Che Qian Zi     | 40.59                     | —                                 |
| Yin Yang Huo    | 41.38                     | —                                 |
| Hou Po          | 41.51                     | —                                 |
| Mu Gua          | 42.99                     | —                                 |
| Ku Shen         | 44.38                     | —                                 |
| Ban Lan Gen     | 44.77                     | —                                 |
| Guang Huo Xiang | 47.67                     | —                                 |
| Gou Qi Zi       | 47.84                     | —                                 |
| Qiang Huo       | 49.01                     | —                                 |
| Hong Jing Tian  | 49.90                     | —                                 |
| Gan Cao         | 49.95                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62423     | 62423                  | 0.00                            | 4.50                               |
| 62424     | 62424                  | 0.00                            | 2.58                               |
| 62631     | 62631                  | 0.00                            | 4.42                               |
| 62632     | 62632                  | 0.00                            | 2.79                               |
| 62801     | 62801                  | 0.00                            | 4.13                               |
| 62802     | 62802                  | 0.00                            | 3.76                               |

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 2.4-2022-02

Validated substance/substance group **Fu Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50884-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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     | G005HS158SP1 | 62699     | 40      | from supplier |
| PhytoComm | Fu Zi     | G005HS158SP1 | 62700     | 40      | from supplier |
| PhytoComm | Fu Zi     | G005HS158TH1 | 62943     | 40      | from supplier |
| PhytoComm | Fu Zi     | G005HS158TH1 | 62944     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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     | G005HS158SP1 | 62699 <sup>†</sup> | 20      |
| PhytoComm | Fu Zi     | G005HS158SP1 | 62700 <sup>†</sup> | 20      |
| PhytoComm | Fu Zi     | G005HS158TH1 | 62943 <sup>†</sup> | 20      |
| PhytoComm | Fu Zi     | G005HS158TH1 | 62944 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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     | g005h0801122 | 1       |
| phytocomm | Fu Zi     | g005h0801322 | 1       |
| Phytocomm | Fu Zi     | G005H0801322 | 1       |
| Phytocomm | Fu Zi     | G005H0801524 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 156           | 4              | 22 280        |
| <b>Type B</b> | 0              | 73            | 7              | 11 317        |
| <b>Type C</b> | 0              | 0             | 4              | 853           |

The substance/substance group *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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 97.5000 % (> 95.6250 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 91.2500 % (> 87.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Shan Yao        | 3.36                      | —                                 |
| Pi Pa Ye        | 4.59                      | —                                 |
| Zi Hua Di Ding  | 4.90                      | —                                 |
| Fu Pen Zi       | 5.26                      | —                                 |
| Zhe Bei Mu      | 6.00                      | —                                 |
| Tian Hua Fen    | 6.17                      | —                                 |
| Ren Dong Teng   | 7.10                      | —                                 |
| Lian Qiao       | 7.47                      | —                                 |
| Ze Xie          | 7.50                      | —                                 |
| Ji Li           | 8.10                      | —                                 |
| Dan Shen        | 8.41                      | —                                 |
| Hou Po          | 8.75                      | —                                 |
| Gu Sui Bu       | 8.81                      | —                                 |
| Mu Zei          | 8.85                      | —                                 |
| Gan Cao         | 9.17                      | —                                 |
| He Huan Pi      | 9.89                      | —                                 |
| Jin Yin Hua     | 9.89                      | —                                 |
| Ling Zhi        | 10.16                     | —                                 |
| Qiang Huo       | 10.34                     | —                                 |
| Yan Hu Suo      | 10.39                     | —                                 |
| Guang Huo Xiang | 10.46                     | —                                 |
| Jing Jie        | 10.57                     | —                                 |
| Bai Zi Ren      | 10.68                     | —                                 |
| Shen Qu         | 10.71                     | —                                 |
| Hong Jing Tian  | 10.83                     | —                                 |
| Huo Ma Ren      | 11.12                     | —                                 |
| Dan Dou Chi     | 12.09                     | —                                 |
| Yin Yang Huo    | 12.18                     | —                                 |
| Ban Lan Gen     | 12.39                     | —                                 |
| Bo He           | 12.61                     | —                                 |
| Bai Shao Yao    | 12.92                     | —                                 |
| Yu Jin          | 13.15                     | —                                 |
| Chai Hu         | 13.32                     | —                                 |
| Che Qian Zi     | 13.41                     | —                                 |
| She Gan         | 13.70                     | —                                 |
| Ce Bai Ye       | 13.76                     | —                                 |
| Lian Zi         | 14.15                     | —                                 |
| Sheng Jiang     | 14.17                     | —                                 |
| Ye Jiao Teng    | 14.55                     | —                                 |
| Ji Xue Teng     | 14.72                     | —                                 |
| Sha Ren         | 14.77                     | —                                 |
| Jiao Gu Lan     | 14.78                     | —                                 |
| Lai Fu Zi       | 14.79                     | —                                 |
| Huang Bai       | 14.97                     | —                                 |
| Ma Huang        | 15.04                     | —                                 |
| Fu Ling         | 15.49                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Gua Lou         | 15.54                     | —                                 |
| Bai Xian Pi     | 15.89                     | —                                 |
| Gui Zhi         | 16.02                     | —                                 |
| Suan Zao Ren    | 16.10                     | —                                 |
| Zhu Ling        | 16.24                     | —                                 |
| Huang Lian      | 16.28                     | —                                 |
| Mao Dong Qing   | 16.39                     | —                                 |
| Zhi Gan Cao     | 16.64                     | —                                 |
| Tu Fu Ling      | 16.66                     | —                                 |
| Du Zhong        | 17.26                     | —                                 |
| Lu Gen          | 17.34                     | —                                 |
| Ren Shen        | 17.36                     | —                                 |
| Zhi Ke          | 17.40                     | —                                 |
| (Fen) Bi Xie    | 17.73                     | —                                 |
| Qing Pi         | 18.59                     | —                                 |
| Tao Ren         | 18.86                     | —                                 |
| Gou Teng        | 18.88                     | —                                 |
| San Qi          | 19.76                     | —                                 |
| Zhu Ru          | 20.24                     | —                                 |
| Rou Gui         | 20.28                     | —                                 |
| Dang Gui        | 20.55                     | —                                 |
| Ku Shen         | 20.55                     | —                                 |
| Di Gu Pi        | 20.59                     | —                                 |
| Cang Zhu        | 22.23                     | —                                 |
| Ci Wu Jia       | 22.54                     | —                                 |
| Qing Hao        | 22.71                     | —                                 |
| Jie Geng        | 22.84                     | —                                 |
| Hong Hua        | 22.97                     | —                                 |
| Ban Xia (Jiang) | 23.26                     | —                                 |
| Bai Jiang Cao   | 23.56                     | —                                 |
| Fu Xiao Mai     | 24.67                     | —                                 |
| Yi Yi Ren       | 26.67                     | —                                 |
| Xie Bai         | 26.68                     | —                                 |
| Ma Huang Gen    | 27.17                     | —                                 |
| Zhi Mu          | 27.74                     | —                                 |
| Gou Qi Zi       | 27.91                     | —                                 |
| Huang Qin       | 28.11                     | —                                 |
| Fo Shou         | 29.07                     | —                                 |
| Chuang Mu Xiang | 30.00                     | —                                 |
| Sang Ye         | 30.34                     | —                                 |
| Pu Gong Ying    | 30.66                     | —                                 |
| Mang Xiao       | 30.81                     | —                                 |
| Chi Shao (Yao)  | 32.28                     | —                                 |
| Long Yan Rou    | 33.28                     | —                                 |
| Mu Gua          | 33.73                     | —                                 |
| Ze Lan          | 34.53                     | —                                 |
| Sang Zhi        | 34.80                     | —                                 |
| Cang Er Zi      | 37.21                     | —                                 |
| Yuan Zhi        | 37.38                     | —                                 |
| Ban Zhi Lian    | 40.19                     | —                                 |
| Fu Shen         | 40.69                     | —                                 |
| Xi Xian Cao     | 42.48                     | —                                 |
| E Zhu           | 47.47                     | —                                 |
| Jiang Huang     | 47.86                     | —                                 |

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                         | 3.65                            |
| 62700     | 62700               | 0.00                         | 3.36                            |
| 62943     | 62943               | 0.00                         | 5.26                            |
| 62944     | 62944               | 0.00                         | 4.90                            |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Gan Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60011-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Gan Cao                   | 3      | 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 |
| PhytoComm | Gan Cao   | G119HS089TL1 | 62879     | 40      | from supplier |
| PhytoComm | Gan Cao   | G119HS089TL1 | 62880     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Gan Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Gan Cao   | G119H0521822 | 62342 <sup>†</sup> | 20      |
| PhytoComm | Gan Cao   | G119H0521823 | 62533 <sup>†</sup> | 20      |
| PhytoComm | Gan Cao   | G119H0521823 | 62534 <sup>†</sup> | 20      |
| PhytoComm | Gan Cao   | G119HS089TL1 | 62879 <sup>†</sup> | 20      |
| PhytoComm | Gan Cao   | G119HS089TL1 | 62880 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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   | G119H0521121 | 4       |
| Phytocomm | Gan Cao   | G119H0521522 | 8       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8244 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zi Hua Di Ding  | 6.34                      | —                                 |
| Zhi Gan Cao     | 7.72                      | —                                 |
| Hong Jing Tian  | 8.82                      | —                                 |
| Jin Yin Hua     | 9.18                      | —                                 |
| Fu Zi           | 9.44                      | —                                 |
| Fu Pen Zi       | 9.46                      | —                                 |
| Dan Shen        | 9.57                      | —                                 |
| Hou Po          | 9.71                      | —                                 |
| Jiao Gu Lan     | 10.87                     | —                                 |
| Zhi Ke          | 11.16                     | —                                 |
| Dan Dou Chi     | 11.85                     | —                                 |
| Ma Huang        | 12.66                     | —                                 |
| Qiang Huo       | 12.81                     | —                                 |
| Ban Lan Gen     | 12.94                     | —                                 |
| Yin Yang Huo    | 13.65                     | —                                 |
| Yan Hu Suo      | 14.75                     | —                                 |
| Pi Pa Ye        | 14.87                     | —                                 |
| Qing Pi         | 14.90                     | —                                 |
| Chai Hu         | 14.90                     | —                                 |
| Huang Bai       | 15.20                     | —                                 |
| Bo He           | 15.36                     | —                                 |
| Ye Jiao Teng    | 15.42                     | —                                 |
| Shan Yao        | 16.27                     | —                                 |
| Bai Shao Yao    | 16.77                     | —                                 |
| Ren Dong Teng   | 16.83                     | —                                 |
| Tian Hua Fen    | 17.28                     | —                                 |
| She Gan         | 17.28                     | —                                 |
| Gu Sui Bu       | 17.68                     | —                                 |
| Guang Huo Xiang | 17.79                     | —                                 |
| Suan Zao Ren    | 18.78                     | —                                 |
| Jing Jie        | 18.98                     | —                                 |
| Hong Hua        | 19.05                     | —                                 |
| Qing Hao        | 19.12                     | —                                 |
| Sha Ren         | 19.23                     | —                                 |
| Chi Shao (Yao)  | 19.34                     | —                                 |
| Mao Dong Qing   | 19.42                     | —                                 |
| Ce Bai Ye       | 19.56                     | —                                 |
| Bai Xian Pi     | 19.75                     | —                                 |
| Mu Zei          | 19.75                     | —                                 |
| Lu Gen          | 19.88                     | —                                 |
| Chuang Mu Xiang | 20.63                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Huang Lian      | 20.73                             | —                                         |
| Yu Jin          | 20.82                             | —                                         |
| Du Zhong        | 20.89                             | —                                         |
| Lian Qiao       | 22.08                             | —                                         |
| Lian Zi         | 22.16                             | —                                         |
| Ji Xue Teng     | 22.33                             | —                                         |
| Che Qian Zi     | 22.59                             | —                                         |
| Gou Qi Zi       | 22.98                             | —                                         |
| Ji Li           | 23.24                             | —                                         |
| Ren Shen        | 23.26                             | —                                         |
| Yuan Zhi        | 24.01                             | —                                         |
| He Huan Pi      | 24.25                             | —                                         |
| Cang Zhu        | 24.84                             | —                                         |
| Shen Qu         | 25.08                             | —                                         |
| (Fen) Bi Xie    | 25.92                             | —                                         |
| Ling Zhi        | 26.21                             | —                                         |
| Bai Jiang Cao   | 26.37                             | —                                         |
| Di Gu Pi        | 26.64                             | —                                         |
| Zhe Bei Mu      | 26.69                             | —                                         |
| Xiang Fu        | 26.72                             | —                                         |
| Tu Fu Ling      | 26.77                             | —                                         |
| Zhu Ling        | 26.84                             | —                                         |
| Ze Xie          | 26.85                             | —                                         |
| Niu Bang Zi     | 27.83                             | —                                         |
| Huang Qin       | 28.00                             | —                                         |
| Ku Shen         | 28.67                             | —                                         |
| Tao Ren         | 28.74                             | —                                         |
| Mang Xiao       | 28.76                             | —                                         |
| Sang Ye         | 29.06                             | —                                         |
| Gua Lou         | 29.67                             | —                                         |
| Xie Bai         | 29.80                             | —                                         |
| Sheng Jiang     | 30.55                             | —                                         |
| Gou Teng        | 31.18                             | —                                         |
| Jie Geng        | 31.61                             | —                                         |
| Fu Ling         | 32.07                             | —                                         |
| Rou Gui         | 32.81                             | —                                         |
| Cang Er Zi      | 33.05                             | —                                         |
| Dang Gui        | 33.31                             | —                                         |
| Bai Zi Ren      | 33.37                             | —                                         |
| Huo Ma Ren      | 33.75                             | —                                         |
| Gui Zhi         | 33.95                             | —                                         |
| Pu Gong Ying    | 35.10                             | —                                         |
| Zi Su Zi        | 35.44                             | —                                         |
| San Qi          | 35.74                             | —                                         |
| Chuan Lian Zi   | 36.00                             | —                                         |
| Ma Huang Gen    | 37.63                             | —                                         |
| Mu Gua          | 37.77                             | —                                         |
| Long Yan Rou    | 38.53                             | —                                         |
| Ze Lan          | 38.95                             | —                                         |
| (Huai) Niu Xi   | 39.39                             | —                                         |
| Sang Zhi        | 40.13                             | —                                         |
| Ci Wu Jia       | 40.21                             | —                                         |
| Lai Fu Zi       | 41.43                             | —                                         |
| Huang Qi        | 41.86                             | —                                         |
| Ban Xia (Jiang) | 42.12                             | —                                         |
| Ban Zhi Lian    | 42.76                             | —                                         |
| Zhi Mu          | 44.29                             | —                                         |
| Yi Yi Ren       | 44.87                             | —                                         |
| Xi Xian Cao     | 45.55                             | —                                         |

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| Substanz      | Distance in<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| Wu Wei Zi     | 45.66                     | —                                 |
| Zhu Ru        | 46.30                     | —                                 |
| Chuan Mu Tong | 47.83                     | —                                 |
| Fu Shen       | 49.74                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62341     | 62341                  | 0.00                            | 19.35                              |
| 62342     | 62342                  | 0.00                            | 19.05                              |
| 62533     | 62533                  | 0.00                            | 22.01                              |
| 62534     | 62534                  | 0.00                            | 22.34                              |
| 62879     | 62879                  | 0.00                            | 6.34                               |
| 62880     | 62880                  | 0.00                            | 7.22                               |

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 2.4-2022-02

Validated substance/substance group **Gan Jiang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10004524-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Gan Jiang; Zingiberis rhizoma

### Special notes

When selecting the *Gan Jiang* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Gan Jiang                 | 1      | 0      | 4      |

### Second-stage model

For differentiation of the substance/substance group *Gan 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 *Gan Jiang*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Gan Jiang | G252H1145021 | 62805     | 40      | from supplier |
| PhytoComm | Gan Jiang | G252H1145021 | 62806     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Gan Jiang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Gan 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 | Gan Jiang | G252H1145021 | 62805 <sup>†</sup> | 20      |
| PhytoComm | Gan Jiang | G252H1145021 | 62806 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Gan Jiang*.
- 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 | Gan Jiang | g252h01145221 | 1       |
| Phytocomm | Gan Jiang | G252H1145221  | 1       |
| Phytocomm | Gan Jiang | G252H1145421  | 1       |
| Phytocomm | Gan Jiang | G252H1145521  | 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 *Gan 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 *Gan 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 3              | 0             | 4              | 850           |

The substance/substance group *Gan 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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 new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

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

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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gan 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Zi Su Zi            | 6.41                      | —                                 |
| Sha Shen (Bei)      | 11.86                     | —                                 |
| Tian Hua Fen        | 13.98                     | —                                 |
| Cang Er Zi          | 14.53                     | —                                 |
| Chuan Lian Zi       | 14.98                     | —                                 |
| Di Gu Pi            | 16.20                     | —                                 |
| Niu Bang Zi         | 16.89                     | —                                 |
| Sang Zhi            | 17.29                     | —                                 |
| (Huai) Niu Xi       | 18.65                     | —                                 |
| Yan Hu Suo          | 19.76                     | —                                 |
| Jie Geng            | 20.61                     | —                                 |
| Mi Huan Jun         | 22.47                     | —                                 |
| E Zhu               | 23.70                     | —                                 |
| Jiang Huang         | 24.00                     | —                                 |
| Shan Yao            | 24.80                     | —                                 |
| Dang Gui            | 25.01                     | —                                 |
| Suan Zao Ren        | 26.26                     | —                                 |
| Lai Fu Zi           | 26.68                     | —                                 |
| (Bai) Dou Kou       | 26.75                     | —                                 |
| Mang Xiao           | 27.40                     | —                                 |
| Xiao Hui Xiang      | 27.97                     | —                                 |
| Chuan Mu Tong       | 28.11                     | —                                 |
| Sha Ren             | 28.45                     | —                                 |
| Ku Shen             | 28.64                     | —                                 |
| Zhi Gan Cao         | 29.13                     | —                                 |
| Huang Qi            | 29.49                     | —                                 |
| Xiang Fu            | 29.67                     | —                                 |
| Lian Qiao           | 29.67                     | —                                 |
| Chuan Niu Xi        | 30.01                     | —                                 |
| Chen Pi             | 30.37                     | —                                 |
| Long Dan (Cao)      | 30.91                     | —                                 |
| Bai Zhi             | 31.04                     | —                                 |
| (Shi) Chang Pu      | 31.13                     | —                                 |
| Bai Zhu             | 34.62                     | —                                 |
| Bai He              | 35.05                     | —                                 |
| Pu Gong Ying        | 35.21                     | —                                 |
| Qin Jiao            | 36.38                     | —                                 |
| Shan Yu Rou         | 37.85                     | —                                 |
| Yi Mu Cao           | 38.78                     | —                                 |
| Bai Hua She She Cao | 41.23                     | —                                 |
| Wu Yao              | 42.19                     | —                                 |
| Ban Zhi Lian        | 43.01                     | —                                 |
| Qiang Huo           | 43.76                     | —                                 |
| He Huan Pi          | 43.95                     | —                                 |
| Huang Lian          | 44.19                     | —                                 |
| Da Zao              | 44.65                     | —                                 |
| Tu Fu Ling          | 44.66                     | —                                 |
| Sang Ji Shend       | 44.98                     | —                                 |
| Dong Gua Zi         | 45.12                     | —                                 |
| Jin Yin Hua         | 45.18                     | —                                 |
| Zhi Ke              | 45.40                     | —                                 |
| Fu Ling             | 45.93                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Du Huo         | 46.15                     | —                                 |
| Fang Feng      | 46.16                     | —                                 |
| Zi Hua Di Ding | 46.54                     | —                                 |
| Bai Xian Pi    | 46.70                     | —                                 |
| Lian Zi        | 46.81                     | —                                 |
| Chi Shao (Yao) | 47.01                     | —                                 |
| Mu Dan Pi      | 47.06                     | —                                 |
| Bo He          | 47.52                     | —                                 |
| Ba Ji Tian     | 48.34                     | —                                 |
| Yuan Zhi       | 48.95                     | —                                 |
| Ju Hua         | 49.23                     | —                                 |
| Sang Ye        | 50.57                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Gan 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62805     | 62805                  | 0.00                            | 6.41                               |
| 62806     | 62806                  | 0.00                            | 6.62                               |

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 2.4-2022-02

Validated substance/substance group **Ge Gen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60050-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ge Gen    | G206H1301822 | 62490 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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    | G206H1301323 | 1       |
| Phytocomm | Ge Gen    | G206H1301422 | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Mang Xiao      | 19.08                     | —                                 |
| Sang Ji Shend  | 23.81                     | —                                 |
| Gu Sui Bu      | 39.13                     | —                                 |
| Jing Jie       | 39.28                     | —                                 |
| He Shou Wu     | 40.55                     | —                                 |
| Hong Jing Tian | 40.55                     | —                                 |
| Gou Teng       | 41.18                     | —                                 |
| Du Zhong       | 47.20                     | —                                 |
| Hua Shi        | 50.69                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62489     | 62489                  | 0.00                            | 19.17                              |
| 62490     | 62490                  | 0.00                            | 19.08                              |

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 2.4-2022-02

Validated substance/substance group **Gou Qi Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60094-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G150HS171TH1 | 62875     | 40      | from supplier |
| PhytoComm | Gou Qi Zi | G150HS171TH1 | 62876     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G150HS171TH1 | 62875 <sup>†</sup> | 20      |
| PhytoComm | Gou Qi Zi | G150HS171TH1 | 62876 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G150H0913221 | 1       |
| Phytocomm | Gou Qi Zi | G150H0913422 | 4       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dang Gui        | 9.96                      | —                                 |
| Cang Zhu        | 12.73                     | —                                 |
| Mu Gua          | 13.84                     | —                                 |
| Jie Geng        | 14.63                     | —                                 |
| Ren Shen        | 15.02                     | —                                 |
| Ku Shen         | 16.81                     | —                                 |
| Xie Bai         | 16.87                     | —                                 |
| Gan Cao         | 17.07                     | —                                 |
| Chuang Mu Xiang | 17.27                     | —                                 |
| Long Yan Rou    | 17.98                     | —                                 |
| Jiao Gu Lan     | 17.98                     | —                                 |
| Yuan Zhi        | 19.13                     | —                                 |
| Lian Qiao       | 19.34                     | —                                 |
| San Qi          | 20.15                     | —                                 |
| Zhi Ke          | 20.20                     | —                                 |
| Zhi Mu          | 20.37                     | —                                 |
| Jin Yin Hua     | 21.13                     | —                                 |
| Shan Yao        | 21.51                     | —                                 |
| Ban Lan Gen     | 21.58                     | —                                 |
| Gua Lou         | 21.64                     | —                                 |
| Pi Pa Ye        | 21.98                     | —                                 |
| Ren Dong Teng   | 22.10                     | —                                 |
| Dan Dou Chi     | 22.20                     | —                                 |
| Zhe Bei Mu      | 22.45                     | —                                 |
| Mu Zei          | 23.42                     | —                                 |
| Ling Zhi        | 24.09                     | —                                 |
| Tian Hua Fen    | 24.71                     | —                                 |
| Bai Shao Yao    | 25.30                     | —                                 |
| Di Gu Pi        | 25.33                     | —                                 |
| Hong Jing Tian  | 25.88                     | —                                 |
| Hou Po          | 26.48                     | —                                 |
| Suan Zao Ren    | 27.62                     | —                                 |
| He Huan Pi      | 28.26                     | —                                 |
| Zi Hua Di Ding  | 28.30                     | —                                 |
| Ji Li           | 29.29                     | —                                 |
| Fu Zi           | 30.21                     | —                                 |
| Ye Jiao Teng    | 30.30                     | —                                 |
| Bai Zi Ren      | 30.31                     | —                                 |
| Huang Qin       | 30.36                     | —                                 |
| Dan Shen        | 30.51                     | —                                 |
| Lai Fu Zi       | 30.55                     | —                                 |
| Ma Huang        | 30.60                     | —                                 |
| Ze Xie          | 30.99                     | —                                 |
| Yan Hu Suo      | 30.99                     | —                                 |
| Mang Xiao       | 31.01                     | —                                 |
| Lu Gen          | 31.60                     | —                                 |
| Zhi Gan Cao     | 31.86                     | —                                 |
| Lian Zi         | 31.89                     | —                                 |
| Hong Hua        | 32.24                     | —                                 |
| Fu Pen Zi       | 32.58                     | —                                 |
| Zhu Ru          | 32.61                     | —                                 |
| Tao Ren         | 32.67                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Chai Hu         | 33.55                     | —                                 |
| Huo Ma Ren      | 34.03                     | —                                 |
| Shen Qu         | 34.18                     | —                                 |
| Gou Teng        | 34.34                     | —                                 |
| Ci Wu Jia       | 34.37                     | —                                 |
| Fo Shou         | 34.52                     | —                                 |
| Sang Zhi        | 34.73                     | —                                 |
| Mao Dong Qing   | 34.95                     | —                                 |
| Yin Yang Huo    | 35.34                     | —                                 |
| Fu Ling         | 35.35                     | —                                 |
| Sheng Jiang     | 35.37                     | —                                 |
| Qing Pi         | 35.41                     | —                                 |
| Gui Zhi         | 35.96                     | —                                 |
| Chi Shao (Yao)  | 36.78                     | —                                 |
| Ji Xue Teng     | 37.07                     | —                                 |
| Tu Fu Ling      | 37.11                     | —                                 |
| Ban Xia (Jiang) | 37.61                     | —                                 |
| Guang Huo Xiang | 38.30                     | —                                 |
| Che Qian Zi     | 38.45                     | —                                 |
| Qiang Huo       | 38.68                     | —                                 |
| Rou Gui         | 40.00                     | —                                 |
| Gu Sui Bu       | 40.41                     | —                                 |
| Cang Er Zi      | 40.75                     | —                                 |
| Huang Lian      | 41.19                     | —                                 |
| Bo He           | 41.61                     | —                                 |
| Bai Xian Pi     | 42.22                     | —                                 |
| Huang Qi        | 42.63                     | —                                 |
| Chuan Lian Zi   | 42.78                     | —                                 |
| She Gan         | 43.06                     | —                                 |
| Sha Ren         | 43.24                     | —                                 |
| Fu Xiao Mai     | 44.15                     | —                                 |
| Sang Ye         | 44.71                     | —                                 |
| Niu Bang Zi     | 44.77                     | —                                 |
| Ce Bai Ye       | 45.60                     | —                                 |
| Yi Yi Ren       | 46.13                     | —                                 |
| Huang Bai       | 47.90                     | —                                 |
| (Fen) Bi Xie    | 48.25                     | —                                 |
| Zhu Ling        | 48.46                     | —                                 |
| Jing Jie        | 48.86                     | —                                 |
| Du Zhong        | 49.40                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62875     | 62875               | 0.00                         | 10.58                           |
| 62876     | 62876               | 0.00                         | 9.96                            |

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



# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Gou Teng**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60097-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Gou Teng  | G247H1210822 | 62314 <sup>†</sup> | 20      |
| PhytoComm | Gou Teng  | G247HS288SG1 | 62629 <sup>†</sup> | 20      |
| PhytoComm | Gou Teng  | G247HS288SG1 | 62630 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 6              | 159           | 1              | 22 274        |
| <b>Type B</b> | 0              | 77            | 3              | 11 317        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9888 % (> 99.9725 %)  | 99.3750 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 96.2500 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Rou Gui         | 3.10                      | —                                 |
| He Huan Pi      | 4.48                      | —                                 |
| Fu Ling         | 5.74                      | —                                 |
| Gui Zhi         | 5.90                      | —                                 |
| Yi Yi Ren       | 6.56                      | —                                 |
| Ma Huang Gen    | 6.62                      | —                                 |
| Mu Zei          | 6.85                      | —                                 |
| Ji Xue Teng     | 7.74                      | —                                 |
| Huo Ma Ren      | 8.07                      | —                                 |
| Sheng Jiang     | 8.50                      | —                                 |
| Lu Gen          | 9.39                      | —                                 |
| Fu Shen         | 10.13                     | —                                 |
| Fu Xiao Mai     | 10.32                     | —                                 |
| Ci Wu Jia       | 11.09                     | —                                 |
| Tao Ren         | 12.09                     | —                                 |
| Ban Xia (Jiang) | 12.54                     | —                                 |
| Ren Dong Teng   | 13.11                     | —                                 |
| Bai Shao Yao    | 13.38                     | —                                 |
| Zhu Ling        | 13.41                     | —                                 |
| Gu Sui Bu       | 13.46                     | —                                 |
| Bai Xian Pi     | 13.49                     | —                                 |
| Lai Fu Zi       | 13.93                     | —                                 |
| Lian Zi         | 14.43                     | —                                 |
| Ling Zhi        | 14.64                     | —                                 |
| (Fen) Bi Xie    | 15.18                     | —                                 |
| Fo Shou         | 15.48                     | —                                 |
| Ye Jiao Teng    | 15.83                     | —                                 |
| Di Gu Pi        | 16.05                     | —                                 |
| She Gan         | 16.45                     | —                                 |
| Ji Li           | 17.28                     | —                                 |
| Zhe Bei Mu      | 17.60                     | —                                 |
| Bai Zi Ren      | 18.14                     | —                                 |
| Shen Qu         | 18.21                     | —                                 |
| Zhu Ru          | 18.37                     | —                                 |
| Suan Zao Ren    | 18.76                     | —                                 |
| Dan Dou Chi     | 20.97                     | —                                 |
| Nü Zhen Zi      | 21.14                     | —                                 |
| Tu Fu Ling      | 21.19                     | —                                 |
| Yu Jin          | 21.58                     | —                                 |
| Tian Hua Fen    | 21.91                     | —                                 |
| Yi Mu Cao       | 23.20                     | —                                 |
| Mang Xiao       | 23.31                     | —                                 |
| Dan Shen        | 24.31                     | —                                 |
| Yan Hu Suo      | 24.47                     | —                                 |
| Lian Qiao       | 24.81                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Ce Bai Ye           | 25.59                     | —                                 |
| Ze Xie              | 25.85                     | —                                 |
| Jing Jie            | 26.30                     | —                                 |
| Pi Pa Ye            | 27.48                     | —                                 |
| Yin Yang Huo        | 27.83                     | —                                 |
| Mao Dong Qing       | 28.63                     | —                                 |
| Shan Yao            | 28.87                     | —                                 |
| Chai Hu             | 29.55                     | —                                 |
| Xuan Fu Hua         | 30.64                     | —                                 |
| Hong Jing Tian      | 31.00                     | —                                 |
| Jiao Gu Lan         | 31.05                     | —                                 |
| Jin Yin Hua         | 31.35                     | —                                 |
| Guang Huo Xiang     | 31.66                     | —                                 |
| Ma Huang            | 33.39                     | —                                 |
| Fu Pen Zi           | 33.40                     | —                                 |
| Fu Zi               | 33.54                     | —                                 |
| Gua Lou             | 33.68                     | —                                 |
| Zhi Ke              | 33.99                     | —                                 |
| Ban Lan Gen         | 35.49                     | —                                 |
| Gan Cao             | 35.93                     | —                                 |
| Sang Ji Shend       | 35.93                     | —                                 |
| Ren Shen            | 36.42                     | —                                 |
| Hou Po              | 36.47                     | —                                 |
| Cang Zhu            | 36.75                     | —                                 |
| Qiang Huo           | 36.82                     | —                                 |
| Jie Geng            | 37.28                     | —                                 |
| Che Qian Zi         | 37.78                     | —                                 |
| Wu Zhu Yu           | 38.91                     | —                                 |
| Dang Gui            | 39.10                     | —                                 |
| Huang Qin           | 39.66                     | —                                 |
| Xin Yi              | 40.79                     | —                                 |
| Zhi Mu              | 41.01                     | —                                 |
| Huang Lian          | 41.14                     | —                                 |
| Zi Hua Di Ding      | 41.23                     | —                                 |
| Sha Ren             | 42.05                     | —                                 |
| San Qi              | 42.49                     | —                                 |
| Wu Jia Pi           | 43.15                     | —                                 |
| Sang Ye             | 43.19                     | —                                 |
| Zhi Shi             | 43.52                     | —                                 |
| Jin Qian Cao        | 43.97                     | —                                 |
| Sang Zhi            | 44.18                     | —                                 |
| Ding Xiang          | 44.19                     | —                                 |
| Sang Bai Pi         | 45.18                     | —                                 |
| Long Yan Rou        | 45.88                     | —                                 |
| Xia Ku Cao          | 46.90                     | —                                 |
| Du Zhong            | 47.58                     | —                                 |
| Mu Gua              | 47.59                     | —                                 |
| Yuan Zhi            | 48.27                     | —                                 |
| Chuang Mu Xiang     | 48.70                     | —                                 |
| Hu Zhang            | 49.13                     | —                                 |
| Gou Qi Zi           | 49.30                     | —                                 |
| Bai Hua She She Cao | 49.53                     | —                                 |
| Han Lian Cao        | 49.89                     | —                                 |
| Yin Chen Hao        | 50.12                     | —                                 |

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                         | 21.14                           |
| 62314     | 62314               | 0.00                         | 22.05                           |
| 62629     | 62629               | 0.00                         | 5.74                            |
| 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 2.4-2022-02

Validated substance/substance group **Gu Sui Bu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002263-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Gu Sui Bu                 | 2      | 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 |
| PhytoComm | Gu Sui Bu | G094HS230TK1 | 62921     | 40      | from supplier |
| PhytoComm | Gu Sui Bu | G094HS230TK1 | 62922     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Gu Sui Bu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Gu Sui Bu | G094H1011921 | 62780 <sup>†</sup> | 20      |
| PhytoComm | Gu Sui Bu | G094HS230TK1 | 62921 <sup>†</sup> | 20      |
| PhytoComm | Gu Sui Bu | G094HS230TK1 | 62922 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 | g094h1011023 | 1       |
| Phytocomm | Gu Sui Bu | g094h1011221 | 1       |
| Phytocomm | Gu Sui Bu | G094H1011221 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 4              | 0             | 6              | 847           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 99.3643 % (> 98.7773 %)  | n/a (n/a)                |

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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Shen Qu         | 5.23                      | —                                 |
| Ren Dong Teng   | 7.06                      | —                                 |
| Mu Zei          | 7.44                      | —                                 |
| Huo Ma Ren      | 7.73                      | —                                 |
| Fu Zi           | 8.54                      | —                                 |
| She Gan         | 9.06                      | —                                 |
| Ce Bai Ye       | 9.40                      | —                                 |
| Pi Pa Ye        | 9.68                      | —                                 |
| (Fen) Bi Xie    | 10.32                     | —                                 |
| Fu Pen Zi       | 10.42                     | —                                 |
| He Huan Pi      | 10.43                     | —                                 |
| Shan Yao        | 10.48                     | —                                 |
| Lu Gen          | 10.49                     | —                                 |
| Zhu Ling        | 11.11                     | —                                 |
| Hou Po          | 11.17                     | —                                 |
| Tian Hua Fen    | 11.25                     | —                                 |
| Gui Zhi         | 11.26                     | —                                 |
| Bai Shao Yao    | 11.27                     | —                                 |
| Ji Li           | 11.28                     | —                                 |
| Ling Zhi        | 11.51                     | —                                 |
| Bai Xian Pi     | 11.71                     | —                                 |
| Dan Dou Chi     | 11.75                     | —                                 |
| Yan Hu Suo      | 11.76                     | —                                 |
| Ji Xue Teng     | 11.80                     | —                                 |
| Ye Jiao Teng    | 12.03                     | —                                 |
| Gou Teng        | 12.25                     | —                                 |
| Lian Qiao       | 12.32                     | —                                 |
| Dan Shen        | 12.56                     | —                                 |
| Fu Ling         | 12.60                     | —                                 |
| Lian Zi         | 12.75                     | —                                 |
| Yu Jin          | 13.25                     | —                                 |
| Ze Xie          | 13.36                     | —                                 |
| Yin Yang Huo    | 13.65                     | —                                 |
| Suan Zao Ren    | 13.87                     | —                                 |
| Jin Yin Hua     | 14.01                     | —                                 |
| Zhe Bei Mu      | 14.10                     | —                                 |
| Tao Ren         | 14.15                     | —                                 |
| Che Qian Zi     | 14.31                     | —                                 |
| Sheng Jiang     | 14.58                     | —                                 |
| Sang Ji Shend   | 14.67                     | —                                 |
| Guang Huo Xiang | 14.80                     | —                                 |
| Ban Lan Gen     | 14.99                     | —                                 |
| Ma Huang        | 15.90                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Chai Hu         | 15.92                             | —                                         |
| He Shou Wu      | 16.03                             | —                                         |
| Sang Bai Pi     | 16.31                             | —                                         |
| Bai Zi Ren      | 16.64                             | —                                         |
| Ma Huang Gen    | 16.92                             | —                                         |
| Hong Jing Tian  | 17.05                             | —                                         |
| Ci Wu Jia       | 17.24                             | —                                         |
| Mao Dong Qing   | 17.62                             | —                                         |
| Gan Cao         | 17.63                             | —                                         |
| Rou Gui         | 18.15                             | —                                         |
| Tu Fu Ling      | 18.24                             | —                                         |
| Qiang Huo       | 18.57                             | —                                         |
| Lai Fu Zi       | 18.70                             | —                                         |
| Jiao Gu Lan     | 18.78                             | —                                         |
| Yin Chen Hao    | 19.60                             | —                                         |
| Fo Shou         | 19.68                             | —                                         |
| Ban Xia (Jiang) | 19.70                             | —                                         |
| Chen Pi         | 19.99                             | —                                         |
| Di Gu Pi        | 20.24                             | —                                         |
| Yi Yi Ren       | 20.84                             | —                                         |
| Gua Lou         | 21.55                             | —                                         |
| Zhu Ru          | 21.97                             | —                                         |
| Ren Shen        | 22.88                             | —                                         |
| Fu Xiao Mai     | 23.09                             | —                                         |
| Jing Jie        | 23.38                             | —                                         |
| Xuan Fu Hua     | 23.52                             | —                                         |
| Jiang Huang     | 23.57                             | —                                         |
| Zhi Gan Cao     | 23.99                             | —                                         |
| Cang Zhu        | 24.51                             | —                                         |
| Zi Hua Di Ding  | 25.24                             | —                                         |
| Dang Gui        | 25.56                             | —                                         |
| Jie Geng        | 25.72                             | —                                         |
| Mang Xiao       | 26.18                             | —                                         |
| Wu Yao          | 26.59                             | —                                         |
| Bu Gu Zhi       | 26.68                             | —                                         |
| Qing Pi         | 26.98                             | —                                         |
| Zhi Ke          | 27.53                             | —                                         |
| Sha Ren         | 27.83                             | —                                         |
| Huang Lian      | 28.11                             | —                                         |
| San Qi          | 28.16                             | —                                         |
| Tu Si Zi        | 29.69                             | —                                         |
| Huang Qin       | 29.71                             | —                                         |
| Bo He           | 30.46                             | —                                         |
| Wu Zhu Yu       | 30.72                             | —                                         |
| (Bai) Dou Kou   | 30.83                             | —                                         |
| Du Zhong        | 30.94                             | —                                         |
| Mu Dan Pi       | 31.50                             | —                                         |
| Yi Mu Cao       | 31.69                             | —                                         |
| Fu Shen         | 32.25                             | —                                         |
| Hu Zhang        | 32.66                             | —                                         |
| Long Yan Rou    | 33.03                             | —                                         |
| Zhi Mu          | 33.06                             | —                                         |
| Ku Shen         | 33.27                             | —                                         |
| Sang Zhi        | 33.63                             | —                                         |
| (Shi) Chang Pu  | 33.64                             | —                                         |
| Huang Bai       | 33.90                             | —                                         |
| Xie Bai         | 34.69                             | —                                         |
| Chuang Mu Xiang | 34.93                             | —                                         |
| Chi Shao (Yao)  | 34.94                             | —                                         |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Nü Zhen Zi          | 36.02                     | —                                 |
| Ge Gen              | 36.50                     | —                                 |
| Gou Qi Zi           | 36.64                     | —                                 |
| E Zhu               | 38.09                     | —                                 |
| Dan Zhu Ye          | 38.30                     | —                                 |
| Shan Yu Rou         | 38.94                     | —                                 |
| Mu Gua              | 39.05                     | —                                 |
| Hong Hua            | 39.96                     | —                                 |
| Xia Ku Cao          | 40.74                     | —                                 |
| Fang Feng           | 42.27                     | —                                 |
| Ju Hua              | 42.36                     | —                                 |
| Yuan Zhi            | 42.38                     | —                                 |
| Xiao Hui Xiang      | 42.89                     | —                                 |
| Bai Jiang Cao       | 44.35                     | —                                 |
| Xi Xian Cao         | 45.28                     | —                                 |
| Cang Er Zi          | 45.52                     | —                                 |
| Xin Yi              | 47.25                     | —                                 |
| Qing Hao            | 47.37                     | —                                 |
| Bai Hua She She Cao | 48.24                     | —                                 |
| Chuan Niu Xi        | 48.79                     | —                                 |
| Jin Qian Cao        | 49.12                     | —                                 |
| Sang Ye             | 50.62                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62779     | 62779                  | 0.00                            | 11.85                              |
| 62780     | 62780                  | 0.00                            | 11.48                              |
| 62921     | 62921                  | 0.00                            | 5.30                               |
| 62922     | 62922                  | 0.00                            | 5.23                               |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Gua Lou**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60128-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Gua Lou                   | 1      | 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   | G241HS202SV1 | 62797     | 40      | from supplier |
| PhytoComm | Gua Lou   | G241HS202SV1 | 62798     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Gua Lou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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   | G241HS202SV1 | 62797 <sup>†</sup> | 20      |
| PhytoComm | Gua Lou   | G241HS202SV1 | 62798 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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   | g241h1096321 | 1       |
| Phytocomm | Gua Lou   | G241H1096321 | 1       |
| Phytocomm | Gua Lou   | G241H1096521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 38            | 2              | 11 357        |
| <b>Type C</b> | 0              | 0             | 3              | 854           |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 95.0000 % (> 87.5000 %)  |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Fo Shou         | 6.47                      | —                                 |
| Bai Shao Yao    | 6.80                      | —                                 |
| Jie Geng        | 7.74                      | —                                 |
| Zhi Mu          | 9.35                      | —                                 |
| Ye Jiao Teng    | 10.26                     | —                                 |
| Pi Pa Ye        | 11.03                     | —                                 |
| San Qi          | 12.34                     | —                                 |
| Di Gu Pi        | 12.51                     | —                                 |
| Shen Qu         | 12.72                     | —                                 |
| Mu Zei          | 13.26                     | —                                 |
| Cang Zhu        | 13.56                     | —                                 |
| Zhe Bei Mu      | 13.79                     | —                                 |
| He Huan Pi      | 13.95                     | —                                 |
| Ji Li           | 14.06                     | —                                 |
| Tian Hua Fen    | 14.35                     | —                                 |
| Jin Yin Hua     | 14.56                     | —                                 |
| Ze Xie          | 14.61                     | —                                 |
| Dang Gui        | 14.82                     | —                                 |
| Bai Zi Ren      | 14.84                     | —                                 |
| Shan Yao        | 15.05                     | —                                 |
| Ci Wu Jia       | 15.29                     | —                                 |
| Mu Gua          | 15.60                     | —                                 |
| Ban Lan Gen     | 15.86                     | —                                 |
| Ren Dong Teng   | 15.90                     | —                                 |
| Tao Ren         | 16.32                     | —                                 |
| Zhu Ru          | 16.50                     | —                                 |
| Lian Zi         | 16.58                     | —                                 |
| Yuan Zhi        | 17.00                     | —                                 |
| Rou Gui         | 17.24                     | —                                 |
| Lian Qiao       | 17.35                     | —                                 |
| Lai Fu Zi       | 17.42                     | —                                 |
| Ku Shen         | 17.53                     | —                                 |
| Ling Zhi        | 17.87                     | —                                 |
| Ban Xia (Jiang) | 18.50                     | —                                 |
| Ren Shen        | 18.60                     | —                                 |
| Sheng Jiang     | 18.62                     | —                                 |
| Tu Fu Ling      | 19.55                     | —                                 |
| Fu Ling         | 20.24                     | —                                 |
| Gou Qi Zi       | 21.05                     | —                                 |
| Lu Gen          | 21.10                     | —                                 |
| Suan Zao Ren    | 21.31                     | —                                 |
| Huo Ma Ren      | 21.51                     | —                                 |
| Gou Teng        | 21.57                     | —                                 |
| Gui Zhi         | 22.04                     | —                                 |
| Long Yan Rou    | 22.09                     | —                                 |
| Jiao Gu Lan     | 22.53                     | —                                 |
| Fu Zi           | 22.93                     | —                                 |
| Fu Pen Zi       | 23.36                     | —                                 |
| Fu Xiao Mai     | 23.92                     | —                                 |
| Ji Xue Teng     | 24.57                     | —                                 |
| Bai Xian Pi     | 24.84                     | —                                 |
| Xie Bai         | 25.04                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Gu Sui Bu       | 25.17                     | —                                 |
| Zhi Ke          | 25.78                     | —                                 |
| Dan Dou Chi     | 26.48                     | —                                 |
| Yi Yi Ren       | 26.90                     | —                                 |
| Ma Huang        | 26.93                     | —                                 |
| Huang Qin       | 27.63                     | —                                 |
| Hou Po          | 27.93                     | —                                 |
| Dan Shen        | 28.26                     | —                                 |
| Hong Jing Tian  | 28.35                     | —                                 |
| Chuang Mu Xiang | 29.17                     | —                                 |
| Mao Dong Qing   | 30.17                     | —                                 |
| Gan Cao         | 30.37                     | —                                 |
| Yin Yang Huo    | 30.57                     | —                                 |
| Ma Huang Gen    | 30.62                     | —                                 |
| (Fen) Bi Xie    | 30.78                     | —                                 |
| Che Qian Zi     | 31.59                     | —                                 |
| Mang Xiao       | 32.35                     | —                                 |
| Chai Hu         | 32.62                     | —                                 |
| Ce Bai Ye       | 33.05                     | —                                 |
| Yan Hu Suo      | 33.35                     | —                                 |
| Yu Jin          | 34.51                     | —                                 |
| She Gan         | 35.25                     | —                                 |
| Fu Shen         | 35.90                     | —                                 |
| Guang Huo Xiang | 36.52                     | —                                 |
| Sang Zhi        | 36.90                     | —                                 |
| Zhu Ling        | 37.32                     | —                                 |
| Qiang Huo       | 37.35                     | —                                 |
| Chi Shao (Yao)  | 38.32                     | —                                 |
| Zhi Gan Cao     | 43.70                     | —                                 |
| Qing Pi         | 44.39                     | —                                 |
| Huang Lian      | 44.82                     | —                                 |
| Jing Jie        | 45.12                     | —                                 |
| Zi Hua Di Ding  | 45.36                     | —                                 |
| Chuan Lian Zi   | 46.11                     | —                                 |
| Bo He           | 46.63                     | —                                 |
| Sha Ren         | 50.03                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62797     | 62797                  | 0.00                            | 6.80                               |
| 62798     | 62798                  | 0.00                            | 6.47                               |

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 2.4-2022-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Guang Huo Xiang</b>                                          |
| Substance class                     | TCM - Granulated herbal extracts (PhytoComm)                    |
| Report date                         | 27/06/2022                                                      |
| Report number                       | 61079-2022-06-27                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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

|                   |                                                                    |
|-------------------|--------------------------------------------------------------------|
| 978-3-7692-7517-9 | <i>European Pharmacopoeia 10th Edition, Basic Version 2020</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]           |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>         |

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Guang Huo Xiang           | 2      | 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 |
| PhytoComm | Guang Huo Xiang | G007HS347TM1 | 63019     | 40      | from supplier |
| PhytoComm | Guang Huo Xiang | G007HS347TM1 | 63020     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Guang Huo Xiang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Guang Huo Xiang | G007H2005822 | 62590 <sup>†</sup> | 20      |
| PhytoComm | Guang Huo Xiang | G007HS347TM1 | 63019 <sup>†</sup> | 20      |
| PhytoComm | Guang Huo Xiang | G007HS347TM1 | 63020 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 159           | 1              | 22 279        |
| <b>Type B</b> | 0              | 75            | 5              | 11 317        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Guang Huo Xiang* 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9963 % (> 99.9799 %)  | 99.3750 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 93.7500 % (> 90.0000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Ce Bai Ye      | 3.84                      | —                                 |
| Dan Dou Chi    | 4.92                      | —                                 |
| Yin Yang Huo   | 5.39                      | —                                 |
| Bai Xian Pi    | 5.74                      | —                                 |
| Hou Po         | 7.74                      | —                                 |
| Tu Fu Ling     | 7.90                      | —                                 |
| Shen Qu        | 8.19                      | —                                 |
| Ren Dong Teng  | 8.23                      | —                                 |
| Ling Zhi       | 8.38                      | —                                 |
| Ye Jiao Teng   | 8.46                      | —                                 |
| Jing Jie       | 8.55                      | —                                 |
| Yu Jin         | 8.82                      | —                                 |
| Chai Hu        | 9.23                      | —                                 |
| Mao Dong Qing  | 9.28                      | —                                 |
| Che Qian Zi    | 9.42                      | —                                 |
| Zhu Ling       | 9.61                      | —                                 |
| Shan Yao       | 9.93                      | —                                 |
| Qiang Huo      | 10.82                     | —                                 |
| Dan Shen       | 11.00                     | —                                 |
| Fu Zi          | 11.03                     | —                                 |
| Gu Sui Bu      | 11.22                     | —                                 |
| Lian Zi        | 12.01                     | —                                 |
| Fu Pen Zi      | 12.08                     | —                                 |
| (Fen) Bi Xie   | 12.17                     | —                                 |
| She Gan        | 12.52                     | —                                 |
| Pi Pa Ye       | 12.81                     | —                                 |
| Yan Hu Suo     | 12.96                     | —                                 |
| Ji Li          | 13.58                     | —                                 |
| Zi Hua Di Ding | 14.00                     | —                                 |
| Jin Yin Hua    | 15.67                     | —                                 |
| Sha Ren        | 16.17                     | —                                 |
| Ma Huang       | 16.19                     | —                                 |
| Ji Xue Teng    | 16.21                     | —                                 |
| Rou Gui        | 16.41                     | —                                 |
| Suan Zao Ren   | 16.45                     | —                                 |
| Hong Jing Tian | 16.49                     | —                                 |
| Gou Teng       | 16.63                     | —                                 |
| Gan Cao        | 16.81                     | —                                 |
| He Huan Pi     | 16.98                     | —                                 |
| Huo Ma Ren     | 17.01                     | —                                 |
| Lian Qiao      | 17.04                     | —                                 |
| Ma Huang Gen   | 17.30                     | —                                 |
| Lu Gen         | 17.33                     | —                                 |
| Mang Xiao      | 17.46                     | —                                 |
| Tian Hua Fen   | 17.77                     | —                                 |
| Bo He          | 18.43                     | —                                 |
| Bai Shao Yao   | 18.49                     | —                                 |
| Fu Ling        | 19.27                     | —                                 |

*continued on the next page*

continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mu Zei          | 19.39                     | —                                 |
| Gui Zhi         | 19.71                     | —                                 |
| Ban Lan Gen     | 19.72                     | —                                 |
| Jiao Gu Lan     | 20.20                     | —                                 |
| Du Zhong        | 20.94                     | —                                 |
| Sheng Jiang     | 21.16                     | —                                 |
| Qing Pi         | 21.45                     | —                                 |
| Huang Bai       | 22.46                     | —                                 |
| Yi Yi Ren       | 23.20                     | —                                 |
| Di Gu Pi        | 23.24                     | —                                 |
| Zhe Bei Mu      | 23.36                     | —                                 |
| Zhi Gan Cao     | 23.99                     | —                                 |
| Tao Ren         | 24.17                     | —                                 |
| Huang Lian      | 24.34                     | —                                 |
| Fo Shou         | 24.40                     | —                                 |
| Zhi Ke          | 26.10                     | —                                 |
| Ren Shen        | 26.63                     | —                                 |
| Ci Wu Jia       | 27.29                     | —                                 |
| Bai Zi Ren      | 28.77                     | —                                 |
| Cang Zhu        | 28.79                     | —                                 |
| Ze Xie          | 28.90                     | —                                 |
| Ban Xia (Jiang) | 29.39                     | —                                 |
| Fu Xiao Mai     | 29.87                     | —                                 |
| Zhu Ru          | 30.27                     | —                                 |
| Chuang Mu Xiang | 30.87                     | —                                 |
| Bai Jiang Cao   | 31.19                     | —                                 |
| Qing Hao        | 32.77                     | —                                 |
| Sang Zhi        | 32.84                     | —                                 |
| Chi Shao (Yao)  | 33.52                     | —                                 |
| Fu Shen         | 33.93                     | —                                 |
| Jie Geng        | 34.79                     | —                                 |
| Dang Gui        | 35.73                     | —                                 |
| Hong Hua        | 35.92                     | —                                 |
| San Qi          | 36.36                     | —                                 |
| Huang Qin       | 36.45                     | —                                 |
| Lai Fu Zi       | 36.89                     | —                                 |
| Gua Lou         | 37.00                     | —                                 |
| Xie Bai         | 37.30                     | —                                 |
| Jiu Da Huang    | 39.45                     | —                                 |
| Long Yan Rou    | 39.52                     | —                                 |
| Ban Zhi Lian    | 40.00                     | —                                 |
| Pu Gong Ying    | 40.50                     | —                                 |
| Cang Er Zi      | 42.78                     | —                                 |
| Ku Shen         | 44.26                     | —                                 |
| Ze Lan          | 44.83                     | —                                 |
| Hua Shi         | 44.87                     | —                                 |
| Bai Zhu         | 45.77                     | —                                 |
| Wu Mei          | 47.10                     | —                                 |
| Sang Ye         | 47.37                     | —                                 |
| Gou Qi Zi       | 48.07                     | —                                 |
| Zhi Mu          | 48.45                     | —                                 |
| E Zhu           | 49.22                     | —                                 |
| Jiang Huang     | 49.93                     | —                                 |
| Shu Di (Huang)  | 52.22                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62589     | 62589               | 0.00                         | 17.58                           |
| 62590     | 62590               | 0.00                         | 17.46                           |
| 63019     | 63019               | 0.00                         | 4.92                            |
| 63020     | 63020               | 0.00                         | 3.84                            |

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 2.4-2022-02

Validated substance/substance group **Gui Zhi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60189-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Gui Zhi                   | 3      | 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   | G070HS205SH1 | 62563     | 40      | from supplier |
| PhytoComm | Gui Zhi   | G070HS205SH1 | 62564     | 40      | from supplier |
| PhytoComm | Gui Zhi   | G070HS205TK1 | 62931     | 40      | from supplier |
| PhytoComm | Gui Zhi   | G070HS205TK1 | 62932     | 40      | from supplier |
| PhytoComm | Gui Zhi   | G070HS205TH1 | 62933     | 40      | from supplier |
| PhytoComm | Gui Zhi   | G070HS205TH1 | 62934     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Gui Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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   | G070HS205SH1 | 62563 <sup>†</sup> | 20      |
| PhytoComm | Gui Zhi   | G070HS205SH1 | 62564 <sup>†</sup> | 20      |
| PhytoComm | Gui Zhi   | G070HS205TK1 | 62931 <sup>†</sup> | 20      |
| PhytoComm | Gui Zhi   | G070HS205TK1 | 62932 <sup>†</sup> | 20      |
| PhytoComm | Gui Zhi   | G070HS205TH1 | 62933 <sup>†</sup> | 20      |
| PhytoComm | Gui Zhi   | G070HS205TH1 | 62934 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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   | G070H1001523 | 2       |
| Phytocomm | Gui Zhi   | G070H100422  | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 239           | 1              | 22 199        |
| <b>Type B</b> | 1              | 112           | 8              | 11 276        |
| <b>Type C</b> | 1              | 0             | 6              | 850           |

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        |
|---------------|-------------------------|-------------------------|
| <b>Type A</b> | 99.9963 % (> 99.9799 %) | 99.5833 % (> 98.3333 %) |
| <b>Type B</b> | 99.9950 % (> 99.9628 %) | 93.3333 % (> 90.8333 %) |
| <b>Type C</b> | 99.7674 % (> 99.1804 %) | n/a (n/a)               |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Rou Gui         | 4.94                      | —                                 |
| Sheng Jiang     | 5.00                      | —                                 |
| He Huan Pi      | 6.22                      | —                                 |
| Ban Xia (Jiang) | 7.04                      | —                                 |
| Mu Zei          | 7.28                      | —                                 |
| Gou Teng        | 7.63                      | —                                 |
| Yi Yi Ren       | 7.66                      | —                                 |
| Ma Huang Gen    | 7.75                      | —                                 |
| Fu Ling         | 8.09                      | —                                 |
| Tao Ren         | 8.10                      | —                                 |
| Ji Xue Teng     | 8.82                      | —                                 |
| Ci Wu Jia       | 8.84                      | —                                 |
| Di Gu Pi        | 8.87                      | —                                 |
| Zhu Ru          | 9.46                      | —                                 |
| Lu Gen          | 9.63                      | —                                 |
| Lai Fu Zi       | 10.29                     | —                                 |
| Fu Xiao Mai     | 10.33                     | —                                 |
| Fu Shen         | 10.81                     | —                                 |
| Gu Sui Bu       | 12.70                     | —                                 |
| Bai Zi Ren      | 13.19                     | —                                 |
| Ji Li           | 13.67                     | —                                 |
| Fo Shou         | 13.69                     | —                                 |
| Lian Zi         | 13.87                     | —                                 |
| Huo Ma Ren      | 13.90                     | —                                 |
| Bai Shao Yao    | 14.18                     | —                                 |
| Bai Xian Pi     | 14.18                     | —                                 |
| Ye Jiao Teng    | 14.42                     | —                                 |
| Ling Zhi        | 14.52                     | —                                 |
| Ren Dong Teng   | 15.90                     | —                                 |
| Shen Qu         | 15.92                     | —                                 |
| Zhe Bei Mu      | 15.92                     | —                                 |
| (Fen) Bi Xie    | 16.48                     | —                                 |
| Suan Zao Ren    | 20.13                     | —                                 |
| Tu Fu Ling      | 21.01                     | —                                 |
| Ze Xie          | 21.16                     | —                                 |
| Tian Hua Fen    | 21.45                     | —                                 |
| She Gan         | 21.88                     | —                                 |
| Zhu Ling        | 21.95                     | —                                 |
| Jin Yin Hua     | 22.20                     | —                                 |
| Ren Shen        | 23.68                     | —                                 |
| Dan Shen        | 23.70                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dan Dou Chi     | 24.38                     | —                                 |
| Yu Jin          | 24.89                     | —                                 |
| Lian Qiao       | 26.10                     | —                                 |
| Pi Pa Ye        | 26.62                     | —                                 |
| Gua Lou         | 27.52                     | —                                 |
| Ma Huang        | 27.56                     | —                                 |
| Dang Gui        | 27.56                     | —                                 |
| Yan Hu Suo      | 27.72                     | —                                 |
| Yin Yang Huo    | 27.77                     | —                                 |
| Ban Lan Gen     | 28.11                     | —                                 |
| Hong Jing Tian  | 28.13                     | —                                 |
| Shan Yao        | 28.13                     | —                                 |
| Ce Bai Ye       | 28.56                     | —                                 |
| Cang Zhu        | 28.59                     | —                                 |
| Zhi Mu          | 29.67                     | —                                 |
| Jie Geng        | 29.68                     | —                                 |
| Jiao Gu Lan     | 30.92                     | —                                 |
| Zhi Ke          | 31.20                     | —                                 |
| Mang Xiao       | 31.50                     | —                                 |
| Mao Dong Qing   | 31.66                     | —                                 |
| Fu Pen Zi       | 31.68                     | —                                 |
| Long Yan Rou    | 31.68                     | —                                 |
| Chai Hu         | 32.13                     | —                                 |
| Guang Huo Xiang | 32.53                     | —                                 |
| Huang Qin       | 33.28                     | —                                 |
| Fu Zi           | 35.21                     | —                                 |
| San Qi          | 35.90                     | —                                 |
| Mu Gua          | 36.35                     | —                                 |
| Gan Cao         | 36.43                     | —                                 |
| Qiang Huo       | 37.63                     | —                                 |
| Hou Po          | 37.71                     | —                                 |
| Yuan Zhi        | 38.43                     | —                                 |
| Sang Zhi        | 38.55                     | —                                 |
| Jing Jie        | 39.04                     | —                                 |
| Huang Lian      | 42.12                     | —                                 |
| Gou Qi Zi       | 43.17                     | —                                 |
| Zi Hua Di Ding  | 43.48                     | —                                 |
| Sha Ren         | 44.14                     | —                                 |
| Chuang Mu Xiang | 44.78                     | —                                 |
| Che Qian Zi     | 45.16                     | —                                 |
| Chi Shao (Yao)  | 46.81                     | —                                 |
| Ku Shen         | 47.61                     | —                                 |
| Bai Zhu         | 50.09                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62563     | 62563               | 0.00                         | 5.08                            |
| 62564     | 62564               | 0.00                         | 5.00                            |
| 62931     | 62931               | 0.00                         | 5.43                            |
| 62932     | 62932               | 0.00                         | 4.94                            |
| 62933     | 62933               | 0.00                         | 6.23                            |
| 62934     | 62934               | 0.00                         | 5.87                            |

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 2.4-2022-02

Validated substance/substance group **Han Lian Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60540-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Han Lian Cao | G095HS141RW1 | 62680 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 | G095H0770321 | 1       |
| PhytoComm | Han Lian Cao | G095H0770321 | 2       |
| Phytocomm | Han Lian Cao | G095H0770521 | 4       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Bai Hua She She Cao | 6.53                      | —                                 |
| Yu Xing Cao         | 10.41                     | —                                 |
| Xi Xian Cao         | 13.39                     | —                                 |
| Xin Yi              | 13.79                     | —                                 |
| Pu Gong Ying        | 15.02                     | —                                 |
| Jiang Huang         | 15.88                     | —                                 |
| Xia Ku Cao          | 16.02                     | —                                 |
| Zhi Shi             | 16.37                     | —                                 |
| Tu Fu Ling          | 16.73                     | —                                 |
| Sang Ye             | 18.80                     | —                                 |
| Huang Lian          | 18.97                     | —                                 |
| Hu Zhang            | 20.10                     | —                                 |
| Shan Yao            | 21.31                     | —                                 |
| Ze Lan              | 21.63                     | —                                 |
| Nü Zhen Zi          | 23.67                     | —                                 |
| Sha Ren             | 25.68                     | —                                 |
| He Huan Pi          | 27.21                     | —                                 |
| Xiang Fu            | 27.48                     | —                                 |
| Mang Xiao           | 28.84                     | —                                 |
| Yi Mu Cao           | 29.97                     | —                                 |
| Yin Chen Hao        | 33.86                     | —                                 |
| Du Zhong            | 34.57                     | —                                 |
| Gu Sui Bu           | 35.79                     | —                                 |
| Qiang Huo           | 37.43                     | —                                 |
| Fu Zi               | 40.40                     | —                                 |
| Yu Jin              | 40.52                     | —                                 |
| Gou Teng            | 42.71                     | —                                 |
| Cang Er Zi          | 44.02                     | —                                 |
| E Zhu               | 44.89                     | —                                 |
| Dan Shen            | 45.27                     | —                                 |
| Hou Po              | 45.45                     | —                                 |
| Niu Bang Zi         | 45.61                     | —                                 |
| Chen Pi             | 46.61                     | —                                 |
| (Bai) Dou Kou       | 47.08                     | —                                 |
| Bo He               | 47.26                     | —                                 |
| Che Qian Zi         | 48.79                     | —                                 |
| Bai Jiang Cao       | 48.95                     | —                                 |
| Zhi Ke              | 49.81                     | —                                 |
| Wu Yao              | 50.29                     | —                                 |

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                         | 6.53                            |
| 62680     | 62680               | 0.00                         | 9.88                            |

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



# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **He Huan Pi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60175-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| He Huan Pi                | 4      | 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 |
| PhytoComm | He Huan Pi | G010HS114SW1 | 62949     | 40      | from supplier |
| PhytoComm | He Huan Pi | G010HS114SW1 | 62950     | 40      | from supplier |
| PhytoComm | He Huan Pi | G010HS114TK1 | 62951     | 40      | from supplier |
| PhytoComm | He Huan Pi | G010HS114TK1 | 62952     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *He Huan Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 22 120 spectra from a total of 278 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | He Huan Pi | G010H0635822 | 62403 <sup>†</sup> | 20      |
| PhytoComm | He Huan Pi | G010HS114SK1 | 62645 <sup>†</sup> | 20      |
| PhytoComm | He Huan Pi | G010HS114SK1 | 62646 <sup>†</sup> | 20      |

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| Supplier  | Substance  | Batch        | Sample ID          | Spectra |
|-----------|------------|--------------|--------------------|---------|
| PhytoComm | He Huan Pi | G010HS114SW1 | 62949 <sup>†</sup> | 20      |
| PhytoComm | He Huan Pi | G010HS114SW1 | 62950 <sup>†</sup> | 20      |
| PhytoComm | He Huan Pi | G010HS114TK1 | 62951 <sup>†</sup> | 20      |
| PhytoComm | He Huan Pi | G010HS114TK1 | 62952 <sup>†</sup> | 20      |

- 11 237 spectra from a total of 278 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 16             | 303           | 17             | 22 104        |
| <b>Type B</b> | 27             | 141           | 19             | 11 210        |
| <b>Type C</b> | 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:

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

|               | <b>Specificity</b>       | <b>Recognition rate</b> |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.8946 % (> 99.8782 %)  | 94.6875 % (> 93.7500 %) |
| <b>Type B</b> | 99.6528 % (> 99.6205 %)  | 88.1250 % (> 86.2500 %) |
| <b>Type C</b> | 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.

### 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.

| <b>Substance</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|------------------|-----------------------------------|-------------------------------------------|
| Rou Gui          | 2.66                              | —                                         |
| Tao Ren          | 3.70                              | —                                         |
| Huo Ma Ren       | 4.38                              | —                                         |
| Sheng Jiang      | 4.71                              | —                                         |
| Ci Wu Jia        | 4.71                              | —                                         |
| Mu Zei           | 5.05                              | —                                         |
| Ma Huang Gen     | 5.17                              | —                                         |
| Gui Zhi          | 5.25                              | —                                         |
| Gou Teng         | 5.79                              | —                                         |
| Lai Fu Zi        | 6.15                              | —                                         |
| Di Gu Pi         | 7.21                              | —                                         |
| Bai Zi Ren       | 7.35                              | —                                         |
| Ji Xue Teng      | 7.59                              | —                                         |
| Lian Zi          | 8.10                              | —                                         |
| Bai Shao Yao     | 8.19                              | —                                         |
| Fu Xiao Mai      | 8.59                              | —                                         |
| Gu Sui Bu        | 8.84                              | —                                         |
| Fu Ling          | 8.86                              | —                                         |
| Lu Gen           | 9.68                              | —                                         |
| Ban Xia (Jiang)  | 9.88                              | —                                         |
| Yi Yi Ren        | 9.94                              | —                                         |
| Ling Zhi         | 10.15                             | —                                         |
| Ji Li            | 10.51                             | —                                         |
| Shen Qu          | 11.15                             | —                                         |
| Zhu Ru           | 11.25                             | —                                         |
| Bai Xian Pi      | 11.54                             | —                                         |
| Zhe Bei Mu       | 11.57                             | —                                         |
| Fu Shen          | 11.75                             | —                                         |
| Ye Jiao Teng     | 12.93                             | —                                         |
| Tian Hua Fen     | 13.46                             | —                                         |
| Fo Shou          | 13.62                             | —                                         |
| Suan Zao Ren     | 14.01                             | —                                         |
| (Fen) Bi Xie     | 14.22                             | —                                         |
| Ze Xie           | 14.42                             | —                                         |
| Ren Dong Teng    | 14.97                             | —                                         |
| Jiang Huang      | 15.48                             | —                                         |

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| <b>Substanz</b>     | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|---------------------|-----------------------------------|-------------------------------------------|
| Zhu Ling            | 15.82                             | —                                         |
| She Gan             | 16.79                             | —                                         |
| Tu Fu Ling          | 17.32                             | —                                         |
| Yu Jin              | 18.96                             | —                                         |
| Ce Bai Ye           | 19.54                             | —                                         |
| Lian Qiao           | 19.55                             | —                                         |
| Pi Pa Ye            | 20.14                             | —                                         |
| Wu Yao              | 20.40                             | —                                         |
| Chen Pi             | 20.47                             | —                                         |
| Shan Yao            | 20.54                             | —                                         |
| (Bai) Dou Kou       | 20.67                             | —                                         |
| Dan Dou Chi         | 21.12                             | —                                         |
| Sha Ren             | 21.44                             | —                                         |
| Dan Shen            | 22.26                             | —                                         |
| Yan Hu Suo          | 22.68                             | —                                         |
| Jin Yin Hua         | 22.99                             | —                                         |
| Fu Pen Zi           | 24.71                             | —                                         |
| Gua Lou             | 24.74                             | —                                         |
| Mao Dong Qing       | 24.96                             | —                                         |
| Chai Hu             | 25.59                             | —                                         |
| Yin Yang Huo        | 25.87                             | —                                         |
| Fu Zi               | 26.19                             | —                                         |
| Cang Zhu            | 26.23                             | —                                         |
| Jiao Gu Lan         | 26.75                             | —                                         |
| Sang Bai Pi         | 27.01                             | —                                         |
| Yi Mu Cao           | 27.26                             | —                                         |
| Ban Lan Gen         | 27.69                             | —                                         |
| Yin Chen Hao        | 27.76                             | —                                         |
| Hong Jing Tian      | 27.77                             | —                                         |
| Guang Huo Xiang     | 28.48                             | —                                         |
| Mang Xiao           | 28.59                             | —                                         |
| Hou Po              | 29.33                             | —                                         |
| Jie Geng            | 29.34                             | —                                         |
| Ma Huang            | 29.54                             | —                                         |
| San Qi              | 30.16                             | —                                         |
| Dang Gui            | 30.27                             | —                                         |
| Zhi Ke              | 30.31                             | —                                         |
| Zhi Mu              | 31.10                             | —                                         |
| Ren Shen            | 31.39                             | —                                         |
| E Zhu               | 31.71                             | —                                         |
| Gan Cao             | 31.90                             | —                                         |
| Che Qian Zi         | 31.99                             | —                                         |
| Qiang Huo           | 33.06                             | —                                         |
| He Shou Wu          | 33.16                             | —                                         |
| (Shi) Chang Pu      | 33.90                             | —                                         |
| Bu Gu Zhi           | 34.35                             | —                                         |
| Huang Qin           | 36.06                             | —                                         |
| Sang Ji Shend       | 36.18                             | —                                         |
| Tu Si Zi            | 36.51                             | —                                         |
| Shan Yu Rou         | 36.66                             | —                                         |
| Hu Zhang            | 37.36                             | —                                         |
| Jing Jie            | 37.75                             | —                                         |
| Wu Zhu Yu           | 38.70                             | —                                         |
| Mu Gua              | 39.37                             | —                                         |
| Yuan Zhi            | 39.62                             | —                                         |
| Zi Hua Di Ding      | 39.89                             | —                                         |
| Bai Hua She She Cao | 39.97                             | —                                         |
| Niu Bang Zi         | 40.04                             | —                                         |
| Huang Lian          | 40.12                             | —                                         |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Long Yan Rou    | 40.22                     | —                                 |
| Gou Qi Zi       | 40.99                     | —                                 |
| Chuang Mu Xiang | 41.04                     | —                                 |
| Xia Ku Cao      | 41.17                     | —                                 |
| Xiao Hui Xiang  | 41.77                     | —                                 |
| Sang Zhi        | 41.92                     | —                                 |
| Mu Dan Pi       | 42.36                     | —                                 |
| Xin Yi          | 42.61                     | —                                 |
| Chuan Niu Xi    | 42.99                     | —                                 |
| Ju Hua          | 43.01                     | —                                 |
| Ze Lan          | 43.30                     | —                                 |
| Xiang Fu        | 43.79                     | —                                 |
| Qing Pi         | 44.74                     | —                                 |
| Ku Shen         | 45.15                     | —                                 |
| Du Zhong        | 45.18                     | —                                 |
| Nü Zhen Zi      | 45.30                     | —                                 |
| Ge Gen          | 45.63                     | —                                 |
| Xi Xian Cao     | 45.80                     | —                                 |
| Fang Feng       | 46.59                     | —                                 |
| Zhi Gan Cao     | 46.94                     | —                                 |
| Bo He           | 47.46                     | —                                 |
| Xie Bai         | 47.97                     | —                                 |
| Xuan Fu Hua     | 48.84                     | —                                 |
| Chi Shao (Yao)  | 50.27                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62402     | 62402                  | 0.00                            | 15.48                              |
| 62403     | 62403                  | 0.00                            | 15.51                              |
| 62645     | 62645                  | 0.00                            | 3.70                               |
| 62646     | 62646                  | 0.00                            | 4.71                               |
| 62949     | 62949                  | 0.00                            | 4.40                               |
| 62950     | 62950                  | 0.00                            | 4.38                               |
| 62951     | 62951                  | 0.00                            | 2.77                               |
| 62952     | 62952                  | 0.00                            | 2.66                               |

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 2.4-2022-02

Validated substance/substance group **He Shou Wu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60101-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | He Shou Wu | G198H0718821 | 62302 <sup>†</sup> | 20      |
| PhytoComm | He Shou Wu | G198H0718921 | 62745 <sup>†</sup> | 20      |
| PhytoComm | He Shou Wu | G198H0718921 | 62746 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G198H0718222 | 1       |
| Phytocomm | He Shou Wu | G198H0718421 | 3       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Xuan Fu Hua         | 6.21                      | —                                 |
| Sang Ji Shend       | 9.93                      | —                                 |
| Yin Chen Hao        | 12.67                     | —                                 |
| Mu Dan Pi           | 14.32                     | —                                 |
| Gu Sui Bu           | 14.41                     | —                                 |
| Jing Jie            | 15.28                     | —                                 |
| He Huan Pi          | 15.97                     | —                                 |
| Sang Bai Pi         | 21.04                     | —                                 |
| Chen Pi             | 23.10                     | —                                 |
| Sha Ren             | 23.52                     | —                                 |
| Mang Xiao           | 24.18                     | —                                 |
| Jin Qian Cao        | 25.91                     | —                                 |
| Shan Yu Rou         | 26.87                     | —                                 |
| Ge Gen              | 26.95                     | —                                 |
| Dan Zhu Ye          | 28.02                     | —                                 |
| Du Zhong            | 28.85                     | —                                 |
| Wu Yao              | 29.08                     | —                                 |
| Jiang Huang         | 29.66                     | —                                 |
| Nü Zhen Zi          | 29.69                     | —                                 |
| Hong Jing Tian      | 29.79                     | —                                 |
| Bu Gu Zhi           | 30.15                     | —                                 |
| Wu Zhu Yu           | 30.45                     | —                                 |
| Gou Teng            | 31.79                     | —                                 |
| Chuan Niu Xi        | 34.57                     | —                                 |
| Tu Si Zi            | 34.99                     | —                                 |
| Dang Gui            | 35.05                     | —                                 |
| (Shi) Chang Pu      | 36.43                     | —                                 |
| (Bai) Dou Kou       | 36.69                     | —                                 |
| Bai Hua She She Cao | 37.12                     | —                                 |
| Shan Yao            | 37.12                     | —                                 |
| E Zhu               | 38.22                     | —                                 |
| Wu Jia Pi           | 38.93                     | —                                 |
| Ding Xiang          | 38.97                     | —                                 |
| Fang Feng           | 39.00                     | —                                 |
| Yi Mu Cao           | 39.72                     | —                                 |
| Sang Ye             | 40.60                     | —                                 |
| Ju Hua              | 41.32                     | —                                 |
| Hu Zhang            | 41.58                     | —                                 |
| Xiang Fu            | 42.11                     | —                                 |
| Bing Lang           | 42.15                     | —                                 |
| Huang Qi            | 42.52                     | —                                 |
| Di Gu Pi            | 42.58                     | —                                 |
| Xiao Hui Xiang      | 45.27                     | —                                 |

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| Substanz      | Distance in<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| Chuan Lian Zi | 47.44                     | —                                 |
| Zhi Ke        | 47.69                     | —                                 |
| Ba Ji Tian    | 47.82                     | —                                 |
| Xia Ku Cao    | 48.09                     | —                                 |
| Xin Yi        | 48.54                     | —                                 |
| Du Huo        | 49.26                     | —                                 |
| Hua Shi       | 49.96                     | —                                 |
| Ku Shen       | 50.11                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62301     | 62301                  | 0.00                            | 6.63                               |
| 62302     | 62302                  | 0.00                            | 6.21                               |
| 62745     | 62745                  | 0.00                            | 14.53                              |
| 62746     | 62746                  | 0.00                            | 14.32                              |

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 2.4-2022-02

Validated substance/substance group **Hong Hua**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60206-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | G057HS173TG1 | 62915     | 40      | from supplier |
| PhytoComm | Hong Hua  | G057HS173TG1 | 62916     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G057HS173TG1 | 62915 <sup>†</sup> | 20      |
| PhytoComm | Hong Hua  | G057HS173TG1 | 62916 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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  | g057h0901121 | 1       |
| Phytocomm | Hong Hua  | G057H0901221 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zhi Gan Cao     | 11.16                     | —                                 |
| Zhi Ke          | 12.50                     | —                                 |
| Jiao Gu Lan     | 14.61                     | —                                 |
| Huang Bai       | 15.24                     | —                                 |
| Chuang Mu Xiang | 15.61                     | —                                 |
| Gan Cao         | 15.77                     | —                                 |
| Shan Yao        | 16.90                     | —                                 |
| Zi Hua Di Ding  | 17.22                     | —                                 |
| Ma Huang        | 17.91                     | —                                 |
| Hong Jing Tian  | 18.82                     | —                                 |
| Qing Pi         | 18.87                     | —                                 |
| Jin Yin Hua     | 19.92                     | —                                 |
| Qing Hao        | 21.12                     | —                                 |
| Dan Dou Chi     | 21.31                     | —                                 |
| Sang Ye         | 21.34                     | —                                 |
| Huang Lian      | 21.36                     | —                                 |
| Mao Dong Qing   | 22.35                     | —                                 |
| Bo He           | 22.50                     | —                                 |
| Sha Ren         | 22.81                     | —                                 |
| Gou Qi Zi       | 22.96                     | —                                 |
| Dan Shen        | 23.12                     | —                                 |
| Hou Po          | 23.24                     | —                                 |
| Ban Lan Gen     | 23.74                     | —                                 |
| Cang Zhu        | 23.87                     | —                                 |
| Fu Zi           | 25.12                     | —                                 |
| Qiang Huo       | 25.19                     | —                                 |
| Fu Pen Zi       | 25.73                     | —                                 |
| Ren Shen        | 25.81                     | —                                 |
| Chai Hu         | 25.82                     | —                                 |
| Suan Zao Ren    | 25.87                     | —                                 |
| Jie Geng        | 26.45                     | —                                 |
| Guang Huo Xiang | 26.76                     | —                                 |
| Ye Jiao Teng    | 27.37                     | —                                 |
| Pu Gong Ying    | 27.49                     | —                                 |
| Xie Bai         | 27.81                     | —                                 |
| Dang Gui        | 28.07                     | —                                 |
| Tian Hua Fen    | 28.08                     | —                                 |
| Yin Yang Huo    | 28.37                     | —                                 |
| Huang Qin       | 28.92                     | —                                 |
| Du Zhong        | 29.22                     | —                                 |
| She Gan         | 29.24                     | —                                 |
| Lian Qiao       | 29.50                     | —                                 |
| Mang Xiao       | 29.64                     | —                                 |
| Ku Shen         | 29.79                     | —                                 |
| Zhe Bei Mu      | 29.91                     | —                                 |
| Ren Dong Teng   | 30.43                     | —                                 |
| Jing Jie        | 30.76                     | —                                 |
| Chi Shao (Yao)  | 30.85                     | —                                 |
| Gu Sui Bu       | 31.70                     | —                                 |
| Mu Zei          | 31.78                     | —                                 |
| Lu Gen          | 31.89                     | —                                 |
| Cang Er Zi      | 31.94                     | —                                 |

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| Substanz      | Distance in<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| Pi Pa Ye      | 32.35                     | —                                 |
| Bai Jiang Cao | 32.91                     | —                                 |
| Yan Hu Suo    | 33.57                     | —                                 |
| He Huan Pi    | 34.17                     | —                                 |
| Tu Fu Ling    | 34.27                     | —                                 |
| Bai Shao Yao  | 34.45                     | —                                 |
| Ze Xie        | 34.99                     | —                                 |
| San Qi        | 36.34                     | —                                 |
| Ji Li         | 37.11                     | —                                 |
| Ze Lan        | 37.71                     | —                                 |
| Ce Bai Ye     | 37.96                     | —                                 |
| Niu Bang Zi   | 38.28                     | —                                 |
| Long Yan Rou  | 38.56                     | —                                 |
| Zi Su Zi      | 38.65                     | —                                 |
| Wu Wei Zi     | 38.81                     | —                                 |
| Tao Ren       | 39.02                     | —                                 |
| Mu Gua        | 39.07                     | —                                 |
| Di Gu Pi      | 39.28                     | —                                 |
| Lian Zi       | 39.32                     | —                                 |
| Ling Zhi      | 39.67                     | —                                 |
| Bai Xian Pi   | 41.09                     | —                                 |
| (Fen) Bi Xie  | 41.77                     | —                                 |
| Che Qian Zi   | 42.10                     | —                                 |
| Gua Lou       | 43.16                     | —                                 |
| Ji Xue Teng   | 43.48                     | —                                 |
| Yu Jin        | 43.52                     | —                                 |
| Zhi Mu        | 45.09                     | —                                 |
| Gou Teng      | 45.34                     | —                                 |
| Rou Gui       | 45.67                     | —                                 |
| Sheng Jiang   | 45.87                     | —                                 |
| Xi Xian Cao   | 46.01                     | —                                 |
| Xiang Fu      | 46.13                     | —                                 |
| Yuan Zhi      | 46.41                     | —                                 |
| Zhu Ling      | 46.84                     | —                                 |
| Lai Fu Zi     | 47.24                     | —                                 |
| Gui Zhi       | 47.46                     | —                                 |
| Bai Zi Ren    | 47.74                     | —                                 |
| Yi Mu Cao     | 47.88                     | —                                 |
| Ban Zhi Lian  | 48.87                     | —                                 |
| Sang Zhi      | 48.95                     | —                                 |
| Chuan Mu Tong | 49.40                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62915     | 62915               | 0.00                         | 11.16                           |
| 62916     | 62916               | 0.00                         | 12.94                           |

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 2.4-2022-02

Validated substance/substance group **Hong Jing Tian**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60031-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Hong Jing Tian | G237H0906821 | 62306 <sup>†</sup> | 20      |
| PhytoComm | Hong Jing Tian | G237HS429SK1 | 62639 <sup>†</sup> | 20      |
| PhytoComm | Hong Jing Tian | G237HS429SK1 | 62640 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 | G237H0906221 | 1       |
| Phytocomm | Hong Jing Tian | G237H0906321 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 159           | 1              | 22 280        |
| <b>Type B</b> | 0              | 78            | 2              | 11 317        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 99.3750 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 97.5000 % (> 93.7500 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jin Yin Hua     | 4.65                      | —                                 |
| Zhi Gan Cao     | 6.13                      | —                                 |
| Dan Shen        | 8.92                      | —                                 |
| Dan Dou Chi     | 10.14                     | —                                 |
| Zi Hua Di Ding  | 10.35                     | —                                 |
| Gan Cao         | 10.97                     | —                                 |
| Hou Po          | 11.60                     | —                                 |
| Guang Huo Xiang | 11.92                     | —                                 |
| Fu Pen Zi       | 12.63                     | —                                 |
| Ban Lan Gen     | 13.51                     | —                                 |
| Pi Pa Ye        | 13.54                     | —                                 |
| Gu Sui Bu       | 14.42                     | —                                 |
| Fu Zi           | 14.63                     | —                                 |
| Ren Dong Teng   | 14.74                     | —                                 |
| Jiao Gu Lan     | 15.14                     | —                                 |
| Chuang Mu Xiang | 15.19                     | —                                 |
| Zhi Ke          | 15.29                     | —                                 |
| Tian Hua Fen    | 15.29                     | —                                 |
| Suan Zao Ren    | 15.30                     | —                                 |
| Ma Huang        | 15.33                     | —                                 |
| She Gan         | 15.92                     | —                                 |
| Shan Yao        | 16.20                     | —                                 |
| Cang Zhu        | 16.39                     | —                                 |
| Yin Yang Huo    | 16.52                     | —                                 |
| Chai Hu         | 16.94                     | —                                 |
| Bai Shao Yao    | 16.99                     | —                                 |
| Ye Jiao Teng    | 17.54                     | —                                 |
| Qiang Huo       | 17.74                     | —                                 |
| Lian Qiao       | 17.88                     | —                                 |
| Mu Zei          | 18.18                     | —                                 |
| Lian Zi         | 18.69                     | —                                 |
| Yan Hu Suo      | 18.76                     | —                                 |
| Hong Hua        | 19.13                     | —                                 |
| Shen Qu         | 19.56                     | —                                 |
| Lu Gen          | 19.59                     | —                                 |
| Bo He           | 19.84                     | —                                 |
| Mao Dong Qing   | 20.29                     | —                                 |
| Ji Li           | 20.29                     | —                                 |
| Ze Xie          | 20.58                     | —                                 |
| Qing Pi         | 20.82                     | —                                 |
| Sang Ji Shend   | 21.09                     | —                                 |
| Ce Bai Ye       | 21.48                     | —                                 |
| Bai Xian Pi     | 21.81                     | —                                 |
| Ren Shen        | 21.87                     | —                                 |
| Huang Bai       | 22.03                     | —                                 |
| He Huan Pi      | 22.47                     | —                                 |
| Zhe Bei Mu      | 22.60                     | —                                 |
| Jing Jie        | 23.01                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Di Gu Pi        | 23.04                             | —                                         |
| Dang Gui        | 23.30                             | —                                         |
| Sha Ren         | 23.33                             | —                                         |
| Che Qian Zi     | 23.33                             | —                                         |
| Ji Xue Teng     | 23.42                             | —                                         |
| Tu Fu Ling      | 23.46                             | —                                         |
| Mang Xiao       | 23.49                             | —                                         |
| Jie Geng        | 23.92                             | —                                         |
| Ku Shen         | 24.07                             | —                                         |
| Yu Jin          | 24.14                             | —                                         |
| Long Yan Rou    | 25.25                             | —                                         |
| Gou Teng        | 25.41                             | —                                         |
| Xie Bai         | 25.49                             | —                                         |
| Ling Zhi        | 25.61                             | —                                         |
| Nü Zhen Zi      | 25.74                             | —                                         |
| Tao Ren         | 26.04                             | —                                         |
| (Fen) Bi Xie    | 26.46                             | —                                         |
| Huang Lian      | 26.70                             | —                                         |
| Ge Gen          | 27.02                             | —                                         |
| Sheng Jiang     | 27.53                             | —                                         |
| Huang Qin       | 27.58                             | —                                         |
| Zhu Ling        | 27.75                             | —                                         |
| Gua Lou         | 27.77                             | —                                         |
| Yi Mu Cao       | 27.86                             | —                                         |
| Gui Zhi         | 27.87                             | —                                         |
| Xuan Fu Hua     | 28.03                             | —                                         |
| Fang Feng       | 28.07                             | —                                         |
| Du Zhong        | 28.07                             | —                                         |
| Chi Shao (Yao)  | 28.38                             | —                                         |
| San Qi          | 28.72                             | —                                         |
| Gou Qi Zi       | 29.07                             | —                                         |
| Huo Ma Ren      | 29.11                             | —                                         |
| Fu Ling         | 29.67                             | —                                         |
| Bai Zi Ren      | 30.10                             | —                                         |
| He Shou Wu      | 30.21                             | —                                         |
| Rou Gui         | 30.87                             | —                                         |
| Cang Er Zi      | 31.67                             | —                                         |
| Ci Wu Jia       | 31.69                             | —                                         |
| Sang Bai Pi     | 33.12                             | —                                         |
| Sang Zhi        | 33.46                             | —                                         |
| Bai Jiang Cao   | 33.58                             | —                                         |
| Chen Pi         | 34.07                             | —                                         |
| Ma Huang Gen    | 34.28                             | —                                         |
| Lai Fu Zi       | 34.46                             | —                                         |
| Qing Hao        | 35.10                             | —                                         |
| Zhi Mu          | 36.02                             | —                                         |
| Wu Zhu Yu       | 36.63                             | —                                         |
| Mu Gua          | 36.64                             | —                                         |
| Sang Ye         | 36.91                             | —                                         |
| Ban Xia (Jiang) | 38.35                             | —                                         |
| Yin Chen Hao    | 39.17                             | —                                         |
| Hu Zhang        | 39.92                             | —                                         |
| Zhu Ru          | 40.09                             | —                                         |
| Fo Shou         | 40.15                             | —                                         |
| Shan Yu Rou     | 41.28                             | —                                         |
| Bu Gu Zhi       | 42.80                             | —                                         |
| Yi Yi Ren       | 43.28                             | —                                         |
| Pu Gong Ying    | 43.44                             | —                                         |
| Fu Xiao Mai     | 43.81                             | —                                         |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Ze Lan         | 44.17                     | —                                 |
| Mu Dan Pi      | 45.24                     | —                                 |
| Yuan Zhi       | 45.82                     | —                                 |
| Ban Zhi Lian   | 46.17                     | —                                 |
| (Shi) Chang Pu | 46.36                     | —                                 |
| Xia Ku Cao     | 47.51                     | —                                 |
| Ju Hua         | 48.26                     | —                                 |
| Niu Bang Zi    | 48.74                     | —                                 |
| Fu Shen        | 49.14                     | —                                 |
| Dan Zhu Ye     | 49.71                     | —                                 |
| Huang Qi       | 49.86                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62305     | 62305                  | 0.00                            | 21.09                              |
| 62306     | 62306                  | 0.00                            | 21.15                              |
| 62639     | 62639                  | 0.00                            | 4.90                               |
| 62640     | 62640                  | 0.00                            | 4.65                               |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Hou Po**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50289-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Hou Po    | G154HS184SH1 | 62614 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 2              | 40            | 0              | 11 355        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

The substance/substance group *Hou Po* 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9802 % (> 99.9481 %)  | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Yu Jin          | 7.00                      | —                                 |
| Chai Hu         | 7.08                      | —                                 |
| Dan Dou Chi     | 7.13                      | —                                 |
| Yan Hu Suo      | 7.54                      | —                                 |
| Ren Dong Teng   | 7.65                      | —                                 |
| Mao Dong Qing   | 7.69                      | —                                 |
| Ce Bai Ye       | 7.75                      | —                                 |
| Shen Qu         | 7.81                      | —                                 |
| Ling Zhi        | 8.13                      | —                                 |
| Che Qian Zi     | 8.25                      | —                                 |
| Shan Yao        | 8.44                      | —                                 |
| Fu Pen Zi       | 8.47                      | —                                 |
| Yin Yang Huo    | 8.70                      | —                                 |
| Fu Zi           | 8.76                      | —                                 |
| Bai Xian Pi     | 9.18                      | —                                 |
| Guang Huo Xiang | 9.20                      | —                                 |
| Qiang Huo       | 9.56                      | —                                 |
| Gu Sui Bu       | 9.71                      | —                                 |
| Pi Pa Ye        | 9.85                      | —                                 |
| Zhu Ling        | 10.26                     | —                                 |
| Jing Jie        | 10.50                     | —                                 |
| Dan Shen        | 10.91                     | —                                 |
| Ji Li           | 12.13                     | —                                 |
| She Gan         | 12.48                     | —                                 |
| Tu Fu Ling      | 12.65                     | —                                 |
| Zi Hua Di Ding  | 13.25                     | —                                 |
| Tian Hua Fen    | 13.29                     | —                                 |
| Lian Zi         | 14.02                     | —                                 |
| Ye Jiao Teng    | 14.75                     | —                                 |
| Hong Jing Tian  | 14.87                     | —                                 |
| Lian Qiao       | 15.12                     | —                                 |
| Gan Cao         | 15.30                     | —                                 |
| Qing Pi         | 15.75                     | —                                 |
| Jin Yin Hua     | 15.98                     | —                                 |
| Du Zhong        | 16.83                     | —                                 |
| Ma Huang        | 17.18                     | —                                 |
| Fu Ling         | 17.22                     | —                                 |
| Jiao Gu Lan     | 17.82                     | —                                 |
| Suan Zao Ren    | 18.54                     | —                                 |
| Ban Lan Gen     | 18.60                     | —                                 |
| Bo He           | 18.70                     | —                                 |
| Mu Zei          | 18.77                     | —                                 |
| Ji Xue Teng     | 18.99                     | —                                 |
| Bai Shao Yao    | 19.13                     | —                                 |
| Sha Ren         | 19.35                     | —                                 |
| (Fen) Bi Xie    | 19.50                     | —                                 |
| He Huan Pi      | 19.57                     | —                                 |
| Lu Gen          | 20.68                     | —                                 |
| Ma Huang Gen    | 20.85                     | —                                 |
| Zhe Bei Mu      | 21.04                     | —                                 |
| Gou Teng        | 21.12                     | —                                 |
| Sheng Jiang     | 21.19                     | —                                 |

*continued on the next page*



continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Qing Hao        | 21.21                     | —                                 |
| Huang Bai       | 21.33                     | —                                 |
| Zhi Gan Cao     | 21.36                     | —                                 |
| Huo Ma Ren      | 22.08                     | —                                 |
| Gui Zhi         | 22.89                     | —                                 |
| Rou Gui         | 23.46                     | —                                 |
| Huang Lian      | 23.76                     | —                                 |
| Ze Xie          | 24.49                     | —                                 |
| Ren Shen        | 24.79                     | —                                 |
| Di Gu Pi        | 25.15                     | —                                 |
| Bai Zi Ren      | 25.31                     | —                                 |
| Yi Yi Ren       | 25.55                     | —                                 |
| Zhi Ke          | 25.74                     | —                                 |
| Tao Ren         | 27.08                     | —                                 |
| Bai Jiang Cao   | 29.19                     | —                                 |
| Cang Zhu        | 30.56                     | —                                 |
| Chuang Mu Xiang | 31.40                     | —                                 |
| Gua Lou         | 31.85                     | —                                 |
| Mang Xiao       | 32.76                     | —                                 |
| Ban Xia (Jiang) | 32.96                     | —                                 |
| Zhu Ru          | 33.31                     | —                                 |
| Ci Wu Jia       | 34.14                     | —                                 |
| Fu Xiao Mai     | 34.78                     | —                                 |
| Jie Geng        | 35.28                     | —                                 |
| Xie Bai         | 35.45                     | —                                 |
| Dang Gui        | 35.54                     | —                                 |
| Hong Hua        | 35.84                     | —                                 |
| Huang Qin       | 35.91                     | —                                 |
| San Qi          | 36.36                     | —                                 |
| Sang Zhi        | 37.41                     | —                                 |
| Chi Shao (Yao)  | 37.60                     | —                                 |
| Ku Shen         | 38.00                     | —                                 |
| Lai Fu Zi       | 38.02                     | —                                 |
| Fo Shou         | 38.13                     | —                                 |
| Pu Gong Ying    | 39.34                     | —                                 |
| Cang Er Zi      | 40.02                     | —                                 |
| Fu Shen         | 41.26                     | —                                 |
| Long Yan Rou    | 41.41                     | —                                 |
| Sang Ye         | 42.23                     | —                                 |
| Ze Lan          | 43.38                     | —                                 |
| Xi Xian Cao     | 45.98                     | —                                 |
| Ban Zhi Lian    | 46.66                     | —                                 |
| Gou Qi Zi       | 47.50                     | —                                 |
| Zhi Mu          | 47.94                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62613     | 62613               | 0.00                         | 7.13                            |
| 62614     | 62614               | 0.00                         | 7.00                            |

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 2.4-2022-02

Validated substance/substance group **Hu Zhang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60130-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Hu Zhang  | G197HS373SK1 | 62566 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Zhi Shi             | 10.86                     | —                                 |
| Han Lian Cao        | 11.57                     | —                                 |
| Yu Xing Cao         | 13.72                     | —                                 |
| Sang Ye             | 16.16                     | —                                 |
| Bai Hua She She Cao | 16.37                     | —                                 |
| Xi Xian Cao         | 18.27                     | —                                 |
| Xin Yi              | 18.28                     | —                                 |
| Huang Lian          | 21.97                     | —                                 |
| Xia Ku Cao          | 24.92                     | —                                 |
| Ze Lan              | 25.01                     | —                                 |
| Pu Gong Ying        | 25.03                     | —                                 |
| Sha Ren             | 25.94                     | —                                 |
| Mang Xiao           | 26.75                     | —                                 |
| Jiang Huang         | 28.46                     | —                                 |
| Yi Mu Cao           | 29.21                     | —                                 |
| Shan Yao            | 30.85                     | —                                 |
| Xiang Fu            | 31.63                     | —                                 |
| Nü Zhen Zi          | 32.25                     | —                                 |
| Tu Fu Ling          | 32.62                     | —                                 |
| Yin Chen Hao        | 36.45                     | —                                 |
| He Huan Pi          | 36.65                     | —                                 |
| Gu Sui Bu           | 38.50                     | —                                 |
| Gou Teng            | 41.07                     | —                                 |
| Bo He               | 47.13                     | —                                 |
| Qiang Huo           | 47.92                     | —                                 |
| Ju Hua              | 49.30                     | —                                 |
| Du Zhong            | 49.50                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62565     | 62565                  | 0.00                            | 10.86                              |
| 62566     | 62566                  | 0.00                            | 10.95                              |

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 2.4-2022-02

Validated substance/substance group **Hua Shi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50308-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Hua Shi   | G238HS289RM1 | 62426 <sup>†</sup> | 20      |
| PhytoComm | Hua Shi   | G238HS289SK1 | 62637 <sup>†</sup> | 20      |
| PhytoComm | Hua Shi   | G238HS289SK1 | 62638 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 65            | 95             | 22 280        |
| <b>Type B</b> | 0              | 29            | 51             | 11 317        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 40.6250 % (> 38.7500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 36.2500 % (> 32.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------|---------------------------|-----------------------------------|
| Mang Xiao | 112.94                    | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62425     | 62425                  | 0.00                            | 112.94                             |
| 62426     | 62426                  | 0.00                            | 114.90                             |
| 62637     | 62637                  | 0.00                            | 146.32                             |
| 62638     | 62638                  | 0.00                            | 144.18                             |

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 2.4-2022-02

Validated substance/substance group **Huang Bai**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60949-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Huang Bai                 | 2      | 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 |
| PhytoComm | Huang Bai | G188HS262SV1 | 62837     | 40      | from supplier |
| PhytoComm | Huang Bai | G188HS262SV1 | 62838     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Bai*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Huang Bai | G188HS262SH1 | 62698 <sup>†</sup> | 20      |
| PhytoComm | Huang Bai | G188HS262SV1 | 62837 <sup>†</sup> | 20      |
| PhytoComm | Huang Bai | G188HS262SV1 | 62838 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.

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

### 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.

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zhi Ke          | 7.10                      | —                                 |
| Bo He           | 7.37                      | —                                 |
| Qing Hao        | 8.29                      | —                                 |
| Jiao Gu Lan     | 8.61                      | —                                 |
| Qing Pi         | 8.80                      | —                                 |
| Fu Zi           | 9.91                      | —                                 |
| Huang Lian      | 9.98                      | —                                 |
| Zi Hua Di Ding  | 10.38                     | —                                 |
| Dan Shen        | 10.40                     | —                                 |
| Qiang Huo       | 11.65                     | —                                 |
| Chai Hu         | 11.75                     | —                                 |
| Tu Fu Ling      | 12.68                     | —                                 |
| Hong Jing Tian  | 13.70                     | —                                 |
| Sha Ren         | 13.99                     | —                                 |
| Gan Cao         | 14.42                     | —                                 |
| Du Zhong        | 14.73                     | —                                 |
| Jing Jie        | 15.62                     | —                                 |
| Bai Jiang Cao   | 15.70                     | —                                 |
| Fu Pen Zi       | 15.86                     | —                                 |
| Yin Yang Huo    | 16.24                     | —                                 |
| Ye Jiao Teng    | 16.47                     | —                                 |
| Shan Yao        | 16.93                     | —                                 |
| Yu Jin          | 16.95                     | —                                 |
| Jin Yin Hua     | 16.98                     | —                                 |
| Hou Po          | 17.11                     | —                                 |
| Mao Dong Qing   | 17.72                     | —                                 |
| Sang Ye         | 17.81                     | —                                 |
| Ma Huang        | 18.99                     | —                                 |
| Ce Bai Ye       | 19.50                     | —                                 |
| Zhi Gan Cao     | 19.58                     | —                                 |
| Yan Hu Suo      | 19.77                     | —                                 |
| Dan Dou Chi     | 19.92                     | —                                 |
| Ban Lan Gen     | 20.02                     | —                                 |
| Pu Gong Ying    | 21.20                     | —                                 |
| Chuang Mu Xiang | 21.62                     | —                                 |
| Hong Hua        | 21.64                     | —                                 |
| Pi Pa Ye        | 21.78                     | —                                 |
| Che Qian Zi     | 22.20                     | —                                 |
| Bai Xian Pi     | 22.84                     | —                                 |
| Bai Shao Yao    | 23.86                     | —                                 |
| Ren Dong Teng   | 24.09                     | —                                 |
| Tian Hua Fen    | 24.89                     | —                                 |
| Gu Sui Bu       | 26.05                     | —                                 |
| Ze Lan          | 26.19                     | —                                 |
| Lian Zi         | 27.53                     | —                                 |
| Suan Zao Ren    | 27.85                     | —                                 |
| Lian Qiao       | 28.11                     | —                                 |
| Ren Shen        | 28.13                     | —                                 |
| She Gan         | 28.43                     | —                                 |
| Di Gu Pi        | 28.46                     | —                                 |
| Ji Li           | 28.55                     | —                                 |
| Ji Xue Teng     | 28.79                     | —                                 |

*continued on the next page*



continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ling Zhi        | 28.86                     | —                                 |
| Lu Gen          | 29.05                     | —                                 |
| Mang Xiao       | 29.65                     | —                                 |
| Mu Zei          | 29.98                     | —                                 |
| Cang Er Zi      | 30.17                     | —                                 |
| He Huan Pi      | 30.61                     | —                                 |
| Zhe Bei Mu      | 30.69                     | —                                 |
| Xi Xian Cao     | 31.56                     | —                                 |
| Guang Huo Xiang | 31.85                     | —                                 |
| (Fen) Bi Xie    | 32.25                     | —                                 |
| Zhu Ling        | 33.17                     | —                                 |
| Cang Zhu        | 34.24                     | —                                 |
| Shen Qu         | 34.26                     | —                                 |
| Huang Qin       | 34.45                     | —                                 |
| Nü Zhen Zi      | 36.10                     | —                                 |
| Tao Ren         | 36.52                     | —                                 |
| Sheng Jiang     | 37.12                     | —                                 |
| Ku Shen         | 37.40                     | —                                 |
| Rou Gui         | 37.87                     | —                                 |
| Chi Shao (Yao)  | 37.87                     | —                                 |
| Ban Zhi Lian    | 38.03                     | —                                 |
| Xie Bai         | 38.09                     | —                                 |
| Jie Geng        | 38.71                     | —                                 |
| Gou Teng        | 40.24                     | —                                 |
| Wu Wei Zi       | 40.36                     | —                                 |
| Zhi Shi         | 40.40                     | —                                 |
| Gua Lou         | 41.06                     | —                                 |
| Ze Xie          | 41.89                     | —                                 |
| Yin Chen Hao    | 42.33                     | —                                 |
| Gou Qi Zi       | 42.69                     | —                                 |
| Fu Ling         | 42.94                     | —                                 |
| Jiang Huang     | 44.48                     | —                                 |
| Xin Yi          | 45.28                     | —                                 |
| Bai Zi Ren      | 45.41                     | —                                 |
| Ma Huang Gen    | 45.56                     | —                                 |
| San Qi          | 45.70                     | —                                 |
| Dang Gui        | 45.88                     | —                                 |
| Huo Ma Ren      | 45.91                     | —                                 |
| Yi Mu Cao       | 46.25                     | —                                 |
| Gui Zhi         | 48.25                     | —                                 |
| Niu Bang Zi     | 48.70                     | —                                 |
| E Zhu           | 48.95                     | —                                 |
| Zi Su Zi        | 49.08                     | —                                 |
| Sang Zhi        | 50.04                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62697     | 62697               | 0.00                         | 8.61                            |
| 62698     | 62698               | 0.00                         | 8.29                            |
| 62837     | 62837               | 0.00                         | 7.37                            |
| 62838     | 62838               | 0.00                         | 7.10                            |

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 2.4-2022-02

Validated substance/substance group **Huang Lian**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60219-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Huang Lian                | 3      | 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 |
| PhytoComm | Huang Lian | G079HS261TK2 | 62919     | 40      | from supplier |
| PhytoComm | Huang Lian | G079HS261TK2 | 62920     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Huang Lian*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Huang Lian | G079HS261RM1 | 62288 <sup>†</sup> | 20      |
| PhytoComm | Huang Lian | G079HS261SK1 | 62707 <sup>†</sup> | 20      |
| PhytoComm | Huang Lian | G079HS261SK1 | 62708 <sup>†</sup> | 20      |
| PhytoComm | Huang Lian | G079HS261TK2 | 62919 <sup>†</sup> | 20      |
| PhytoComm | Huang Lian | G079HS261TK2 | 62920 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | 1       |
| Phytocomm | Huang Lian | G079H1205321 | 2       |
| PhytoComm | Huang Lian | G079H1205321 | 4       |
| Phytocomm | Huang Lian | G079H1205421 | 1       |
| Phytocomm | Huang Lian | G079H1205521 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8248 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Bai Jiang Cao       | 12.92                     | —                                 |
| Huang Bai           | 13.22                     | —                                 |
| Ze Lan              | 13.34                     | —                                 |
| Hu Zhang            | 13.84                     | —                                 |
| Pu Gong Ying        | 13.92                     | —                                 |
| Sang Ye             | 14.50                     | —                                 |
| Yin Chen Hao        | 17.61                     | —                                 |
| Sha Ren             | 17.69                     | —                                 |
| Tu Fu Ling          | 19.88                     | —                                 |
| Zhi Shi             | 20.50                     | —                                 |
| Han Lian Cao        | 21.04                     | —                                 |
| Bo He               | 21.11                     | —                                 |
| Xin Yi              | 21.56                     | —                                 |
| Shan Yao            | 21.68                     | —                                 |
| Ma Huang            | 21.77                     | —                                 |
| Bai Hua She She Cao | 24.06                     | —                                 |
| Yu Xing Cao         | 24.86                     | —                                 |
| Xi Xian Cao         | 24.98                     | —                                 |
| Zhi Ke              | 25.40                     | —                                 |
| Qiang Huo           | 25.49                     | —                                 |
| Fu Zi               | 25.75                     | —                                 |
| Jing Jie            | 25.87                     | —                                 |
| Nü Zhen Zi          | 26.26                     | —                                 |
| Qing Pi             | 26.84                     | —                                 |
| Mang Xiao           | 27.07                     | —                                 |
| Dan Shen            | 27.19                     | —                                 |
| Chai Hu             | 28.49                     | —                                 |
| Hou Po              | 28.59                     | —                                 |
| Fu Pen Zi           | 29.35                     | —                                 |
| Yin Yang Huo        | 29.60                     | —                                 |
| Du Zhong            | 29.64                     | —                                 |
| Ye Jiao Teng        | 30.55                     | —                                 |
| Yu Jin              | 30.89                     | —                                 |
| Hong Jing Tian      | 31.17                     | —                                 |
| Jiao Gu Lan         | 31.51                     | —                                 |
| Xia Ku Cao          | 31.99                     | —                                 |
| Mao Dong Qing       | 32.43                     | —                                 |
| Qing Hao            | 32.71                     | —                                 |
| Yi Mu Cao           | 33.50                     | —                                 |
| Che Qian Zi         | 34.47                     | —                                 |
| Dan Dou Chi         | 34.61                     | —                                 |

*continued on the next page*

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zi Hua Di Ding  | 34.79                     | —                                 |
| Hong Hua        | 36.01                     | —                                 |
| Gan Cao         | 36.19                     | —                                 |
| Jiang Huang     | 37.97                     | —                                 |
| Zhi Gan Cao     | 38.40                     | —                                 |
| Jin Yin Hua     | 39.30                     | —                                 |
| Xiang Fu        | 39.64                     | —                                 |
| Pi Pa Ye        | 40.44                     | —                                 |
| Suan Zao Ren    | 40.95                     | —                                 |
| Bai Xian Pi     | 41.06                     | —                                 |
| Wu Wei Zi       | 41.24                     | —                                 |
| Chuang Mu Xiang | 41.59                     | —                                 |
| Huang Qin       | 42.24                     | —                                 |
| Cang Er Zi      | 42.74                     | —                                 |
| Bai Shao Yao    | 43.25                     | —                                 |
| He Huan Pi      | 44.23                     | —                                 |
| Yan Hu Suo      | 45.05                     | —                                 |
| Gou Teng        | 46.14                     | —                                 |
| Gu Sui Bu       | 46.61                     | —                                 |
| Lian Qiao       | 47.53                     | —                                 |
| Ce Bai Ye       | 47.98                     | —                                 |
| Di Gu Pi        | 48.63                     | —                                 |
| Ren Dong Teng   | 48.74                     | —                                 |
| Lian Zi         | 48.97                     | —                                 |
| Lu Gen          | 49.67                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62287     | 62287                  | 0.00                            | 13.34                              |
| 62288     | 62288                  | 0.00                            | 12.92                              |
| 62707     | 62707                  | 0.00                            | 14.06                              |
| 62708     | 62708                  | 0.00                            | 13.84                              |
| 62919     | 62919                  | 0.00                            | 17.56                              |
| 62920     | 62920                  | 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 2.4-2022-02

Validated substance/substance group **Huang Qi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60154-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Huang Qi                  | 3      | 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 |
| PhytoComm | Huang Qi  | G040H1202924 | 62973     | 40      | from supplier |
| PhytoComm | Huang Qi  | G040H1202924 | 62974     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Huang Qi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Huang Qi  | G040H1202822 | 62384 <sup>†</sup> | 20      |
| PhytoComm | Huang Qi  | G040H1202823 | 62511 <sup>†</sup> | 20      |
| PhytoComm | Huang Qi  | G040H1202823 | 62512 <sup>†</sup> | 20      |
| PhytoComm | Huang Qi  | G040H1202924 | 62973 <sup>†</sup> | 20      |
| PhytoComm | Huang Qi  | G040H1202924 | 62974 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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  | G040H1202321 | 1       |
| Phytocomm | Huang Qi  | G040H1202423 | 2       |
| Phytocomm | Huang Qi  | G040H1202521 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 6              | 3             | 7              | 841           |

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:

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

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 99.5208 % (> 98.9333 %)  | n/a (n/a)                |

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

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

| <b>Substance</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|------------------|-----------------------------------|-------------------------------------------|
| Mu Gua           | 6.68                              | —                                         |
| Zhi Gan Cao      | 8.05                              | —                                         |
| Chi Shao (Yao)   | 10.58                             | —                                         |
| Bai Zhu          | 12.34                             | —                                         |
| Jie Geng         | 15.37                             | —                                         |
| (Huai) Niu Xi    | 18.27                             | —                                         |
| Sang Zhi         | 20.19                             | —                                         |
| Long Dan (Cao)   | 20.66                             | —                                         |
| Yuan Zhi         | 21.93                             | —                                         |
| Di Gu Pi         | 22.19                             | —                                         |
| Chuan Lian Zi    | 22.52                             | —                                         |
| Bing Lang        | 25.68                             | —                                         |
| Mang Xiao        | 27.21                             | —                                         |
| Qin Jiao         | 27.54                             | —                                         |
| Tian Hua Fen     | 28.95                             | —                                         |
| Bai He           | 30.47                             | —                                         |
| Lian Qiao        | 31.43                             | —                                         |
| Gan Cao          | 32.57                             | —                                         |
| Dang Gui         | 34.09                             | —                                         |
| Zi Su Zi         | 34.22                             | —                                         |
| Zhi Ke           | 34.67                             | —                                         |
| Chuan Niu Xi     | 34.98                             | —                                         |
| Chuan Mu Tong    | 35.39                             | —                                         |
| Bai Zhi          | 35.53                             | —                                         |
| Ban Zhi Lian     | 37.33                             | —                                         |
| Tu Fu Ling       | 37.58                             | —                                         |
| Shan Yao         | 37.90                             | —                                         |
| Bai Shao Yao     | 38.65                             | —                                         |
| Lai Fu Zi        | 38.98                             | —                                         |
| Sha Shen (Bei)   | 39.01                             | —                                         |
| (Shi) Chang Pu   | 39.28                             | —                                         |
| Gan Jiang        | 40.69                             | —                                         |
| Lian Zi          | 40.98                             | —                                         |
| E Zhu            | 40.98                             | —                                         |
| Cang Zhu         | 41.40                             | —                                         |
| Bai Xian Pi      | 41.56                             | —                                         |

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| Substanz     | Distance in<br>main model | Distance in<br>second-stage model |
|--------------|---------------------------|-----------------------------------|
| Suan Zao Ren | 42.33                     | —                                 |
| Du Huo       | 42.73                     | —                                 |
| Ma Huang     | 43.64                     | —                                 |
| Ju Hua       | 43.73                     | —                                 |
| Chai Hu      | 44.14                     | —                                 |
| Jin Yin Hua  | 44.28                     | —                                 |
| She Gan      | 44.46                     | —                                 |
| Zhe Bei Mu   | 44.46                     | —                                 |
| Huang Qin    | 44.68                     | —                                 |
| Xiang Fu     | 44.75                     | —                                 |
| Rou Gui      | 45.37                     | —                                 |
| Yan Hu Suo   | 45.44                     | —                                 |
| Ku Shen      | 45.63                     | —                                 |
| Niu Bang Zi  | 46.10                     | —                                 |
| Gu Sui Bu    | 46.40                     | —                                 |
| Ji Xue Teng  | 46.74                     | —                                 |
| Ye Jiao Teng | 46.93                     | —                                 |
| Fu Zi        | 47.13                     | —                                 |
| Huang Bai    | 47.25                     | —                                 |
| Cang Er Zi   | 47.37                     | —                                 |
| Gou Teng     | 47.49                     | —                                 |
| Jiao Gu Lan  | 47.69                     | —                                 |
| Fo Shou      | 47.74                     | —                                 |
| Ji Li        | 47.90                     | —                                 |
| Fu Ling      | 48.84                     | —                                 |
| San Qi       | 49.04                     | —                                 |
| Ce Bai Ye    | 49.24                     | —                                 |
| Chen Pi      | 49.71                     | —                                 |
| Dan Shen     | 50.31                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62383     | 62383                  | 0.00                            | 7.55                               |
| 62384     | 62384                  | 0.00                            | 6.68                               |
| 62511     | 62511                  | 0.00                            | 8.12                               |
| 62512     | 62512                  | 0.00                            | 8.05                               |
| 62973     | 62973                  | 0.00                            | 9.45                               |
| 62974     | 62974                  | 0.00                            | 10.29                              |

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 2.4-2022-02

Validated substance/substance group **Huang Qin**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60012-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Huang Qin                 | 3      | 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 |
| PhytoComm | Huang Qin | G225HS259TH2 | 62789     | 40      | from supplier |
| PhytoComm | Huang Qin | G225HS259TH2 | 62790     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Huang Qin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Huang Qin | G225HS259RM1 | 62282 <sup>†</sup> | 20      |
| PhytoComm | Huang Qin | G225HS259SM1 | 62709 <sup>†</sup> | 20      |
| PhytoComm | Huang Qin | G225HS259SM1 | 62710 <sup>†</sup> | 20      |
| PhytoComm | Huang Qin | G225HS259TH2 | 62789 <sup>†</sup> | 20      |
| PhytoComm | Huang Qin | G225HS259TH2 | 62790 <sup>†</sup> | 20      |



- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | g225h1204121 | 1       |
| Phytocomm | Huang Qin | G225H1204221 | 1       |
| PhytoComm | Huang Qin | G225H1204221 | 1       |
| PhytoComm | Huang Qin | G225H1204322 | 5       |
| Phytocomm | Huang Qin | G225H1204522 | 3       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8248 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mang Xiao       | 23.71                     | —                                 |
| Ma Huang        | 23.91                     | —                                 |
| Jin Yin Hua     | 27.69                     | —                                 |
| Lian Qiao       | 28.44                     | —                                 |
| Zhi Ke          | 29.39                     | —                                 |
| Ye Jiao Teng    | 29.92                     | —                                 |
| Jiao Gu Lan     | 30.49                     | —                                 |
| Fu Pen Zi       | 31.05                     | —                                 |
| Hou Po          | 31.69                     | —                                 |
| Fu Zi           | 33.50                     | —                                 |
| Yin Yang Huo    | 33.82                     | —                                 |
| Gan Cao         | 34.39                     | —                                 |
| Tian Hua Fen    | 34.59                     | —                                 |
| Yan Hu Suo      | 35.34                     | —                                 |
| Bai Shao Yao    | 36.52                     | —                                 |
| Ren Shen        | 37.54                     | —                                 |
| He Huan Pi      | 37.75                     | —                                 |
| Cang Zhu        | 38.05                     | —                                 |
| Zi Hua Di Ding  | 38.40                     | —                                 |
| Gou Qi Zi       | 39.79                     | —                                 |
| Dang Gui        | 40.09                     | —                                 |
| Guang Huo Xiang | 40.10                     | —                                 |
| San Qi          | 40.26                     | —                                 |
| Pi Pa Ye        | 40.37                     | —                                 |
| Ban Lan Gen     | 41.15                     | —                                 |
| Lu Gen          | 41.39                     | —                                 |
| Ku Shen         | 41.82                     | —                                 |
| Hong Jing Tian  | 42.95                     | —                                 |
| Chi Shao (Yao)  | 43.76                     | —                                 |
| Tao Ren         | 44.11                     | —                                 |
| Huang Lian      | 44.51                     | —                                 |
| Shan Yao        | 45.29                     | —                                 |
| Rou Gui         | 45.82                     | —                                 |
| Qiang Huo       | 45.82                     | —                                 |
| Di Gu Pi        | 46.41                     | —                                 |
| Zhe Bei Mu      | 46.82                     | —                                 |
| Gua Lou         | 47.00                     | —                                 |
| Dan Dou Chi     | 47.72                     | —                                 |
| Gou Teng        | 48.03                     | —                                 |
| Suan Zao Ren    | 48.61                     | —                                 |
| Hong Hua        | 48.65                     | —                                 |

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| Substanz    | Distance in<br>main model | Distance in<br>second-stage model |
|-------------|---------------------------|-----------------------------------|
| Ci Wu Jia   | 48.99                     | —                                 |
| Ze Xie      | 49.31                     | —                                 |
| Ji Xue Teng | 49.77                     | —                                 |
| Hua Shi     | 57.33                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62281     | 62281                  | 0.00                            | 24.45                              |
| 62282     | 62282                  | 0.00                            | 23.91                              |
| 62709     | 62709                  | 0.00                            | 23.85                              |
| 62710     | 62710                  | 0.00                            | 23.76                              |
| 62789     | 62789                  | 0.00                            | 23.79                              |
| 62790     | 62790                  | 0.00                            | 23.71                              |

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 2.4-2022-02

Validated substance/substance group **Huo Ma Ren**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60234-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Huo Ma Ren | G141HS061SP1 | 62712 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 2              | 76            | 4              | 22 358        |
| <b>Type B</b> | 3              | 37            | 3              | 11 354        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Huo Ma 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9907 % (> 99.9744 %)  | 95.0000 % (> 91.2500 %) |
| <b>Type B</b> | 99.9888 % (> 99.9568 %)  | 92.5000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| He Huan Pi      | 3.64                      | —                                 |
| Mu Zei          | 4.72                      | —                                 |
| Bai Shao Yao    | 6.86                      | —                                 |
| Gu Sui Bu       | 6.92                      | —                                 |
| Gou Teng        | 7.38                      | —                                 |
| Shen Qu         | 7.71                      | —                                 |
| Tao Ren         | 7.82                      | —                                 |
| Lu Gen          | 8.28                      | —                                 |
| Lian Zi         | 8.69                      | —                                 |
| Gui Zhi         | 8.98                      | —                                 |
| Sheng Jiang     | 9.05                      | —                                 |
| Ling Zhi        | 9.59                      | —                                 |
| Ji Xue Teng     | 9.82                      | —                                 |
| Fu Ling         | 9.84                      | —                                 |
| Ji Li           | 9.91                      | —                                 |
| Ci Wu Jia       | 10.55                     | —                                 |
| Tian Hua Fen    | 10.63                     | —                                 |
| Zhe Bei Mu      | 10.68                     | —                                 |
| Rou Gui         | 10.73                     | —                                 |
| Bai Xian Pi     | 11.05                     | —                                 |
| Ren Dong Teng   | 11.36                     | —                                 |
| (Fen) Bi Xie    | 11.46                     | —                                 |
| She Gan         | 11.64                     | —                                 |
| Ye Jiao Teng    | 11.86                     | —                                 |
| Bai Zi Ren      | 11.97                     | —                                 |
| Zhu Ling        | 12.00                     | —                                 |
| Yi Yi Ren       | 12.46                     | —                                 |
| Suan Zao Ren    | 12.54                     | —                                 |
| Lai Fu Zi       | 12.62                     | —                                 |
| Fu Xiao Mai     | 13.26                     | —                                 |
| Di Gu Pi        | 13.35                     | —                                 |
| Ban Xia (Jiang) | 14.21                     | —                                 |
| Ma Huang Gen    | 14.34                     | —                                 |
| Fo Shou         | 15.59                     | —                                 |
| Ce Bai Ye       | 15.60                     | —                                 |
| Lian Qiao       | 15.78                     | —                                 |
| Yu Jin          | 15.95                     | —                                 |
| Ze Xie          | 16.13                     | —                                 |
| Tu Fu Ling      | 16.26                     | —                                 |
| Pi Pa Ye        | 16.60                     | —                                 |
| Zhu Ru          | 16.68                     | —                                 |
| Shan Yao        | 16.87                     | —                                 |
| Dan Dou Chi     | 17.49                     | —                                 |
| Yan Hu Suo      | 18.96                     | —                                 |
| Dan Shen        | 19.02                     | —                                 |
| Fu Zi           | 19.58                     | —                                 |
| Fu Pen Zi       | 20.57                     | —                                 |
| Yin Yang Huo    | 21.12                     | —                                 |
| Jin Yin Hua     | 21.51                     | —                                 |
| Chai Hu         | 21.59                     | —                                 |
| Mao Dong Qing   | 22.10                     | —                                 |
| Guang Huo Xiang | 23.43                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jiao Gu Lan     | 23.85                     | —                                 |
| Hou Po          | 23.99                     | —                                 |
| Gua Lou         | 24.24                     | —                                 |
| Hong Jing Tian  | 24.36                     | —                                 |
| Ma Huang        | 25.59                     | —                                 |
| Ban Lan Gen     | 25.61                     | —                                 |
| Che Qian Zi     | 25.72                     | —                                 |
| Cang Zhu        | 26.42                     | —                                 |
| Fu Shen         | 26.45                     | —                                 |
| Gan Cao         | 27.05                     | —                                 |
| Qiang Huo       | 28.40                     | —                                 |
| Zhi Ke          | 29.00                     | —                                 |
| Ren Shen        | 29.07                     | —                                 |
| Jie Geng        | 29.28                     | —                                 |
| Dang Gui        | 30.16                     | —                                 |
| San Qi          | 30.72                     | —                                 |
| Jing Jie        | 32.20                     | —                                 |
| Mang Xiao       | 33.19                     | —                                 |
| Huang Qin       | 34.72                     | —                                 |
| Zi Hua Di Ding  | 34.78                     | —                                 |
| Zhi Mu          | 35.22                     | —                                 |
| Huang Lian      | 36.04                     | —                                 |
| Sha Ren         | 36.53                     | —                                 |
| Chuang Mu Xiang | 38.99                     | —                                 |
| Qing Pi         | 39.10                     | —                                 |
| Sang Zhi        | 39.70                     | —                                 |
| Du Zhong        | 39.80                     | —                                 |
| Long Yan Rou    | 39.86                     | —                                 |
| Gou Qi Zi       | 40.06                     | —                                 |
| Zhi Gan Cao     | 40.25                     | —                                 |
| Mu Gua          | 40.27                     | —                                 |
| Bo He           | 42.14                     | —                                 |
| Yuan Zhi        | 42.36                     | —                                 |
| Ku Shen         | 42.54                     | —                                 |
| Xie Bai         | 44.39                     | —                                 |
| Chi Shao (Yao)  | 45.89                     | —                                 |
| Huang Bai       | 46.16                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62711     | 62711                  | 0.00                            | 4.90                               |
| 62712     | 62712                  | 0.00                            | 3.64                               |

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 2.4-2022-02

Validated substance/substance group **Ji Li**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60110-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ji Li                     | 2      | 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     | 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 34 694 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 Li*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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     | G240HS305SK1 | 62545 <sup>†</sup> | 20      |
| PhytoComm | Ji Li     | G240HS305SK1 | 62546 <sup>†</sup> | 20      |
| PhytoComm | Ji Li     | G240HS305SQ1 | 62721 <sup>†</sup> | 20      |
| PhytoComm | Ji Li     | G240HS305SQ1 | 62722 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 160           | 0              | 22 279        |
| <b>Type B</b> | 3              | 75            | 5              | 11 314        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 99.9963 % (> 99.9799 %)  | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 99.9777 % (> 99.9455 %)  | 93.7500 % (> 90.0000 %)  |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Lai Fu Zi       | 4.34                      | —                                 |
| Ling Zhi        | 4.65                      | —                                 |
| Lian Qiao       | 5.11                      | —                                 |
| Tian Hua Fen    | 6.05                      | —                                 |
| Bai Shao Yao    | 6.34                      | —                                 |
| Shen Qu         | 6.47                      | —                                 |
| Bai Zi Ren      | 7.08                      | —                                 |
| Sheng Jiang     | 7.27                      | —                                 |
| Zhe Bei Mu      | 7.27                      | —                                 |
| Mu Zei          | 7.35                      | —                                 |
| Lian Zi         | 7.83                      | —                                 |
| Huo Ma Ren      | 8.13                      | —                                 |
| He Huan Pi      | 8.58                      | —                                 |
| Fu Zi           | 8.75                      | —                                 |
| Pi Pa Ye        | 9.68                      | —                                 |
| Zhu Ru          | 9.84                      | —                                 |
| Shan Yao        | 10.04                     | —                                 |
| Ren Dong Teng   | 10.16                     | —                                 |
| Ci Wu Jia       | 10.24                     | —                                 |
| Gu Sui Bu       | 10.26                     | —                                 |
| Tao Ren         | 10.83                     | —                                 |
| Fu Ling         | 12.06                     | —                                 |
| Gui Zhi         | 12.08                     | —                                 |
| Hou Po          | 12.18                     | —                                 |
| Di Gu Pi        | 12.20                     | —                                 |
| Mao Dong Qing   | 12.89                     | —                                 |
| Fu Xiao Mai     | 13.38                     | —                                 |
| Ye Jiao Teng    | 13.44                     | —                                 |
| Yu Jin          | 13.53                     | —                                 |
| Che Qian Zi     | 14.13                     | —                                 |
| Chai Hu         | 14.20                     | —                                 |
| Ze Xie          | 14.31                     | —                                 |
| Suan Zao Ren    | 14.44                     | —                                 |
| Gou Teng        | 14.64                     | —                                 |
| Ban Xia (Jiang) | 14.84                     | —                                 |
| Fu Pen Zi       | 14.96                     | —                                 |
| Yi Yi Ren       | 15.47                     | —                                 |
| Gua Lou         | 15.55                     | —                                 |
| Dan Shen        | 15.62                     | —                                 |
| Bai Xian Pi     | 15.78                     | —                                 |
| Jiao Gu Lan     | 15.88                     | —                                 |
| Tu Fu Ling      | 16.33                     | —                                 |
| Dan Dou Chi     | 16.36                     | —                                 |
| Lu Gen          | 16.47                     | —                                 |
| Rou Gui         | 16.52                     | —                                 |
| Ji Xue Teng     | 16.54                     | —                                 |
| Ce Bai Ye       | 16.74                     | —                                 |
| Zhu Ling        | 17.26                     | —                                 |
| Jin Yin Hua     | 17.82                     | —                                 |

*continued on the next page*

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Fo Shou         | 18.01                     | —                                 |
| She Gan         | 18.15                     | —                                 |
| San Qi          | 18.57                     | —                                 |
| Yan Hu Suo      | 18.90                     | —                                 |
| Guang Huo Xiang | 19.85                     | —                                 |
| Ban Lan Gen     | 20.47                     | —                                 |
| Ren Shen        | 20.71                     | —                                 |
| (Fen) Bi Xie    | 20.93                     | —                                 |
| Dang Gui        | 21.13                     | —                                 |
| Jie Geng        | 21.30                     | —                                 |
| Yin Yang Huo    | 22.13                     | —                                 |
| Qiang Huo       | 22.86                     | —                                 |
| Ma Huang Gen    | 23.08                     | —                                 |
| Zhi Mu          | 23.46                     | —                                 |
| Cang Zhu        | 24.41                     | —                                 |
| Zhi Gan Cao     | 24.60                     | —                                 |
| Hong Jing Tian  | 24.75                     | —                                 |
| Ku Shen         | 24.83                     | —                                 |
| Gan Cao         | 25.63                     | —                                 |
| Xie Bai         | 25.63                     | —                                 |
| Qing Pi         | 26.88                     | —                                 |
| Gou Qi Zi       | 27.72                     | —                                 |
| Zhi Ke          | 28.01                     | —                                 |
| Mu Gua          | 28.70                     | —                                 |
| Huang Qin       | 28.89                     | —                                 |
| Ma Huang        | 29.61                     | —                                 |
| Yuan Zhi        | 29.72                     | —                                 |
| Du Zhong        | 29.87                     | —                                 |
| Zi Hua Di Ding  | 31.38                     | —                                 |
| Jing Jie        | 31.92                     | —                                 |
| Chuang Mu Xiang | 32.98                     | —                                 |
| Long Yan Rou    | 33.22                     | —                                 |
| Fu Shen         | 33.30                     | —                                 |
| Mang Xiao       | 33.53                     | —                                 |
| Bo He           | 33.56                     | —                                 |
| Huang Lian      | 33.62                     | —                                 |
| Sha Ren         | 35.00                     | —                                 |
| Sang Zhi        | 37.64                     | —                                 |
| Huang Bai       | 37.81                     | —                                 |
| Chi Shao (Yao)  | 39.13                     | —                                 |
| Cang Er Zi      | 40.68                     | —                                 |
| Hong Hua        | 47.08                     | —                                 |
| Qing Hao        | 47.48                     | —                                 |
| Bai Jiang Cao   | 48.77                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62545     | 62545               | 0.00                         | 4.86                            |
| 62546     | 62546               | 0.00                         | 4.65                            |
| 62721     | 62721               | 0.00                         | 4.35                            |
| 62722     | 62722               | 0.00                         | 4.34                            |

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 2.4-2022-02

Validated substance/substance group **Ji Xue Teng**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60099-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ji Xue Teng | G159HS337SK1 | 62560 <sup>†</sup> | 20      |
| PhytoComm | Ji Xue Teng | G159HS337SQ1 | 62723 <sup>†</sup> | 20      |
| PhytoComm | Ji Xue Teng | G159HS337SQ1 | 62724 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | g159h2101122 | 1       |
| Phytocomm | Ji Xue Teng | G159H2101423 | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 3              | 154           | 6              | 22 277        |
| <b>Type B</b> | 2              | 78            | 2              | 11 315        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9851 % (> 99.9688 %)  | 96.2500 % (> 94.3750 %) |
| <b>Type B</b> | 99.9777 % (> 99.9455 %)  | 97.5000 % (> 93.7500 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Lu Gen          | 4.03                      | —                                 |
| Ye Jiao Teng    | 4.22                      | —                                 |
| He Huan Pi      | 5.41                      | —                                 |
| Rou Gui         | 6.12                      | —                                 |
| Ma Huang Gen    | 6.83                      | —                                 |
| Ren Dong Teng   | 7.93                      | —                                 |
| Gou Teng        | 9.39                      | —                                 |
| (Fen) Bi Xie    | 10.39                     | —                                 |
| Mu Zei          | 10.54                     | —                                 |
| Fo Shou         | 10.78                     | —                                 |
| Gui Zhi         | 10.81                     | —                                 |
| Bai Shao Yao    | 11.44                     | —                                 |
| Huo Ma Ren      | 11.76                     | —                                 |
| Bai Xian Pi     | 12.00                     | —                                 |
| She Gan         | 12.08                     | —                                 |
| Fu Ling         | 12.09                     | —                                 |
| Dan Dou Chi     | 14.20                     | —                                 |
| Yi Yi Ren       | 14.28                     | —                                 |
| Sheng Jiang     | 14.66                     | —                                 |
| Gu Sui Bu       | 15.38                     | —                                 |
| Tu Fu Ling      | 15.83                     | —                                 |
| Ling Zhi        | 16.37                     | —                                 |
| Tao Ren         | 16.51                     | —                                 |
| Shen Qu         | 16.65                     | —                                 |
| Dan Shen        | 16.66                     | —                                 |
| Lian Zi         | 16.87                     | —                                 |
| Ci Wu Jia       | 17.12                     | —                                 |
| Zhu Ling        | 17.26                     | —                                 |
| Ban Xia (Jiang) | 17.31                     | —                                 |
| Fu Shen         | 17.65                     | —                                 |
| Suan Zao Ren    | 18.03                     | —                                 |
| Ma Huang        | 18.97                     | —                                 |
| Yin Yang Huo    | 19.44                     | —                                 |
| Yan Hu Suo      | 20.12                     | —                                 |
| Yu Jin          | 20.44                     | —                                 |
| Guang Huo Xiang | 20.57                     | —                                 |
| Lai Fu Zi       | 20.71                     | —                                 |
| Fu Xiao Mai     | 20.84                     | —                                 |
| Zhe Bei Mu      | 20.92                     | —                                 |
| Di Gu Pi        | 21.77                     | —                                 |
| Ji Li           | 22.96                     | —                                 |
| Lian Qiao       | 23.17                     | —                                 |
| Jin Yin Hua     | 23.54                     | —                                 |
| Ce Bai Ye       | 23.68                     | —                                 |
| Tian Hua Fen    | 23.84                     | —                                 |

*continued on the next page*

continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bai Zi Ren      | 24.86                     | —                                 |
| Ze Xie          | 25.33                     | —                                 |
| Pi Pa Ye        | 25.75                     | —                                 |
| Chai Hu         | 26.07                     | —                                 |
| Mao Dong Qing   | 26.31                     | —                                 |
| Hong Jing Tian  | 26.37                     | —                                 |
| Fu Zi           | 26.45                     | —                                 |
| Fu Pen Zi       | 26.49                     | —                                 |
| Gan Cao         | 27.74                     | —                                 |
| Zhu Ru          | 28.06                     | —                                 |
| Jing Jie        | 28.11                     | —                                 |
| Hou Po          | 28.31                     | —                                 |
| Zhi Ke          | 28.66                     | —                                 |
| Jiao Gu Lan     | 28.78                     | —                                 |
| Shan Yao        | 28.78                     | —                                 |
| Qiang Huo       | 30.14                     | —                                 |
| Ban Lan Gen     | 30.70                     | —                                 |
| Mang Xiao       | 30.80                     | —                                 |
| Cang Zhu        | 31.75                     | —                                 |
| Zi Hua Di Ding  | 32.22                     | —                                 |
| Sha Ren         | 32.74                     | —                                 |
| Ren Shen        | 32.90                     | —                                 |
| Che Qian Zi     | 32.94                     | —                                 |
| Huang Lian      | 32.99                     | —                                 |
| Huang Qin       | 34.49                     | —                                 |
| Gua Lou         | 34.79                     | —                                 |
| Jie Geng        | 35.13                     | —                                 |
| Dang Gui        | 35.15                     | —                                 |
| Zhi Mu          | 39.24                     | —                                 |
| Long Yan Rou    | 39.49                     | —                                 |
| Sang Zhi        | 39.63                     | —                                 |
| Du Zhong        | 39.73                     | —                                 |
| Bo He           | 39.95                     | —                                 |
| Chuang Mu Xiang | 41.66                     | —                                 |
| San Qi          | 42.45                     | —                                 |
| Huang Bai       | 42.96                     | —                                 |
| Chi Shao (Yao)  | 43.40                     | —                                 |
| Zhi Gan Cao     | 44.86                     | —                                 |
| Gou Qi Zi       | 45.50                     | —                                 |
| Mu Gua          | 46.32                     | —                                 |
| Qing Pi         | 47.12                     | —                                 |
| Ban Zhi Lian    | 47.22                     | —                                 |
| Hong Hua        | 48.84                     | —                                 |

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                         | 4.47                            |
| 62560     | 62560               | 0.00                         | 4.22                            |
| 62723     | 62723               | 0.00                         | 4.03                            |
| 62724     | 62724               | 0.00                         | 5.14                            |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Jiang Huang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60181-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Jiang Huang               | 1      | 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 | G085H1716821 | 62519     | 40      | from supplier |
| PhytoComm | Jiang Huang | G085H1716821 | 62520     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Jiang Huang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G085H1716821 | 62519 <sup>†</sup> | 20      |
| PhytoComm | Jiang Huang | G085H1716821 | 62520 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 | G085H1716321 | 1       |
| Phytocomm | Jiang Huang | G085H1716422 | 3       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 3              | 0             | 5              | 849           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 99.3023 % (> 98.7155 %)  | n/a (n/a)                |

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

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

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

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Sha Ren             | 14.06                     | —                                 |
| (Bai) Dou Kou       | 19.17                     | —                                 |
| He Huan Pi          | 20.45                     | —                                 |
| Bai Hua She She Cao | 20.51                     | —                                 |
| E Zhu               | 23.52                     | —                                 |
| Shan Yao            | 24.35                     | —                                 |
| Wang Bu Liu Xing    | 25.28                     | —                                 |
| Yi Mu Cao           | 26.00                     | —                                 |
| Cang Er Zi          | 27.84                     | —                                 |
| Niu Bang Zi         | 28.35                     | —                                 |
| Ze Lan              | 28.36                     | —                                 |
| Chen Pi             | 28.77                     | —                                 |
| Yan Hu Suo          | 28.95                     | —                                 |
| Huang Lian          | 29.00                     | —                                 |
| Mang Xiao           | 30.01                     | —                                 |
| Xin Yi              | 30.24                     | —                                 |
| Xiang Fu            | 31.60                     | —                                 |
| Hu Zhang            | 31.81                     | —                                 |
| Zhi Ke              | 32.65                     | —                                 |
| Zi Su Zi            | 34.01                     | —                                 |
| Wu Yao              | 34.65                     | —                                 |
| Di Gu Pi            | 34.81                     | —                                 |
| Yin Chen Hao        | 34.96                     | —                                 |
| Du Zhong            | 35.14                     | —                                 |
| Mao Dong Qing       | 35.78                     | —                                 |
| Pu Gong Ying        | 35.86                     | —                                 |
| Xi Xian Cao         | 35.99                     | —                                 |
| Sang Ye             | 36.61                     | —                                 |
| Suan Zao Ren        | 37.45                     | —                                 |
| Xiao Hui Xiang      | 37.58                     | —                                 |
| Gan Jiang           | 37.68                     | —                                 |
| Gu Sui Bu           | 38.13                     | —                                 |
| Qiang Huo           | 40.72                     | —                                 |
| Nü Zhen Zi          | 42.13                     | —                                 |
| Bo He               | 42.82                     | —                                 |
| Sha Shen (Bei)      | 44.68                     | —                                 |
| Mi Huan Jun         | 45.02                     | —                                 |
| Sang Ji Shend       | 45.03                     | —                                 |
| Tian Hua Fen        | 45.98                     | —                                 |
| Dan Dou Chi         | 45.98                     | —                                 |
| Hong Jing Tian      | 46.30                     | —                                 |
| Xia Ku Cao          | 46.33                     | —                                 |
| Jiao Gu Lan         | 46.39                     | —                                 |
| Shan Yu Rou         | 46.43                     | —                                 |
| Tu Fu Ling          | 46.53                     | —                                 |
| Xu Duan             | 46.90                     | —                                 |
| Han Lian Cao        | 47.13                     | —                                 |
| He Shou Wu          | 47.35                     | —                                 |
| Dang Gui            | 47.62                     | —                                 |
| Chuan Niu Xi        | 48.09                     | —                                 |
| Yu Xing Cao         | 48.75                     | —                                 |
| Lian Qiao           | 48.93                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62519     | 62519               | 0.00                         | 14.06                           |
| 62520     | 62520               | 0.00                         | 14.50                           |

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



# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Jiao Gu Lan**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60332-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Jiao Gu Lan               | 3      | 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 |
| PhytoComm | Jiao Gu Lan | G065HS424TL1 | 62907     | 40      | from supplier |
| PhytoComm | Jiao Gu Lan | G065HS424TL1 | 62908     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Jiao Gu Lan*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Jiao Gu Lan | G065HS424RR1 | 62442 <sup>†</sup> | 20      |
| PhytoComm | Jiao Gu Lan | G065HS424SG1 | 62665 <sup>†</sup> | 20      |
| PhytoComm | Jiao Gu Lan | G065HS424SG1 | 62666 <sup>†</sup> | 20      |
| PhytoComm | Jiao Gu Lan | G065HS424TL1 | 62907 <sup>†</sup> | 20      |
| PhytoComm | Jiao Gu Lan | G065HS424TL1 | 62908 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jin Yin Hua     | 8.24                      | —                                 |
| Shan Yao        | 9.75                      | —                                 |
| Zhi Gan Cao     | 11.11                     | —                                 |
| Suan Zao Ren    | 11.32                     | —                                 |
| Dan Shen        | 11.74                     | —                                 |
| Lian Qiao       | 11.88                     | —                                 |
| Zi Hua Di Ding  | 11.92                     | —                                 |
| Ji Li           | 13.97                     | —                                 |
| Chai Hu         | 14.08                     | —                                 |
| Xie Bai         | 14.46                     | —                                 |
| Qing Pi         | 14.69                     | —                                 |
| Ku Shen         | 14.84                     | —                                 |
| Hong Jing Tian  | 15.20                     | —                                 |
| Mao Dong Qing   | 15.61                     | —                                 |
| Qing Hao        | 15.70                     | —                                 |
| Zhi Ke          | 16.18                     | —                                 |
| Ling Zhi        | 16.45                     | —                                 |
| Ban Lan Gen     | 16.57                     | —                                 |
| Hong Hua        | 16.72                     | —                                 |
| Bai Zi Ren      | 17.98                     | —                                 |
| Gan Cao         | 18.39                     | —                                 |
| Guang Huo Xiang | 18.54                     | —                                 |
| Dan Dou Chi     | 18.77                     | —                                 |
| Zhe Bei Mu      | 18.84                     | —                                 |
| Tian Hua Fen    | 18.94                     | —                                 |
| Pi Pa Ye        | 19.15                     | —                                 |
| Chuang Mu Xiang | 19.26                     | —                                 |
| Ren Shen        | 20.93                     | —                                 |
| Hou Po          | 21.16                     | —                                 |
| Lian Zi         | 21.72                     | —                                 |
| Qiang Huo       | 21.85                     | —                                 |
| She Gan         | 22.41                     | —                                 |
| Cang Er Zi      | 22.48                     | —                                 |
| Ren Dong Teng   | 22.52                     | —                                 |
| Yan Hu Suo      | 22.56                     | —                                 |
| Bo He           | 22.76                     | —                                 |
| Gu Sui Bu       | 22.96                     | —                                 |
| Huang Bai       | 23.78                     | —                                 |
| Bai Shao Yao    | 24.09                     | —                                 |
| Fu Ling         | 24.15                     | —                                 |
| Sang Ye         | 25.02                     | —                                 |
| Fu Zi           | 25.09                     | —                                 |
| Du Zhong        | 25.13                     | —                                 |
| Shen Qu         | 25.55                     | —                                 |
| Yin Yang Huo    | 25.67                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ye Jiao Teng    | 25.72                     | —                                 |
| Cang Zhu        | 25.96                     | —                                 |
| Ma Huang        | 26.17                     | —                                 |
| Fu Pen Zi       | 26.19                     | —                                 |
| San Qi          | 26.20                     | —                                 |
| Sha Ren         | 26.23                     | —                                 |
| He Huan Pi      | 26.38                     | —                                 |
| Mu Zei          | 26.49                     | —                                 |
| Di Gu Pi        | 26.60                     | —                                 |
| Jie Geng        | 27.87                     | —                                 |
| Ze Xie          | 27.91                     | —                                 |
| Lu Gen          | 28.35                     | —                                 |
| Dang Gui        | 28.47                     | —                                 |
| Ce Bai Ye       | 28.51                     | —                                 |
| Gou Qi Zi       | 28.82                     | —                                 |
| Huo Ma Ren      | 28.93                     | —                                 |
| Bai Xian Pi     | 29.18                     | —                                 |
| Sheng Jiang     | 29.52                     | —                                 |
| Huang Lian      | 30.26                     | —                                 |
| Che Qian Zi     | 30.66                     | —                                 |
| Zhi Mu          | 30.89                     | —                                 |
| Yu Jin          | 30.96                     | —                                 |
| Gua Lou         | 31.06                     | —                                 |
| Chi Shao (Yao)  | 31.34                     | —                                 |
| Wu Wei Zi       | 31.36                     | —                                 |
| Jing Jie        | 31.73                     | —                                 |
| Zhu Ru          | 31.80                     | —                                 |
| Zhu Ling        | 31.82                     | —                                 |
| Mang Xiao       | 32.17                     | —                                 |
| Ji Xue Teng     | 32.18                     | —                                 |
| Gou Teng        | 33.41                     | —                                 |
| Bai Jiang Cao   | 34.10                     | —                                 |
| Huang Qin       | 34.77                     | —                                 |
| Long Yan Rou    | 35.32                     | —                                 |
| Mu Gua          | 35.70                     | —                                 |
| Gui Zhi         | 36.59                     | —                                 |
| Tao Ren         | 36.88                     | —                                 |
| Tu Fu Ling      | 38.00                     | —                                 |
| Yuan Zhi        | 38.49                     | —                                 |
| Sang Zhi        | 38.85                     | —                                 |
| Rou Gui         | 40.18                     | —                                 |
| (Fen) Bi Xie    | 40.46                     | —                                 |
| Lai Fu Zi       | 41.39                     | —                                 |
| Ci Wu Jia       | 41.78                     | —                                 |
| Niu Bang Zi     | 42.82                     | —                                 |
| Pu Gong Ying    | 42.98                     | —                                 |
| Yi Yi Ren       | 43.30                     | —                                 |
| Ze Lan          | 44.74                     | —                                 |
| Xi Xian Cao     | 45.47                     | —                                 |
| Ma Huang Gen    | 45.78                     | —                                 |
| Fu Xiao Mai     | 46.13                     | —                                 |
| Ban Xia (Jiang) | 49.38                     | —                                 |
| Zi Su Zi        | 49.50                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62441     | 62441               | 0.00                         | 8.24                            |
| 62442     | 62442               | 0.00                         | 9.75                            |
| 62665     | 62665               | 0.00                         | 9.75                            |
| 62666     | 62666               | 0.00                         | 10.06                           |
| 62907     | 62907               | 0.00                         | 10.21                           |
| 62908     | 62908               | 0.00                         | 9.86                            |

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 2.4-2022-02

Validated substance/substance group **Jie Geng**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60034-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Jie Geng                  | 3      | 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  | G193H1015821 | 62365     | 40      | from supplier |
| PhytoComm | Jie Geng  | G193H1015821 | 62366     | 40      | from supplier |
| PhytoComm | Jie Geng  | G193H1015921 | 62843     | 40      | from supplier |
| PhytoComm | Jie Geng  | G193H1015921 | 62844     | 40      | from supplier |
| PhytoComm | Jie Geng  | G193HS221TP1 | 63029     | 40      | from supplier |
| PhytoComm | Jie Geng  | G193HS221TP1 | 63030     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Jie Geng*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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  | G193H1015821 | 62365 <sup>†</sup> | 20      |
| PhytoComm | Jie Geng  | G193H1015821 | 62366 <sup>†</sup> | 20      |
| PhytoComm | Jie Geng  | G193H1015921 | 62843 <sup>†</sup> | 20      |
| PhytoComm | Jie Geng  | G193H1015921 | 62844 <sup>†</sup> | 20      |
| PhytoComm | Jie Geng  | G193HS221TP1 | 63029 <sup>†</sup> | 20      |
| PhytoComm | Jie Geng  | G193HS221TP1 | 63030 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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  | G193H1015521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 3              | 120           | 0              | 11 274        |
| <b>Type C</b> | 4              | 2             | 3              | 848           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 99.9826 % (> 99.9504 %)  | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 99.3798 % (> 98.7930 %)  | n/a (n/a)                |

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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Gua Lou        | 7.21                      | —                                 |
| Cang Zhu       | 7.95                      | —                                 |
| Bai Zhu        | 9.34                      | —                                 |
| Zhi Mu         | 9.43                      | —                                 |
| Dang Gui       | 9.56                      | —                                 |
| Bai Shao Yao   | 9.85                      | —                                 |
| Chuan Lian Zi  | 10.31                     | —                                 |
| Fo Shou        | 11.20                     | —                                 |
| Sang Zhi       | 11.21                     | —                                 |
| Di Gu Pi       | 12.46                     | —                                 |
| Zhi Gan Cao    | 13.33                     | —                                 |
| San Qi         | 13.34                     | —                                 |
| Ye Jiao Teng   | 13.55                     | —                                 |
| Yuan Zhi       | 13.55                     | —                                 |
| Mu Gua         | 13.74                     | —                                 |
| Pi Pa Ye       | 14.20                     | —                                 |
| Long Dan (Cao) | 14.82                     | —                                 |
| Gou Qi Zi      | 15.30                     | —                                 |
| Huang Qi       | 15.84                     | —                                 |
| Ren Shen       | 16.04                     | —                                 |
| Zhe Bei Mu     | 16.09                     | —                                 |
| Tian Hua Fen   | 16.60                     | —                                 |
| Mu Zei         | 17.25                     | —                                 |
| Bai He         | 17.42                     | —                                 |
| Ji Li          | 17.60                     | —                                 |
| Jin Yin Hua    | 17.61                     | —                                 |
| Ren Dong Teng  | 17.72                     | —                                 |
| Qin Jiao       | 17.72                     | —                                 |
| Ban Lan Gen    | 17.74                     | —                                 |
| Shen Qu        | 17.91                     | —                                 |
| He Huan Pi     | 18.08                     | —                                 |
| Long Yan Rou   | 18.09                     | —                                 |
| Shan Yao       | 18.60                     | —                                 |
| Lian Qiao      | 18.72                     | —                                 |
| Ci Wu Jia      | 19.09                     | —                                 |
| Lai Fu Zi      | 19.72                     | —                                 |
| Ku Shen        | 19.88                     | —                                 |
| Zhu Ru         | 20.51                     | —                                 |
| Rou Gui        | 20.82                     | —                                 |
| Lian Zi        | 21.39                     | —                                 |
| Bai Zi Ren     | 21.50                     | —                                 |
| Ze Xie         | 21.62                     | —                                 |
| Xie Bai        | 22.13                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Tao Ren         | 22.46                             | —                                         |
| Jiao Gu Lan     | 22.59                             | —                                         |
| Ling Zhi        | 22.97                             | —                                         |
| Chi Shao (Yao)  | 23.29                             | —                                         |
| Sheng Jiang     | 23.76                             | —                                         |
| Gou Teng        | 24.92                             | —                                         |
| Gan Jiang       | 24.95                             | —                                         |
| Suan Zao Ren    | 24.97                             | —                                         |
| Dan Dou Chi     | 25.02                             | —                                         |
| Ban Xia (Jiang) | 25.04                             | —                                         |
| Zhi Ke          | 25.06                             | —                                         |
| Fu Ling         | 25.09                             | —                                         |
| Tu Fu Ling      | 25.13                             | —                                         |
| Chuang Mu Xiang | 25.26                             | —                                         |
| Huo Ma Ren      | 25.99                             | —                                         |
| Lu Gen          | 26.15                             | —                                         |
| Zi Su Zi        | 26.18                             | —                                         |
| Fu Pen Zi       | 26.22                             | —                                         |
| Hong Jing Tian  | 26.33                             | —                                         |
| Sha Shen (Bei)  | 26.39                             | —                                         |
| (Huai) Niu Xi   | 26.45                             | —                                         |
| Fu Xiao Mai     | 26.86                             | —                                         |
| Fu Zi           | 27.47                             | —                                         |
| Gui Zhi         | 27.55                             | —                                         |
| Ma Huang        | 27.56                             | —                                         |
| Gan Cao         | 27.66                             | —                                         |
| Huang Qin       | 28.08                             | —                                         |
| Ji Xue Teng     | 28.10                             | —                                         |
| Hou Po          | 28.17                             | —                                         |
| Chuan Mu Tong   | 29.09                             | —                                         |
| Mang Xiao       | 29.69                             | —                                         |
| Dan Shen        | 30.60                             | —                                         |
| Bai Xian Pi     | 31.04                             | —                                         |
| Gu Sui Bu       | 31.06                             | —                                         |
| E Zhu           | 31.51                             | —                                         |
| Cang Er Zi      | 32.93                             | —                                         |
| Yin Yang Huo    | 33.16                             | —                                         |
| Mao Dong Qing   | 33.27                             | —                                         |
| Yi Yi Ren       | 33.86                             | —                                         |
| Ban Zhi Lian    | 33.93                             | —                                         |
| Che Qian Zi     | 34.01                             | —                                         |
| Chai Hu         | 34.66                             | —                                         |
| Guang Huo Xiang | 34.96                             | —                                         |
| Ma Huang Gen    | 36.70                             | —                                         |
| Yan Hu Suo      | 36.78                             | —                                         |
| Bai Zhi         | 37.44                             | —                                         |
| Chuan Niu Xi    | 37.49                             | —                                         |
| Niu Bang Zi     | 37.52                             | —                                         |
| Bing Lang       | 38.05                             | —                                         |
| (Fen) Bi Xie    | 38.28                             | —                                         |
| Mi Huan Jun     | 38.76                             | —                                         |
| Ce Bai Ye       | 38.90                             | —                                         |
| Qiang Huo       | 40.10                             | —                                         |
| Fu Shen         | 40.45                             | —                                         |
| Yu Jin          | 41.13                             | —                                         |
| She Gan         | 41.55                             | —                                         |
| (Shi) Chang Pu  | 42.36                             | —                                         |
| Zi Hua Di Ding  | 42.64                             | —                                         |
| Zhu Ling        | 43.83                             | —                                         |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Chen Pi        | 44.02                     | —                                 |
| Bo He          | 45.10                     | —                                 |
| Qing Pi        | 46.31                     | —                                 |
| Jiang Huang    | 46.46                     | —                                 |
| Huang Lian     | 47.89                     | —                                 |
| Hong Hua       | 48.42                     | —                                 |
| Da Zao         | 48.49                     | —                                 |
| Xiao Hui Xiang | 49.23                     | —                                 |
| Sha Ren        | 49.61                     | —                                 |
| Dong Gua Zi    | 49.65                     | —                                 |
| Jing Jie       | 49.97                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62365     | 62365                  | 0.00                            | 9.34                               |
| 62366     | 62366                  | 0.00                            | 10.31                              |
| 62843     | 62843                  | 0.00                            | 12.30                              |
| 62844     | 62844                  | 0.00                            | 13.69                              |
| 63029     | 63029                  | 0.00                            | 7.95                               |
| 63030     | 63030                  | 0.00                            | 7.21                               |

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 2.4-2022-02

Validated substance/substance group **Jin Qian Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50293-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Jin Qian Cao | G151H0847821 | 62466 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Sang Ye          | 16.59                     | —                                 |
| Ding Xiang       | 17.43                     | —                                 |
| Wu Jia Pi        | 19.39                     | —                                 |
| Jing Jie         | 20.15                     | —                                 |
| Mang Xiao        | 21.31                     | —                                 |
| Du Zhong         | 24.29                     | —                                 |
| Sang Ji Shend    | 26.14                     | —                                 |
| Gou Teng         | 28.02                     | —                                 |
| Yu Xing Cao      | 31.89                     | —                                 |
| Hong Jing Tian   | 32.71                     | —                                 |
| Dan Zhu Ye       | 35.75                     | —                                 |
| Ge Gen           | 36.47                     | —                                 |
| Xuan Fu Hua      | 38.20                     | —                                 |
| Yin Chen Hao     | 40.04                     | —                                 |
| Xuan Shen        | 40.16                     | —                                 |
| Xian Mao         | 42.65                     | —                                 |
| Nü Zhen Zi       | 42.91                     | —                                 |
| He Shou Wu       | 47.03                     | —                                 |
| (Sheng) Di Huang | 48.55                     | —                                 |
| Hua Shi          | 48.76                     | —                                 |
| Yi Mu Cao        | 52.55                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62465     | 62465                  | 0.00                            | 16.59                              |
| 62466     | 62466                  | 0.00                            | 16.98                              |

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 2.4-2022-02

Validated substance/substance group **Jin Yin Hua**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60350-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Jin Yin Hua               | 2      | 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 |
| PhytoComm | Jin Yin Hua | G145HS311TH2 | 62897     | 40      | from supplier |
| PhytoComm | Jin Yin Hua | G145HS311TH2 | 62898     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Jin Yin Hua*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Jin Yin Hua | G145HS311SK1 | 62578 <sup>†</sup> | 20      |
| PhytoComm | Jin Yin Hua | G145HS311TH2 | 62897 <sup>†</sup> | 20      |
| PhytoComm | Jin Yin Hua | G145HS311TH2 | 62898 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 2              | 80            | 0              | 11 315        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 99.9851 % (> 99.9529 %)  | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.

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

### 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.

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ma Huang        | 8.61                      | —                                 |
| Jiao Gu Lan     | 9.53                      | —                                 |
| Ban Lan Gen     | 10.61                     | —                                 |
| Pi Pa Ye        | 11.39                     | —                                 |
| Zhe Bei Mu      | 11.65                     | —                                 |
| Lian Qiao       | 11.93                     | —                                 |
| Fu Zi           | 12.14                     | —                                 |
| Yan Hu Suo      | 12.18                     | —                                 |
| Ze Xie          | 12.20                     | —                                 |
| Hou Po          | 12.48                     | —                                 |
| Tian Hua Fen    | 12.52                     | —                                 |
| Guang Huo Xiang | 12.91                     | —                                 |
| Dan Dou Chi     | 13.40                     | —                                 |
| Ku Shen         | 13.86                     | —                                 |
| Zhi Gan Cao     | 13.93                     | —                                 |
| Shan Yao        | 13.94                     | —                                 |
| Zhi Ke          | 14.06                     | —                                 |
| Ren Dong Teng   | 14.56                     | —                                 |
| Bai Shao Yao    | 14.81                     | —                                 |
| Dang Gui        | 14.89                     | —                                 |
| Ye Jiao Teng    | 15.01                     | —                                 |
| Gua Lou         | 16.18                     | —                                 |
| He Huan Pi      | 16.36                     | —                                 |
| Cang Zhu        | 16.46                     | —                                 |
| Ling Zhi        | 16.83                     | —                                 |
| Chai Hu         | 16.92                     | —                                 |
| Huang Qin       | 17.08                     | —                                 |
| Fu Pen Zi       | 17.51                     | —                                 |
| Lu Gen          | 17.57                     | —                                 |
| Ji Li           | 17.64                     | —                                 |
| Ren Shen        | 17.65                     | —                                 |
| Mu Zei          | 17.67                     | —                                 |
| Suan Zao Ren    | 17.74                     | —                                 |
| Dan Shen        | 17.76                     | —                                 |
| Qing Pi         | 17.81                     | —                                 |
| Tao Ren         | 18.07                     | —                                 |
| Zi Hua Di Ding  | 18.29                     | —                                 |
| Hong Jing Tian  | 18.44                     | —                                 |
| Xie Bai         | 19.03                     | —                                 |
| Gan Cao         | 19.12                     | —                                 |
| San Qi          | 19.76                     | —                                 |
| Gui Zhi         | 19.85                     | —                                 |
| Gu Sui Bu       | 20.11                     | —                                 |
| Jie Geng        | 20.43                     | —                                 |
| She Gan         | 20.44                     | —                                 |
| Bai Zi Ren      | 20.70                     | —                                 |
| Di Gu Pi        | 20.97                     | —                                 |
| Rou Gui         | 21.21                     | —                                 |
| Gou Qi Zi       | 21.45                     | —                                 |
| Qiang Huo       | 21.86                     | —                                 |
| Lian Zi         | 21.87                     | —                                 |
| Ji Xue Teng     | 21.98                     | —                                 |

*continued on the next page*



continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ci Wu Jia       | 22.02                     | —                                 |
| Chuang Mu Xiang | 22.06                     | —                                 |
| Yin Yang Huo    | 22.35                     | —                                 |
| Mao Dong Qing   | 22.50                     | —                                 |
| Lai Fu Zi       | 23.71                     | —                                 |
| Ban Xia (Jiang) | 24.07                     | —                                 |
| Huo Ma Ren      | 24.17                     | —                                 |
| Zhi Mu          | 24.48                     | —                                 |
| Shen Qu         | 24.50                     | —                                 |
| Ce Bai Ye       | 24.83                     | —                                 |
| Sheng Jiang     | 25.17                     | —                                 |
| Gou Teng        | 25.24                     | —                                 |
| Long Yan Rou    | 26.00                     | —                                 |
| Che Qian Zi     | 26.21                     | —                                 |
| Fu Ling         | 27.02                     | —                                 |
| Hong Hua        | 27.07                     | —                                 |
| Tu Fu Ling      | 27.48                     | —                                 |
| Bai Xian Pi     | 27.53                     | —                                 |
| Bo He           | 27.99                     | —                                 |
| Fo Shou         | 28.09                     | —                                 |
| Zhu Ling        | 28.43                     | —                                 |
| Yu Jin          | 29.16                     | —                                 |
| Mu Gua          | 29.40                     | —                                 |
| Zhu Ru          | 29.51                     | —                                 |
| Huang Lian      | 29.86                     | —                                 |
| Du Zhong        | 29.96                     | —                                 |
| Sha Ren         | 30.33                     | —                                 |
| Mang Xiao       | 30.73                     | —                                 |
| Chi Shao (Yao)  | 31.81                     | —                                 |
| Huang Bai       | 31.91                     | —                                 |
| (Fen) Bi Xie    | 32.23                     | —                                 |
| Sang Ye         | 32.27                     | —                                 |
| Yi Yi Ren       | 32.57                     | —                                 |
| Yuan Zhi        | 32.81                     | —                                 |
| Cang Er Zi      | 33.06                     | —                                 |
| Jing Jie        | 33.06                     | —                                 |
| Fu Xiao Mai     | 33.19                     | —                                 |
| Qing Hao        | 35.57                     | —                                 |
| Fu Shen         | 37.28                     | —                                 |
| Sang Zhi        | 37.88                     | —                                 |
| Ma Huang Gen    | 39.76                     | —                                 |
| Bai Jiang Cao   | 40.69                     | —                                 |
| Wu Wei Zi       | 44.57                     | —                                 |
| Ze Lan          | 49.47                     | —                                 |

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                         | 9.84                            |
| 62578     | 62578               | 0.00                         | 9.53                            |
| 62897     | 62897               | 0.00                         | 10.21                           |
| 62898     | 62898               | 0.00                         | 8.61                            |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Jing Jie**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60088-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Jing Jie                  | 3      | 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 |
| PhytoComm | Jing Jie  | G221HS218TH1 | 62785     | 40      | from supplier |
| PhytoComm | Jing Jie  | G221HS218TH1 | 62786     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Jing Jie*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Jing Jie  | G221H1038822 | 62498 <sup>†</sup> | 20      |
| PhytoComm | Jing Jie  | G221H1038823 | 62751 <sup>†</sup> | 20      |
| PhytoComm | Jing Jie  | G221H1038823 | 62752 <sup>†</sup> | 20      |
| PhytoComm | Jing Jie  | G221HS218TH1 | 62785 <sup>†</sup> | 20      |
| PhytoComm | Jing Jie  | G221HS218TH1 | 62786 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 238           | 2              | 22 199        |
| <b>Type B</b> | 1              | 117           | 3              | 11 276        |
| <b>Type C</b> | 5              | 0             | 2              | 850           |

The substance/substance group *Jing Jie* 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        |
|---------------|-------------------------|-------------------------|
| <b>Type A</b> | 99.9963 % (> 99.9799 %) | 99.1667 % (> 97.9167 %) |
| <b>Type B</b> | 99.9851 % (> 99.9529 %) | 97.5000 % (> 95.0000 %) |
| <b>Type C</b> | 99.5930 % (> 99.0081 %) | n/a (n/a)               |

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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Hou Po          | 4.91                      | —                                 |
| Mao Dong Qing   | 5.71                      | —                                 |
| Chai Hu         | 5.88                      | —                                 |
| Yu Jin          | 5.97                      | —                                 |
| Qiang Huo       | 5.98                      | —                                 |
| Yin Yang Huo    | 6.24                      | —                                 |
| Du Zhong        | 7.07                      | —                                 |
| Zi Hua Di Ding  | 7.58                      | —                                 |
| Dan Dou Chi     | 7.85                      | —                                 |
| Bai Xian Pi     | 7.88                      | —                                 |
| Fu Zi           | 7.90                      | —                                 |
| Ling Zhi        | 8.39                      | —                                 |
| Che Qian Zi     | 9.64                      | —                                 |
| Ce Bai Ye       | 9.82                      | —                                 |
| Shan Yao        | 9.90                      | —                                 |
| Bo He           | 10.36                     | —                                 |
| Yan Hu Suo      | 10.42                     | —                                 |
| Sha Ren         | 10.93                     | —                                 |
| Shen Qu         | 11.02                     | —                                 |
| Fu Pen Zi       | 11.73                     | —                                 |
| Guang Huo Xiang | 12.08                     | —                                 |
| Dan Shen        | 12.33                     | —                                 |
| Ren Dong Teng   | 12.75                     | —                                 |
| Ye Jiao Teng    | 13.09                     | —                                 |
| Zhu Ling        | 13.65                     | —                                 |
| Pi Pa Ye        | 13.66                     | —                                 |
| Yin Chen Hao    | 13.74                     | —                                 |
| Qing Pi         | 14.49                     | —                                 |
| Qing Hao        | 15.05                     | —                                 |
| Gu Sui Bu       | 15.33                     | —                                 |
| Hong Jing Tian  | 15.85                     | —                                 |
| Ji Li           | 15.98                     | —                                 |
| Lian Zi         | 15.99                     | —                                 |
| Huang Bai       | 16.22                     | —                                 |
| Tian Hua Fen    | 16.36                     | —                                 |
| Tu Fu Ling      | 16.90                     | —                                 |
| Wu Jia Pi       | 17.06                     | —                                 |
| Sang Ji Shend   | 17.07                     | —                                 |
| Ma Huang        | 17.22                     | —                                 |
| Ji Xue Teng     | 18.53                     | —                                 |
| He Shou Wu      | 18.71                     | —                                 |
| Jiao Gu Lan     | 19.04                     | —                                 |
| Jin Yin Hua     | 19.07                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Jin Qian Cao    | 20.04                             | —                                         |
| Bai Jiang Cao   | 20.15                             | —                                         |
| Gan Cao         | 20.69                             | —                                         |
| Huang Lian      | 20.70                             | —                                         |
| (Fen) Bi Xie    | 21.02                             | —                                         |
| Suan Zao Ren    | 21.08                             | —                                         |
| Lian Qiao       | 21.11                             | —                                         |
| Bai Shao Yao    | 21.32                             | —                                         |
| Ban Lan Gen     | 21.56                             | —                                         |
| Dan Zhu Ye      | 21.67                             | —                                         |
| She Gan         | 21.77                             | —                                         |
| He Huan Pi      | 21.95                             | —                                         |
| Xuan Fu Hua     | 22.47                             | —                                         |
| Ma Huang Gen    | 22.48                             | —                                         |
| Gou Teng        | 23.18                             | —                                         |
| Mang Xiao       | 24.02                             | —                                         |
| Zhi Ke          | 24.33                             | —                                         |
| Di Gu Pi        | 24.43                             | —                                         |
| Mu Zei          | 24.67                             | —                                         |
| Fu Ling         | 24.91                             | —                                         |
| Lu Gen          | 25.01                             | —                                         |
| Rou Gui         | 25.10                             | —                                         |
| Bu Gu Zhi       | 25.12                             | —                                         |
| Zhi Gan Cao     | 25.53                             | —                                         |
| Ren Shen        | 25.88                             | —                                         |
| Sheng Jiang     | 26.25                             | —                                         |
| Huo Ma Ren      | 26.58                             | —                                         |
| Ding Xiang      | 27.75                             | —                                         |
| Zhe Bei Mu      | 27.77                             | —                                         |
| Gui Zhi         | 28.21                             | —                                         |
| Yu Xing Cao     | 29.12                             | —                                         |
| Nü Zhen Zi      | 29.78                             | —                                         |
| Yi Yi Ren       | 30.04                             | —                                         |
| Pu Gong Ying    | 30.15                             | —                                         |
| Sang Bai Pi     | 30.86                             | —                                         |
| Ge Gen          | 31.69                             | —                                         |
| Chuang Mu Xiang | 31.88                             | —                                         |
| Tao Ren         | 31.98                             | —                                         |
| Sang Ye         | 32.24                             | —                                         |
| Hong Hua        | 32.24                             | —                                         |
| Cang Zhu        | 32.89                             | —                                         |
| Ze Lan          | 34.92                             | —                                         |
| Wu Zhu Yu       | 35.01                             | —                                         |
| Bai Zi Ren      | 35.30                             | —                                         |
| Chi Shao (Yao)  | 35.55                             | —                                         |
| Ze Xie          | 35.63                             | —                                         |
| Sang Zhi        | 36.43                             | —                                         |
| Ci Wu Jia       | 37.63                             | —                                         |
| Ban Xia (Jiang) | 37.70                             | —                                         |
| Xi Xian Cao     | 37.91                             | —                                         |
| Jie Geng        | 38.47                             | —                                         |
| Huang Qin       | 38.73                             | —                                         |
| Zhu Ru          | 38.90                             | —                                         |
| Cang Er Zi      | 39.12                             | —                                         |
| Ban Zhi Lian    | 39.53                             | —                                         |
| Xie Bai         | 39.54                             | —                                         |
| Fo Shou         | 39.92                             | —                                         |
| Fu Xiao Mai     | 41.25                             | —                                         |
| Dang Gui        | 41.28                             | —                                         |

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| Substanz     | Distance in<br>main model | Distance in<br>second-stage model |
|--------------|---------------------------|-----------------------------------|
| Xian Mao     | 41.28                     | —                                 |
| Yi Mu Cao    | 41.41                     | —                                 |
| Gua Lou      | 41.87                     | —                                 |
| Fu Shen      | 42.13                     | —                                 |
| San Qi       | 43.26                     | —                                 |
| Long Yan Rou | 43.55                     | —                                 |
| E Zhu        | 43.56                     | —                                 |
| Jiang Huang  | 44.69                     | —                                 |
| Chen Pi      | 46.61                     | —                                 |
| Ku Shen      | 47.34                     | —                                 |
| Lai Fu Zi    | 47.92                     | —                                 |
| Hua Shi      | 48.80                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62497     | 62497                  | 0.00                            | 7.07                               |
| 62498     | 62498                  | 0.00                            | 7.64                               |
| 62751     | 62751                  | 0.00                            | 14.05                              |
| 62752     | 62752                  | 0.00                            | 13.74                              |
| 62785     | 62785                  | 0.00                            | 5.05                               |
| 62786     | 62786                  | 0.00                            | 4.91                               |

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 2.4-2022-02

Validated substance/substance group **Jiu Da Huang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 61389-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Jiu Da Huang; Rhei radix et rhizoma praeparata

### Special notes

When selecting the *Jiu Da Huang* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Jiu Da Huang              | 1      | 0      | 0      |

### Second-stage model

For differentiation of the substance/substance group *Jiu 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 *Jiu Da Huang*:

| Supplier  | Substance    | Batch        | Sample ID | Spectra | Certificate   |
|-----------|--------------|--------------|-----------|---------|---------------|
| PhytoComm | Jiu Da Huang | G561HS013SW1 | 62821     | 40      | from supplier |
| PhytoComm | Jiu Da Huang | G561HS013SW1 | 62822     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Jiu Da Huang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Jiu 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 | Jiu Da Huang | G561HS013SW1 | 62821 <sup>†</sup> | 20      |
| PhytoComm | Jiu Da Huang | G561HS013SW1 | 62822 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Jiu Da Huang*.
- 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 *Jiu 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 *Jiu 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 0              | 857           |

The substance/substance group *Jiu 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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 *Jiu 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.

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

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mang Xiao       | 15.90                     | —                                 |
| Xuan Shen       | 30.36                     | —                                 |
| Guang Huo Xiang | 33.54                     | —                                 |
| Ding Xiang      | 46.42                     | —                                 |
| Hua Shi         | 47.17                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Jiu 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62821     | 62821                  | 0.00                            | 15.94                              |
| 62822     | 62822                  | 0.00                            | 15.90                              |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Ju Hua**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002256-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ju Hua    | G064H1231822 | 62776 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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    | G064H1231421 | 1       |
| PhytoComm | Ju Hua    | G064H1231521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Chen Pi             | 16.24                     | —                                 |
| Fang Feng           | 17.70                     | —                                 |
| Xiang Fu            | 18.29                     | —                                 |
| Chuan Niu Xi        | 18.51                     | —                                 |
| (Shi) Chang Pu      | 20.88                     | —                                 |
| Shan Yu Rou         | 23.39                     | —                                 |
| Dang Gui            | 24.90                     | —                                 |
| Wu Yao              | 25.49                     | —                                 |
| Bing Lang           | 26.09                     | —                                 |
| Mang Xiao           | 26.12                     | —                                 |
| Gu Sui Bu           | 26.61                     | —                                 |
| He Huan Pi          | 28.45                     | —                                 |
| Sha Ren             | 28.45                     | —                                 |
| Huang Qi            | 28.83                     | —                                 |
| Chuan Lian Zi       | 29.18                     | —                                 |
| Zhi Gan Cao         | 30.09                     | —                                 |
| Ba Ji Tian          | 31.07                     | —                                 |
| Wu Zhu Yu           | 31.89                     | —                                 |
| He Shou Wu          | 32.33                     | —                                 |
| Chi Shao (Yao)      | 32.65                     | —                                 |
| Hong Jing Tian      | 33.55                     | —                                 |
| Xu Duan             | 34.16                     | —                                 |
| Yi Mu Cao           | 34.24                     | —                                 |
| Ku Shen             | 34.57                     | —                                 |
| Bai Zhi             | 36.03                     | —                                 |
| Shan Yao            | 38.29                     | —                                 |
| Jiang Huang         | 38.91                     | —                                 |
| Mu Dan Pi           | 39.77                     | —                                 |
| Sang Ji Shend       | 39.94                     | —                                 |
| Ge Gen              | 40.16                     | —                                 |
| Tian Hua Fen        | 40.33                     | —                                 |
| Sang Zhi            | 40.52                     | —                                 |
| Cang Er Zi          | 40.94                     | —                                 |
| Xiao Hui Xiang      | 41.39                     | —                                 |
| Sang Bai Pi         | 41.99                     | —                                 |
| (Huai) Niu Xi       | 42.21                     | —                                 |
| Di Gu Pi            | 42.26                     | —                                 |
| E Zhu               | 42.72                     | —                                 |
| Xin Yi              | 42.91                     | —                                 |
| Zhi Ke              | 42.92                     | —                                 |
| Du Huo              | 42.97                     | —                                 |
| Bai Hua She She Cao | 43.71                     | —                                 |
| Bai Zhu             | 43.75                     | —                                 |
| Zi Su Zi            | 43.77                     | —                                 |
| Lian Qiao           | 43.89                     | —                                 |
| Yuan Zhi            | 44.07                     | —                                 |
| Gan Cao             | 44.13                     | —                                 |
| Niu Bang Zi         | 44.39                     | —                                 |
| Jie Geng            | 44.39                     | —                                 |
| Pu Gong Ying        | 44.66                     | —                                 |
| (Bai) Dou Kou       | 45.86                     | —                                 |
| Yan Hu Suo          | 47.49                     | —                                 |

*continued on the next page*



continued from previous page

| Substanz | Distance in<br>main model | Distance in<br>second-stage model |
|----------|---------------------------|-----------------------------------|
| Sang Ye  | 50.32                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62775     | 62775                  | 0.00                            | 16.36                              |
| 62776     | 62776                  | 0.00                            | 16.24                              |

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



# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Jue Ming Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002262-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G059H1097021 | 62927     | 40      | from supplier |
| PhytoComm | Jue Ming Zi | G059H1097021 | 62928     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Jue Ming Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G059H1097021 | 62927 <sup>†</sup> | 20      |
| PhytoComm | Jue Ming Zi | G059H1097021 | 62928 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 2              | 0             | 4              | 851           |

The substance/substance group *Jue Ming 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Mang Xiao        | 15.67                     | —                                 |
| Guang Huo Xiang  | 31.22                     | —                                 |
| Shu Di (Huang)   | 34.95                     | —                                 |
| Hua Shi          | 41.01                     | —                                 |
| (Sheng) Di Huang | 41.11                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62927     | 62927                  | 0.00                            | 15.75                              |
| 62928     | 62928                  | 0.00                            | 15.67                              |

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 2.4-2022-02

Validated substance/substance group **Ku Shen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60112-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ku Shen                   | 2      | 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 |
| PhytoComm | Ku Shen   | G233HS180TK1 | 62795     | 40      | from supplier |
| PhytoComm | Ku Shen   | G233HS180TK1 | 62796     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Ku Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Ku Shen   | G233H0908822 | 62500 <sup>†</sup> | 20      |
| PhytoComm | Ku Shen   | G233HS180TK1 | 62795 <sup>†</sup> | 20      |
| PhytoComm | Ku Shen   | G233HS180TK1 | 62796 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 2              | 0             | 2              | 853           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 99.7287 % (> 99.1438 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| San Qi        | 6.71                      | —                                 |
| Lian Qiao     | 8.11                      | —                                 |
| Zhe Bei Mu    | 9.01                      | —                                 |
| Jin Yin Hua   | 10.17                     | —                                 |
| Bai Zi Ren    | 10.68                     | —                                 |
| Shan Yao      | 10.95                     | —                                 |
| Ji Li         | 11.11                     | —                                 |
| Jiao Gu Lan   | 11.31                     | —                                 |
| Zhi Mu        | 12.19                     | —                                 |
| Pi Pa Ye      | 12.57                     | —                                 |
| Suan Zao Ren  | 12.65                     | —                                 |
| Ling Zhi      | 13.66                     | —                                 |
| Lai Fu Zi     | 15.21                     | —                                 |
| Tian Hua Fen  | 15.26                     | —                                 |
| Ren Shen      | 16.25                     | —                                 |
| Xie Bai       | 16.47                     | —                                 |
| Hou Po        | 17.11                     | —                                 |
| Huo Ma Ren    | 17.25                     | —                                 |
| Niu Bang Zi   | 17.41                     | —                                 |
| Lian Zi       | 18.35                     | —                                 |
| He Huan Pi    | 18.52                     | —                                 |
| Bai Shao Yao  | 18.96                     | —                                 |
| Jie Geng      | 19.09                     | —                                 |
| Zhu Ru        | 19.19                     | —                                 |
| Gua Lou       | 19.22                     | —                                 |
| Fu Zi         | 19.27                     | —                                 |
| Mu Zei        | 19.40                     | —                                 |
| Cang Zhu      | 19.42                     | —                                 |
| Ren Dong Teng | 19.54                     | —                                 |
| Gou Qi Zi     | 20.02                     | —                                 |
| Fu Ling       | 20.44                     | —                                 |
| Sheng Jiang   | 20.68                     | —                                 |
| Dang Gui      | 20.87                     | —                                 |
| Mao Dong Qing | 20.99                     | —                                 |
| Ze Xie        | 21.00                     | —                                 |
| Yi Mu Cao     | 21.51                     | —                                 |
| Cang Er Zi    | 21.56                     | —                                 |
| Zhi Ke        | 22.07                     | —                                 |
| Shen Qu       | 22.75                     | —                                 |
| Mu Gua        | 22.89                     | —                                 |
| Dan Dou Chi   | 23.46                     | —                                 |
| Di Gu Pi      | 23.54                     | —                                 |
| Ji Xue Teng   | 23.90                     | —                                 |
| (Huai) Niu Xi | 23.97                     | —                                 |
| Ban Lan Gen   | 24.25                     | —                                 |

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*continued from previous page*

| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Yan Hu Suo      | 24.48                             | —                                         |
| Yuan Zhi        | 24.54                             | —                                         |
| Guang Huo Xiang | 24.55                             | —                                         |
| Xiang Fu        | 25.01                             | —                                         |
| Xiao Hui Xiang  | 25.27                             | —                                         |
| Dan Shen        | 25.42                             | —                                         |
| Tu Fu Ling      | 26.33                             | —                                         |
| Chai Hu         | 26.85                             | —                                         |
| Gu Sui Bu       | 27.20                             | —                                         |
| Gui Zhi         | 27.42                             | —                                         |
| Fu Pen Zi       | 28.08                             | —                                         |
| Lu Gen          | 28.10                             | —                                         |
| Ye Jiao Teng    | 28.25                             | —                                         |
| Che Qian Zi     | 29.10                             | —                                         |
| Qing Pi         | 29.29                             | —                                         |
| Yu Jin          | 29.59                             | —                                         |
| Yi Yi Ren       | 29.64                             | —                                         |
| Gan Cao         | 29.77                             | —                                         |
| Gou Teng        | 29.79                             | —                                         |
| Zhi Gan Cao     | 30.11                             | —                                         |
| Ci Wu Jia       | 31.08                             | —                                         |
| Dong Gua Zi     | 31.15                             | —                                         |
| Huang Qin       | 31.26                             | —                                         |
| Chuang Mu Xiang | 31.62                             | —                                         |
| Tao Ren         | 31.71                             | —                                         |
| Mang Xiao       | 31.82                             | —                                         |
| Zhu Ling        | 31.95                             | —                                         |
| Fu Xiao Mai     | 32.00                             | —                                         |
| Qiang Huo       | 32.53                             | —                                         |
| Rou Gui         | 33.04                             | —                                         |
| Ban Xia (Jiang) | 33.06                             | —                                         |
| Bai Xian Pi     | 33.09                             | —                                         |
| Ce Bai Ye       | 33.20                             | —                                         |
| Ma Huang        | 33.49                             | —                                         |
| Yin Yang Huo    | 33.63                             | —                                         |
| Zi Hua Di Ding  | 33.71                             | —                                         |
| Zi Su Zi        | 33.79                             | —                                         |
| Gan Jiang       | 34.87                             | —                                         |
| Hong Jing Tian  | 34.92                             | —                                         |
| Xu Duan         | 35.20                             | —                                         |
| She Gan         | 35.25                             | —                                         |
| Chi Shao (Yao)  | 36.38                             | —                                         |
| Long Yan Rou    | 36.41                             | —                                         |
| Huang Qi        | 36.67                             | —                                         |
| Jiang Huang     | 36.98                             | —                                         |
| Du Zhong        | 37.02                             | —                                         |
| Sang Zhi        | 38.89                             | —                                         |
| Huang Lian      | 39.21                             | —                                         |
| (Bai) Dou Kou   | 40.61                             | —                                         |
| Bo He           | 41.15                             | —                                         |
| Hong Hua        | 41.46                             | —                                         |
| Shan Yu Rou     | 41.58                             | —                                         |
| (Fen) Bi Xie    | 41.90                             | —                                         |
| Sang Ye         | 41.92                             | —                                         |
| Fo Shou         | 41.98                             | —                                         |
| Pu Gong Ying    | 42.04                             | —                                         |
| Sha Ren         | 43.80                             | —                                         |
| Ma Huang Gen    | 44.45                             | —                                         |
| Ze Lan          | 44.48                             | —                                         |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Chen Pi        | 44.95                     | —                                 |
| Chuan Lian Zi  | 46.09                     | —                                 |
| Huang Bai      | 47.13                     | —                                 |
| Sha Shen (Bei) | 48.30                     | —                                 |
| Chuan Niu Xi   | 48.33                     | —                                 |
| Qing Hao       | 48.58                     | —                                 |
| E Zhu          | 49.96                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62499     | 62499                  | 0.00                            | 17.48                              |
| 62500     | 62500                  | 0.00                            | 17.41                              |
| 62795     | 62795                  | 0.00                            | 6.71                               |
| 62796     | 62796                  | 0.00                            | 7.43                               |

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 2.4-2022-02

Validated substance/substance group **Lai Fu Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60067-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Lai Fu Zi                 | 2      | 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 |
| PhytoComm | Lai Fu Zi | G209HS278TN1 | 63031     | 40      | from supplier |
| PhytoComm | Lai Fu Zi | G209HS278TN1 | 63032     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Lai Fu Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Lai Fu Zi | G209H1220821 | 62492 <sup>†</sup> | 20      |
| PhytoComm | Lai Fu Zi | G209HS278TN1 | 63031 <sup>†</sup> | 20      |
| PhytoComm | Lai Fu Zi | G209HS278TN1 | 63032 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 160           | 0              | 22 279        |
| <b>Type B</b> | 5              | 73            | 7              | 11 312        |
| <b>Type C</b> | 0              | 0             | 3              | 854           |

The substance/substance group *Lai 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 99.9981 % (> 99.9818 %)  | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 99.9330 % (> 99.9008 %)  | 91.2500 % (> 87.5000 %)  |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bai Shao Yao    | 4.16                      | —                                 |
| He Huan Pi      | 4.42                      | —                                 |
| Di Gu Pi        | 6.20                      | —                                 |
| Bai Zi Ren      | 6.25                      | —                                 |
| Shen Qu         | 6.41                      | —                                 |
| Sheng Jiang     | 6.70                      | —                                 |
| Ci Wu Jia       | 7.16                      | —                                 |
| Zhu Ru          | 7.93                      | —                                 |
| Tao Ren         | 7.94                      | —                                 |
| Ji Li           | 8.53                      | —                                 |
| Gui Zhi         | 8.68                      | —                                 |
| Zhe Bei Mu      | 8.68                      | —                                 |
| Huo Ma Ren      | 9.19                      | —                                 |
| Lian Zi         | 9.20                      | —                                 |
| Mu Zei          | 9.50                      | —                                 |
| Tian Hua Fen    | 10.98                     | —                                 |
| Ye Jiao Teng    | 11.48                     | —                                 |
| Fu Xiao Mai     | 11.55                     | —                                 |
| Ling Zhi        | 11.74                     | —                                 |
| Ze Xie          | 12.29                     | —                                 |
| Gou Teng        | 13.57                     | —                                 |
| Rou Gui         | 13.68                     | —                                 |
| Yi Yi Ren       | 13.83                     | —                                 |
| Pi Pa Ye        | 13.94                     | —                                 |
| Ban Xia (Jiang) | 14.04                     | —                                 |
| Shan Yao        | 14.52                     | —                                 |
| Gu Sui Bu       | 15.05                     | —                                 |
| Ren Dong Teng   | 15.28                     | —                                 |
| Fu Ling         | 15.34                     | —                                 |
| Fo Shou         | 15.37                     | —                                 |
| Bai Xian Pi     | 15.89                     | —                                 |
| Lian Qiao       | 16.64                     | —                                 |
| Lu Gen          | 16.86                     | —                                 |
| Suan Zao Ren    | 17.40                     | —                                 |
| Ji Xue Teng     | 17.74                     | —                                 |
| Jin Yin Hua     | 18.40                     | —                                 |
| Tu Fu Ling      | 19.24                     | —                                 |
| Gua Lou         | 19.35                     | —                                 |
| Sang Zhi        | 19.92                     | —                                 |
| Yu Jin          | 21.20                     | —                                 |
| Cang Zhu        | 21.60                     | —                                 |
| Ma Huang Gen    | 21.91                     | —                                 |
| Fu Zi           | 22.03                     | —                                 |
| Fu Pen Zi       | 22.85                     | —                                 |
| Jie Geng        | 22.92                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Zhi Mu          | 23.35                             | —                                         |
| Dang Gui        | 23.41                             | —                                         |
| San Qi          | 23.57                             | —                                         |
| Chuan Lian Zi   | 23.73                             | —                                         |
| Ce Bai Ye       | 24.37                             | —                                         |
| Zhu Ling        | 24.52                             | —                                         |
| Yan Hu Suo      | 24.86                             | —                                         |
| (Fen) Bi Xie    | 24.95                             | —                                         |
| Bai He          | 25.36                             | —                                         |
| Jiao Gu Lan     | 25.42                             | —                                         |
| Dan Shen        | 25.59                             | —                                         |
| Ban Lan Gen     | 25.91                             | —                                         |
| Bai Zhu         | 26.05                             | —                                         |
| Dan Dou Chi     | 26.88                             | —                                         |
| She Gan         | 27.29                             | —                                         |
| Hou Po          | 27.42                             | —                                         |
| Ren Shen        | 27.60                             | —                                         |
| Zhi Ke          | 27.62                             | —                                         |
| Sha Shen (Bei)  | 28.04                             | —                                         |
| Mao Dong Qing   | 28.06                             | —                                         |
| Mang Xiao       | 28.46                             | —                                         |
| Che Qian Zi     | 29.13                             | —                                         |
| Fu Shen         | 29.59                             | —                                         |
| Yin Yang Huo    | 30.06                             | —                                         |
| Chai Hu         | 30.09                             | —                                         |
| Guang Huo Xiang | 30.74                             | —                                         |
| Mu Gua          | 32.01                             | —                                         |
| Yuan Zhi        | 32.57                             | —                                         |
| Cang Er Zi      | 32.68                             | —                                         |
| Ma Huang        | 32.80                             | —                                         |
| Ku Shen         | 32.85                             | —                                         |
| Gou Qi Zi       | 32.89                             | —                                         |
| Huang Qin       | 32.93                             | —                                         |
| E Zhu           | 33.97                             | —                                         |
| Hong Jing Tian  | 35.38                             | —                                         |
| Gan Cao         | 36.38                             | —                                         |
| Qiang Huo       | 36.43                             | —                                         |
| Long Yan Rou    | 38.71                             | —                                         |
| Chuang Mu Xiang | 39.08                             | —                                         |
| Gan Jiang       | 39.23                             | —                                         |
| Zi Su Zi        | 39.34                             | —                                         |
| Xie Bai         | 41.72                             | —                                         |
| Jiang Huang     | 42.05                             | —                                         |
| Huang Qi        | 43.16                             | —                                         |
| Huang Lian      | 43.34                             | —                                         |
| Qing Pi         | 45.10                             | —                                         |
| Zi Hua Di Ding  | 45.17                             | —                                         |
| Jing Jie        | 46.00                             | —                                         |
| Da Zao          | 46.20                             | —                                         |
| Chuan Mu Tong   | 47.49                             | —                                         |
| Long Dan (Cao)  | 48.09                             | —                                         |
| Qin Jiao        | 48.64                             | —                                         |
| Du Zhong        | 49.10                             | —                                         |
| Chi Shao (Yao)  | 49.26                             | —                                         |
| Sha Ren         | 49.30                             | —                                         |
| Zhi Gan Cao     | 49.44                             | —                                         |
| Ban Zhi Lian    | 49.55                             | —                                         |
| Bo He           | 50.49                             | —                                         |

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                         | 19.92                           |
| 62492     | 62492               | 0.00                         | 19.92                           |
| 63031     | 63031               | 0.00                         | 4.42                            |
| 63032     | 63032               | 0.00                         | 4.16                            |

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 2.4-2022-02

Validated substance/substance group **Lian Qiao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60146-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Lian Qiao                 | 3      | 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 |
| PhytoComm | Lian Qiao | G105H1132021 | 63005     | 40      | from supplier |
| PhytoComm | Lian Qiao | G105H1132021 | 63006     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Lian Qiao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Lian Qiao | G105H1132821 | 62338 <sup>†</sup> | 20      |
| PhytoComm | Lian Qiao | G105HS252RW1 | 62685 <sup>†</sup> | 20      |
| PhytoComm | Lian Qiao | G105HS252RW1 | 62686 <sup>†</sup> | 20      |
| PhytoComm | Lian Qiao | G105H1132021 | 63005 <sup>†</sup> | 20      |
| PhytoComm | Lian Qiao | G105H1132021 | 63006 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G105H1132321 | 1       |
| Phytocomm | Lian Qiao | G105H1132521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 2              | 120           | 0              | 11 275        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 99.9851 % (> 99.9529 %)  | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8280 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ji Li           | 5.15                      | —                                 |
| Ling Zhi        | 6.17                      | —                                 |
| Shan Yao        | 6.46                      | —                                 |
| Zhe Bei Mu      | 8.09                      | —                                 |
| Bai Zi Ren      | 9.45                      | —                                 |
| Lian Zi         | 9.86                      | —                                 |
| Pi Pa Ye        | 10.76                     | —                                 |
| Suan Zao Ren    | 10.96                     | —                                 |
| Niu Bang Zi     | 11.17                     | —                                 |
| Jiao Gu Lan     | 11.60                     | —                                 |
| Shen Qu         | 12.75                     | —                                 |
| Fu Zi           | 13.23                     | —                                 |
| Hou Po          | 13.45                     | —                                 |
| Mao Dong Qing   | 13.61                     | —                                 |
| Tian Hua Fen    | 13.64                     | —                                 |
| Ze Xie          | 14.05                     | —                                 |
| He Huan Pi      | 14.29                     | —                                 |
| Fu Ling         | 14.88                     | —                                 |
| Jin Yin Hua     | 15.08                     | —                                 |
| Guang Huo Xiang | 15.48                     | —                                 |
| Huo Ma Ren      | 15.82                     | —                                 |
| San Qi          | 15.95                     | —                                 |
| Ku Shen         | 16.31                     | —                                 |
| Ren Dong Teng   | 16.33                     | —                                 |
| Bai Shao Yao    | 16.66                     | —                                 |
| Dan Shen        | 16.77                     | —                                 |
| Chai Hu         | 16.78                     | —                                 |
| Mu Zei          | 17.10                     | —                                 |
| Gu Sui Bu       | 17.61                     | —                                 |
| Dan Dou Chi     | 17.77                     | —                                 |
| Sheng Jiang     | 17.90                     | —                                 |
| Gua Lou         | 18.55                     | —                                 |
| Yu Jin          | 19.26                     | —                                 |
| Tu Fu Ling      | 19.76                     | —                                 |
| Xie Bai         | 19.81                     | —                                 |
| Fu Pen Zi       | 20.26                     | —                                 |
| (Huai) Niu Xi   | 20.81                     | —                                 |
| She Gan         | 21.02                     | —                                 |
| Yan Hu Suo      | 21.10                     | —                                 |
| Bai Xian Pi     | 21.55                     | —                                 |
| Zhu Ru          | 21.81                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Di Gu Pi        | 21.86                             | —                                         |
| Che Qian Zi     | 22.20                             | —                                         |
| Zi Su Zi        | 22.27                             | —                                         |
| Ban Lan Gen     | 22.37                             | —                                         |
| Cang Zhu        | 22.58                             | —                                         |
| Ce Bai Ye       | 22.99                             | —                                         |
| Gui Zhi         | 23.34                             | —                                         |
| Zhu Ling        | 23.47                             | —                                         |
| Zhi Gan Cao     | 23.71                             | —                                         |
| Lu Gen          | 23.89                             | —                                         |
| Gan Cao         | 23.94                             | —                                         |
| Ren Shen        | 24.90                             | —                                         |
| Lai Fu Zi       | 24.92                             | —                                         |
| Gou Teng        | 25.15                             | —                                         |
| Ji Xue Teng     | 25.25                             | —                                         |
| Qiang Huo       | 25.54                             | —                                         |
| Qing Pi         | 25.96                             | —                                         |
| Ye Jiao Teng    | 26.01                             | —                                         |
| Zhi Ke          | 26.22                             | —                                         |
| Yin Yang Huo    | 26.30                             | —                                         |
| Hong Jing Tian  | 27.10                             | —                                         |
| Chi Shao (Yao)  | 27.12                             | —                                         |
| Xiang Fu        | 27.12                             | —                                         |
| Jie Geng        | 27.14                             | —                                         |
| Dang Gui        | 27.29                             | —                                         |
| Yuan Zhi        | 27.62                             | —                                         |
| Xiao Hui Xiang  | 28.01                             | —                                         |
| Tao Ren         | 28.27                             | —                                         |
| Chuang Mu Xiang | 29.18                             | —                                         |
| Yi Yi Ren       | 29.52                             | —                                         |
| Du Zhong        | 29.53                             | —                                         |
| Mang Xiao       | 29.86                             | —                                         |
| Rou Gui         | 29.87                             | —                                         |
| Ci Wu Jia       | 29.97                             | —                                         |
| Yi Mu Cao       | 30.29                             | —                                         |
| Fu Xiao Mai     | 30.67                             | —                                         |
| Zi Hua Di Ding  | 31.11                             | —                                         |
| Zhi Mu          | 31.26                             | —                                         |
| Gou Qi Zi       | 31.90                             | —                                         |
| Ban Xia (Jiang) | 32.83                             | —                                         |
| (Fen) Bi Xie    | 33.09                             | —                                         |
| Ma Huang        | 33.11                             | —                                         |
| Cang Er Zi      | 33.19                             | —                                         |
| Bo He           | 33.55                             | —                                         |
| Ma Huang Gen    | 34.02                             | —                                         |
| Mu Gua          | 34.78                             | —                                         |
| Huang Qin       | 35.25                             | —                                         |
| Huang Lian      | 35.28                             | —                                         |
| Chuan Lian Zi   | 36.85                             | —                                         |
| Huang Bai       | 37.23                             | —                                         |
| Du Huo          | 37.32                             | —                                         |
| Jing Jie        | 37.79                             | —                                         |
| Sang Zhi        | 37.81                             | —                                         |
| Sha Ren         | 38.00                             | —                                         |
| Huang Qi        | 38.08                             | —                                         |
| Bai Zhi         | 38.31                             | —                                         |
| (Shi) Chang Pu  | 38.43                             | —                                         |
| Ju Hua          | 39.83                             | —                                         |
| Qing Hao        | 40.21                             | —                                         |

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| Substanz      | Distance in<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| Long Yan Rou  | 40.29                     | —                                 |
| Hong Hua      | 40.70                     | —                                 |
| Fo Shou       | 41.43                     | —                                 |
| Shan Yu Rou   | 42.01                     | —                                 |
| Gan Jiang     | 42.10                     | —                                 |
| Qin Jiao      | 43.51                     | —                                 |
| Wu Yao        | 43.53                     | —                                 |
| Jiang Huang   | 43.98                     | —                                 |
| Pu Gong Ying  | 44.27                     | —                                 |
| Fang Feng     | 44.39                     | —                                 |
| Dong Gua Zi   | 44.52                     | —                                 |
| Chen Pi       | 45.35                     | —                                 |
| Sang Ye       | 45.38                     | —                                 |
| (Bai) Dou Kou | 45.65                     | —                                 |
| Chuan Niu Xi  | 47.01                     | —                                 |
| Ze Lan        | 47.39                     | —                                 |
| Xu Duan       | 47.59                     | —                                 |
| Bai Jiang Cao | 47.77                     | —                                 |
| Wu Wei Zi     | 49.33                     | —                                 |
| Fu Shen       | 49.44                     | —                                 |
| Chuan Mu Tong | 49.52                     | —                                 |
| E Zhu         | 49.87                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62337     | 62337                  | 0.00                            | 18.25                              |
| 62338     | 62338                  | 0.00                            | 18.06                              |
| 62685     | 62685                  | 0.00                            | 5.71                               |
| 62686     | 62686                  | 0.00                            | 5.15                               |
| 63005     | 63005                  | 0.00                            | 11.29                              |
| 63006     | 63006                  | 0.00                            | 11.17                              |

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 2.4-2022-02

Validated substance/substance group **Lian Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60248-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Lian Zi   | G171HS312SK1 | 62568 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Suan Zao Ren    | 6.36                      | —                                 |
| Ling Zhi        | 7.24                      | —                                 |
| Ji Li           | 7.63                      | —                                 |
| Shen Qu         | 9.46                      | —                                 |
| Huo Ma Ren      | 10.03                     | —                                 |
| Ren Dong Teng   | 10.82                     | —                                 |
| Fu Ling         | 10.89                     | —                                 |
| Bai Shao Yao    | 11.14                     | —                                 |
| Tu Fu Ling      | 11.23                     | —                                 |
| He Huan Pi      | 11.32                     | —                                 |
| She Gan         | 11.78                     | —                                 |
| Bai Xian Pi     | 12.49                     | —                                 |
| Bai Zi Ren      | 12.81                     | —                                 |
| Sheng Jiang     | 12.85                     | —                                 |
| Zhe Bei Mu      | 13.32                     | —                                 |
| Tao Ren         | 13.95                     | —                                 |
| Lian Qiao       | 14.77                     | —                                 |
| Shan Yao        | 14.80                     | —                                 |
| Lu Gen          | 14.81                     | —                                 |
| Ce Bai Ye       | 14.82                     | —                                 |
| Gu Sui Bu       | 14.96                     | —                                 |
| Gui Zhi         | 15.08                     | —                                 |
| Ze Xie          | 15.17                     | —                                 |
| Mu Zei          | 15.42                     | —                                 |
| Dan Dou Chi     | 15.50                     | —                                 |
| Chai Hu         | 15.51                     | —                                 |
| Pi Pa Ye        | 15.51                     | —                                 |
| Ye Jiao Teng    | 16.16                     | —                                 |
| Tian Hua Fen    | 16.56                     | —                                 |
| Mao Dong Qing   | 16.94                     | —                                 |
| Guang Huo Xiang | 16.98                     | —                                 |
| Ci Wu Jia       | 17.13                     | —                                 |
| Yu Jin          | 17.15                     | —                                 |
| Gou Teng        | 17.67                     | —                                 |
| Fu Zi           | 17.76                     | —                                 |
| Di Gu Pi        | 18.04                     | —                                 |
| Rou Gui         | 18.54                     | —                                 |
| Zhu Ru          | 18.81                     | —                                 |
| (Fen) Bi Xie    | 18.93                     | —                                 |
| Zhu Ling        | 19.94                     | —                                 |
| Hou Po          | 20.00                     | —                                 |
| Yi Yi Ren       | 20.03                     | —                                 |
| Jiao Gu Lan     | 20.05                     | —                                 |
| Dan Shen        | 20.29                     | —                                 |
| Fu Pen Zi       | 20.47                     | —                                 |
| Jin Yin Hua     | 21.10                     | —                                 |
| Fu Xiao Mai     | 21.41                     | —                                 |
| Ban Lan Gen     | 21.83                     | —                                 |
| Hong Jing Tian  | 21.87                     | —                                 |
| Ji Xue Teng     | 21.89                     | —                                 |
| San Qi          | 21.96                     | —                                 |
| Gua Lou         | 22.34                     | —                                 |
| Che Qian Zi     | 22.43                     | —                                 |
| Cang Zhu        | 22.66                     | —                                 |
| Lai Fu Zi       | 22.68                     | —                                 |
| Ma Huang Gen    | 23.72                     | —                                 |
| Fo Shou         | 23.87                     | —                                 |
| Yin Yang Huo    | 24.11                     | —                                 |
| Gan Cao         | 24.85                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ban Xia (Jiang) | 25.47                     | —                                 |
| Qiang Huo       | 26.61                     | —                                 |
| Chuang Mu Xiang | 27.57                     | —                                 |
| Yan Hu Suo      | 27.73                     | —                                 |
| Zhi Ke          | 28.37                     | —                                 |
| Jing Jie        | 29.13                     | —                                 |
| Jie Geng        | 29.18                     | —                                 |
| Ma Huang        | 29.60                     | —                                 |
| Zi Hua Di Ding  | 31.29                     | —                                 |
| Dang Gui        | 31.60                     | —                                 |
| Ren Shen        | 31.62                     | —                                 |
| Xie Bai         | 31.70                     | —                                 |
| Zhi Gan Cao     | 33.17                     | —                                 |
| Mang Xiao       | 33.78                     | —                                 |
| Bo He           | 35.37                     | —                                 |
| Qing Pi         | 35.43                     | —                                 |
| Fu Shen         | 36.30                     | —                                 |
| Sha Ren         | 37.33                     | —                                 |
| Du Zhong        | 38.06                     | —                                 |
| Ku Shen         | 38.09                     | —                                 |
| Huang Lian      | 38.39                     | —                                 |
| Sang Zhi        | 38.84                     | —                                 |
| Zhi Mu          | 39.03                     | —                                 |
| Huang Bai       | 39.04                     | —                                 |
| Huang Qin       | 39.15                     | —                                 |
| Mu Gua          | 39.19                     | —                                 |
| Long Yan Rou    | 40.04                     | —                                 |
| Yuan Zhi        | 41.10                     | —                                 |
| Gou Qi Zi       | 42.91                     | —                                 |
| Chi Shao (Yao)  | 44.63                     | —                                 |
| Cang Er Zi      | 48.72                     | —                                 |
| Bai Zhu         | 48.77                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62567     | 62567                  | 0.00                            | 6.36                               |
| 62568     | 62568                  | 0.00                            | 7.24                               |

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

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Ling Zhi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60187-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ling Zhi                  | 2      | 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 |
| PhytoComm | Ling Zhi  | G109HS355TG1 | 62941     | 40      | from supplier |
| PhytoComm | Ling Zhi  | G109HS355TG1 | 62942     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Ling Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Ling Zhi  | G109HS355RP1 | 62454 <sup>†</sup> | 20      |
| PhytoComm | Ling Zhi  | G109HS355TG1 | 62941 <sup>†</sup> | 20      |
| PhytoComm | Ling Zhi  | G109HS355TG1 | 62942 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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  | G109F-B2405221 | 1       |
| Phytocomm | Ling Zhi  | g109fb2405321  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 159           | 1              | 22 279        |
| <b>Type B</b> | 5              | 79            | 1              | 11 312        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Ling 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9926 % (> 99.9762 %)  | 99.3750 % (> 97.5000 %) |
| <b>Type B</b> | 99.9554 % (> 99.9232 %)  | 98.7500 % (> 95.0000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ji Li           | 4.84                      | —                                 |
| Ren Dong Teng   | 5.24                      | —                                 |
| Lian Zi         | 5.82                      | —                                 |
| Ce Bai Ye       | 5.93                      | —                                 |
| Bai Xian Pi     | 7.09                      | —                                 |
| Yu Jin          | 7.17                      | —                                 |
| Dan Dou Chi     | 7.22                      | —                                 |
| Chai Hu         | 7.59                      | —                                 |
| Hou Po          | 8.09                      | —                                 |
| He Huan Pi      | 8.18                      | —                                 |
| Shen Qu         | 8.54                      | —                                 |
| Lian Qiao       | 9.51                      | —                                 |
| Bai Zi Ren      | 9.89                      | —                                 |
| Mao Dong Qing   | 9.94                      | —                                 |
| Zhe Bei Mu      | 10.17                     | —                                 |
| Huo Ma Ren      | 10.43                     | —                                 |
| Bai Shao Yao    | 10.91                     | —                                 |
| Che Qian Zi     | 11.33                     | —                                 |
| Zhu Ling        | 11.53                     | —                                 |
| Guang Huo Xiang | 11.63                     | —                                 |
| Sheng Jiang     | 11.70                     | —                                 |
| Tu Fu Ling      | 11.82                     | —                                 |
| Tian Hua Fen    | 11.86                     | —                                 |
| Ze Xie          | 12.19                     | —                                 |
| Gu Sui Bu       | 12.32                     | —                                 |
| Fu Zi           | 12.87                     | —                                 |
| Fu Ling         | 12.98                     | —                                 |
| She Gan         | 13.28                     | —                                 |
| Yin Yang Huo    | 13.66                     | —                                 |
| Shan Yao        | 13.74                     | —                                 |
| Mu Zei          | 13.99                     | —                                 |
| Ye Jiao Teng    | 14.17                     | —                                 |
| Suan Zao Ren    | 14.33                     | —                                 |
| Fu Pen Zi       | 14.62                     | —                                 |
| Pi Pa Ye        | 15.31                     | —                                 |
| Gui Zhi         | 15.46                     | —                                 |
| Zhu Ru          | 15.71                     | —                                 |
| Di Gu Pi        | 16.06                     | —                                 |
| Dan Shen        | 16.19                     | —                                 |
| Yan Hu Suo      | 16.20                     | —                                 |
| Jiao Gu Lan     | 16.88                     | —                                 |
| Qiang Huo       | 17.11                     | —                                 |
| (Fen) Bi Xie    | 17.33                     | —                                 |
| Gou Teng        | 17.43                     | —                                 |
| Lai Fu Zi       | 17.87                     | —                                 |

*continued on the next page*

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Lu Gen          | 18.16                     | —                                 |
| Tao Ren         | 18.46                     | —                                 |
| Fu Xiao Mai     | 18.58                     | —                                 |
| Rou Gui         | 19.53                     | —                                 |
| Yi Yi Ren       | 19.54                     | —                                 |
| Jing Jie        | 19.58                     | —                                 |
| Ji Xue Teng     | 19.98                     | —                                 |
| Gan Cao         | 20.04                     | —                                 |
| Jin Yin Hua     | 21.00                     | —                                 |
| Zi Hua Di Ding  | 21.67                     | —                                 |
| San Qi          | 21.78                     | —                                 |
| Ci Wu Jia       | 21.79                     | —                                 |
| Du Zhong        | 21.94                     | —                                 |
| Hong Jing Tian  | 22.14                     | —                                 |
| Ma Huang Gen    | 22.33                     | —                                 |
| Qing Pi         | 22.67                     | —                                 |
| Cang Zhu        | 24.35                     | —                                 |
| Ban Lan Gen     | 24.62                     | —                                 |
| Ban Xia (Jiang) | 24.88                     | —                                 |
| Gua Lou         | 25.35                     | —                                 |
| Ma Huang        | 26.68                     | —                                 |
| Sha Ren         | 26.69                     | —                                 |
| Zhi Ke          | 26.97                     | —                                 |
| Zhi Gan Cao     | 27.10                     | —                                 |
| Bo He           | 27.18                     | —                                 |
| Huang Bai       | 27.73                     | —                                 |
| Ren Shen        | 28.42                     | —                                 |
| Ku Shen         | 29.41                     | —                                 |
| Chuang Mu Xiang | 29.68                     | —                                 |
| Qing Hao        | 30.03                     | —                                 |
| Jie Geng        | 30.71                     | —                                 |
| Huang Lian      | 30.79                     | —                                 |
| Fo Shou         | 31.37                     | —                                 |
| Dang Gui        | 31.57                     | —                                 |
| Xie Bai         | 32.43                     | —                                 |
| Mang Xiao       | 33.84                     | —                                 |
| Zhi Mu          | 37.45                     | —                                 |
| Huang Qin       | 38.24                     | —                                 |
| Fu Shen         | 39.38                     | —                                 |
| Bai Jiang Cao   | 39.60                     | —                                 |
| Gou Qi Zi       | 39.80                     | —                                 |
| Mu Gua          | 40.64                     | —                                 |
| Sang Zhi        | 41.08                     | —                                 |
| Yuan Zhi        | 42.90                     | —                                 |
| Chi Shao (Yao)  | 43.64                     | —                                 |
| Cang Er Zi      | 43.98                     | —                                 |
| Long Yan Rou    | 46.57                     | —                                 |
| Hong Hua        | 49.88                     | —                                 |

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                         | 7.17                            |
| 62454     | 62454               | 0.00                         | 5.24                            |
| 62941     | 62941               | 0.00                         | 5.12                            |
| 62942     | 62942               | 0.00                         | 4.84                            |

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 2.4-2022-02

Validated substance/substance group **Long Dan (Cao)**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60227-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Long Dan (Cao)            | 2      | 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 |
| PhytoComm | Long Dan (Cao) | G112H1705921 | 62871     | 40      | from supplier |
| PhytoComm | Long Dan (Cao) | G112H1705921 | 62872     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Dan (Cao)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Long Dan (Cao) | G112H1705821 | 62532 <sup>†</sup> | 20      |
| PhytoComm | Long Dan (Cao) | G112H1705921 | 62871 <sup>†</sup> | 20      |
| PhytoComm | Long Dan (Cao) | G112H1705921 | 62872 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 1              | 3             | 1              | 852           |

The substance/substance group *Long Dan (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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 99.9612 % (> 99.3747 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Qin Jiao       | 8.39                      | —                                 |
| Huang Qi       | 14.19                     | —                                 |
| Da Zao         | 17.02                     | —                                 |
| Bai He         | 18.14                     | —                                 |
| Bai Zhu        | 18.83                     | —                                 |
| Jie Geng       | 18.87                     | —                                 |
| Dang Gui       | 19.76                     | —                                 |
| Zhi Gan Cao    | 20.67                     | —                                 |
| Mang Xiao      | 21.04                     | —                                 |
| Chuan Mu Tong  | 21.81                     | —                                 |
| Sang Zhi       | 22.80                     | —                                 |
| Lai Fu Zi      | 23.30                     | —                                 |
| Chuan Lian Zi  | 23.36                     | —                                 |
| Sha Shen (Bei) | 24.19                     | —                                 |
| E Zhu          | 24.77                     | —                                 |
| Chuan Niu Xi   | 26.25                     | —                                 |
| Tian Hua Fen   | 26.29                     | —                                 |
| Mu Gua         | 27.08                     | —                                 |
| Mi Huan Jun    | 27.10                     | —                                 |
| Di Gu Pi       | 27.31                     | —                                 |
| (Huai) Niu Xi  | 28.12                     | —                                 |
| Chi Shao (Yao) | 29.85                     | —                                 |
| Zi Su Zi       | 30.30                     | —                                 |
| Bing Lang      | 30.97                     | —                                 |
| Bai Zhi        | 33.19                     | —                                 |
| Yuan Zhi       | 34.80                     | —                                 |
| Jiang Huang    | 35.02                     | —                                 |
| Gan Jiang      | 36.63                     | —                                 |
| He Huan Pi     | 37.42                     | —                                 |
| Sha Ren        | 38.62                     | —                                 |
| Chen Pi        | 39.78                     | —                                 |
| Mu Dan Pi      | 40.57                     | —                                 |
| Shan Yao       | 42.44                     | —                                 |
| Lian Qiao      | 42.68                     | —                                 |
| Ban Zhi Lian   | 44.10                     | —                                 |
| Ba Ji Tian     | 44.53                     | —                                 |
| (Shi) Chang Pu | 45.25                     | —                                 |
| Cang Er Zi     | 45.47                     | —                                 |
| Tu Fu Ling     | 46.35                     | —                                 |
| Lian Zi        | 49.33                     | —                                 |
| Bai Shao Yao   | 49.73                     | —                                 |
| (Bai) Dou Kou  | 49.99                     | —                                 |
| Rou Gui        | 50.28                     | —                                 |



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                         | 18.01                           |
| 62532     | 62532               | 0.00                         | 17.02                           |
| 62871     | 62871               | 0.00                         | 8.39                            |
| 62872     | 62872               | 0.00                         | 9.11                            |

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 2.4-2022-02

Validated substance/substance group **Long Yan Rou**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60463-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Long Yan Rou              | 1      | 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 | G144HS324SQ1 | 62727     | 40      | from supplier |
| PhytoComm | Long Yan Rou | G144HS324SQ1 | 62728     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Yan Rou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 | G144HS324SQ1 | 62727 <sup>†</sup> | 20      |
| PhytoComm | Long Yan Rou | G144HS324SQ1 | 62728 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Cang Zhu        | 11.96                     | —                                 |
| Dang Gui        | 12.31                     | —                                 |
| Ren Shen        | 13.52                     | —                                 |
| Jie Geng        | 14.88                     | —                                 |
| Fo Shou         | 14.96                     | —                                 |
| Bai Shao Yao    | 17.44                     | —                                 |
| Ye Jiao Teng    | 17.64                     | —                                 |
| Zhe Bei Mu      | 18.62                     | —                                 |
| Jin Yin Hua     | 18.74                     | —                                 |
| Di Gu Pi        | 18.84                     | —                                 |
| Ma Huang        | 19.78                     | —                                 |
| Ze Xie          | 19.79                     | —                                 |
| Mu Gua          | 19.90                     | —                                 |
| Gou Qi Zi       | 20.16                     | —                                 |
| Tao Ren         | 20.69                     | —                                 |
| Mu Zei          | 20.81                     | —                                 |
| Zhi Mu          | 20.91                     | —                                 |
| Chuang Mu Xiang | 21.04                     | —                                 |
| Hong Jing Tian  | 21.15                     | —                                 |
| San Qi          | 21.79                     | —                                 |
| Ban Lan Gen     | 22.19                     | —                                 |
| Tian Hua Fen    | 22.32                     | —                                 |
| Shen Qu         | 22.84                     | —                                 |
| Ren Dong Teng   | 23.16                     | —                                 |
| Lu Gen          | 24.08                     | —                                 |
| Ban Xia (Jiang) | 24.12                     | —                                 |
| Ling Zhi        | 24.28                     | —                                 |
| Dan Dou Chi     | 24.35                     | —                                 |
| Zhi Ke          | 24.48                     | —                                 |
| Fu Pen Zi       | 24.48                     | —                                 |
| He Huan Pi      | 24.58                     | —                                 |
| Rou Gui         | 24.59                     | —                                 |
| Pi Pa Ye        | 24.60                     | —                                 |
| Tu Fu Ling      | 24.76                     | —                                 |
| Gu Sui Bu       | 24.89                     | —                                 |
| Suan Zao Ren    | 25.03                     | —                                 |
| Gou Teng        | 25.15                     | —                                 |
| Lian Zi         | 25.19                     | —                                 |
| Xie Bai         | 25.84                     | —                                 |
| Gua Lou         | 25.96                     | —                                 |
| Shan Yao        | 26.39                     | —                                 |
| Ci Wu Jia       | 26.76                     | —                                 |
| Lian Qiao       | 26.85                     | —                                 |
| Gui Zhi         | 26.98                     | —                                 |
| Dan Shen        | 27.09                     | —                                 |
| Huang Qin       | 27.11                     | —                                 |
| Gan Cao         | 27.55                     | —                                 |
| Bai Zi Ren      | 27.78                     | —                                 |
| Bai Xian Pi     | 27.96                     | —                                 |
| Yuan Zhi        | 28.46                     | —                                 |
| Yin Yang Huo    | 28.61                     | —                                 |
| Ku Shen         | 28.66                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ji Li           | 28.88                     | —                                 |
| Fu Xiao Mai     | 28.93                     | —                                 |
| Lai Fu Zi       | 29.09                     | —                                 |
| Jiao Gu Lan     | 29.29                     | —                                 |
| Ji Xue Teng     | 29.33                     | —                                 |
| Mang Xiao       | 30.05                     | —                                 |
| Sheng Jiang     | 30.36                     | —                                 |
| Fu Ling         | 30.67                     | —                                 |
| Sang Zhi        | 30.89                     | —                                 |
| Hou Po          | 30.91                     | —                                 |
| Huo Ma Ren      | 30.91                     | —                                 |
| Fu Zi           | 30.96                     | —                                 |
| Hong Hua        | 31.88                     | —                                 |
| She Gan         | 32.17                     | —                                 |
| Ma Huang Gen    | 32.82                     | —                                 |
| Chi Shao (Yao)  | 33.11                     | —                                 |
| (Fen) Bi Xie    | 33.97                     | —                                 |
| Zi Hua Di Ding  | 34.31                     | —                                 |
| Chai Hu         | 34.45                     | —                                 |
| Chuan Lian Zi   | 35.13                     | —                                 |
| Zhu Ru          | 35.30                     | —                                 |
| Mao Dong Qing   | 35.72                     | —                                 |
| Yan Hu Suo      | 35.83                     | —                                 |
| Fu Shen         | 36.44                     | —                                 |
| Guang Huo Xiang | 37.26                     | —                                 |
| Yu Jin          | 37.30                     | —                                 |
| Huang Qi        | 37.31                     | —                                 |
| Ce Bai Ye       | 37.77                     | —                                 |
| Zhi Gan Cao     | 37.80                     | —                                 |
| Che Qian Zi     | 38.02                     | —                                 |
| Qiang Huo       | 38.66                     | —                                 |
| Jing Jie        | 39.15                     | —                                 |
| Yi Yi Ren       | 41.05                     | —                                 |
| Bo He           | 42.33                     | —                                 |
| Zhu Ling        | 43.17                     | —                                 |
| Sha Ren         | 44.41                     | —                                 |
| Huang Lian      | 44.52                     | —                                 |
| Bai Zhu         | 46.13                     | —                                 |
| Huang Bai       | 46.45                     | —                                 |
| Bai He          | 49.51                     | —                                 |
| Qing Pi         | 49.82                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62727     | 62727               | 0.00                         | 11.96                           |
| 62728     | 62728               | 0.00                         | 12.83                           |

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 2.4-2022-02

Validated substance/substance group **Lu Gen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10004528-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Lu Gen; Phragmitis communis rhizoma

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Lu Gen                    | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Lu 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 *Lu Gen*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Lu Gen    | G189HS348TG1 | 62839     | 40      | from supplier |
| PhytoComm | Lu Gen    | G189HS348TG1 | 62840     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Lu Gen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Lu 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 | Lu Gen    | G189HS348TG1 | 62839 <sup>†</sup> | 20      |
| PhytoComm | Lu Gen    | G189HS348TG1 | 62840 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Lu Gen*.
- 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 | Lu Gen    | G189H2014221 | 1       |
| Phytocomm | Lu Gen    | G189H2014521 | 1       |
| PhytoComm | Lu Gen    | G189H2014521 | 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 *Lu 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 *Lu 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 4              | 79            | 1              | 22 356        |
| <b>Type B</b> | 2              | 37            | 3              | 11 355        |
| <b>Type C</b> | 0              | 0             | 4              | 853           |

The substance/substance group *Lu 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9851 % (> 99.9688 %)  | 98.7500 % (> 95.0000 %) |
| <b>Type B</b> | 99.9851 % (> 99.9531 %)  | 92.5000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lu 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ji Xue Teng     | 3.54                      | —                                 |
| He Huan Pi      | 5.86                      | —                                 |
| Ren Dong Teng   | 6.74                      | —                                 |
| Ye Jiao Teng    | 6.86                      | —                                 |
| Mu Zei          | 6.92                      | —                                 |
| (Fen) Bi Xie    | 7.24                      | —                                 |
| Gou Teng        | 7.35                      | —                                 |
| Gui Zhi         | 7.72                      | —                                 |
| Rou Gui         | 7.90                      | —                                 |
| Huo Ma Ren      | 8.02                      | —                                 |
| Bai Shao Yao    | 9.00                      | —                                 |
| Gu Sui Bu       | 9.59                      | —                                 |
| Ma Huang Gen    | 9.60                      | —                                 |
| Fo Shou         | 9.65                      | —                                 |
| She Gan         | 9.70                      | —                                 |
| Bai Xian Pi     | 10.47                     | —                                 |
| Fu Ling         | 10.67                     | —                                 |
| Tao Ren         | 11.30                     | —                                 |
| Sheng Jiang     | 13.52                     | —                                 |
| Suan Zao Ren    | 13.64                     | —                                 |
| Ling Zhi        | 13.68                     | —                                 |
| Shen Qu         | 13.72                     | —                                 |
| Lian Zi         | 13.96                     | —                                 |
| Ban Xia (Jiang) | 14.08                     | —                                 |
| Ci Wu Jia       | 14.16                     | —                                 |
| Tu Fu Ling      | 14.92                     | —                                 |
| Dan Dou Chi     | 15.03                     | —                                 |
| Yi Yi Ren       | 15.27                     | —                                 |
| Zhu Ling        | 16.26                     | —                                 |
| Zhe Bei Mu      | 16.42                     | —                                 |
| Dan Shen        | 16.64                     | —                                 |
| Lai Fu Zi       | 17.00                     | —                                 |
| Ma Huang        | 18.59                     | —                                 |
| Ji Li           | 18.61                     | —                                 |
| Yu Jin          | 18.65                     | —                                 |
| Ce Bai Ye       | 18.75                     | —                                 |
| Fu Xiao Mai     | 18.77                     | —                                 |
| Yin Yang Huo    | 18.99                     | —                                 |
| Guang Huo Xiang | 19.05                     | —                                 |
| Jin Yin Hua     | 19.17                     | —                                 |
| Di Gu Pi        | 19.25                     | —                                 |
| Yan Hu Suo      | 19.48                     | —                                 |
| Ze Xie          | 19.64                     | —                                 |
| Tian Hua Fen    | 20.43                     | —                                 |
| Lian Qiao       | 20.46                     | —                                 |
| Bai Zi Ren      | 20.63                     | —                                 |
| Fu Shen         | 21.33                     | —                                 |
| Pi Pa Ye        | 21.63                     | —                                 |
| Hong Jing Tian  | 22.06                     | —                                 |
| Fu Pen Zi       | 22.23                     | —                                 |
| Fu Zi           | 23.24                     | —                                 |
| Zhu Ru          | 23.67                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Shan Yao        | 23.79                     | —                                 |
| Mao Dong Qing   | 24.19                     | —                                 |
| Ban Lan Gen     | 24.29                     | —                                 |
| Chai Hu         | 25.67                     | —                                 |
| Hou Po          | 25.77                     | —                                 |
| Gan Cao         | 25.78                     | —                                 |
| Jiao Gu Lan     | 26.18                     | —                                 |
| Cang Zhu        | 27.12                     | —                                 |
| Zhi Ke          | 27.28                     | —                                 |
| Qiang Huo       | 28.49                     | —                                 |
| Jing Jie        | 28.50                     | —                                 |
| Gua Lou         | 28.68                     | —                                 |
| Ren Shen        | 28.92                     | —                                 |
| Dang Gui        | 30.05                     | —                                 |
| Jie Geng        | 30.12                     | —                                 |
| Mang Xiao       | 31.76                     | —                                 |
| Che Qian Zi     | 32.14                     | —                                 |
| Zi Hua Di Ding  | 32.50                     | —                                 |
| Huang Qin       | 32.54                     | —                                 |
| Long Yan Rou    | 33.41                     | —                                 |
| Sha Ren         | 33.91                     | —                                 |
| Zhi Mu          | 34.25                     | —                                 |
| Huang Lian      | 34.34                     | —                                 |
| San Qi          | 35.78                     | —                                 |
| Sang Zhi        | 36.87                     | —                                 |
| Chuang Mu Xiang | 38.54                     | —                                 |
| Bo He           | 40.01                     | —                                 |
| Mu Gua          | 40.41                     | —                                 |
| Zhi Gan Cao     | 41.19                     | —                                 |
| Du Zhong        | 41.38                     | —                                 |
| Gou Qi Zi       | 41.62                     | —                                 |
| Chi Shao (Yao)  | 42.52                     | —                                 |
| Qing Pi         | 43.17                     | —                                 |
| Huang Bai       | 44.15                     | —                                 |
| Yuan Zhi        | 44.88                     | —                                 |
| Ku Shen         | 45.89                     | —                                 |
| Xie Bai         | 48.48                     | —                                 |
| Hong Hua        | 49.20                     | —                                 |
| Bai Zhu         | 49.68                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lu 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62839     | 62839                  | 0.00                            | 3.54                               |
| 62840     | 62840                  | 0.00                            | 4.25                               |

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 2.4-2022-02

Validated substance/substance group **Ma Huang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50283-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | G097HS255SL1 | 62693     | 40      | from supplier |
| PhytoComm | Ma Huang  | G097HS255SL1 | 62694     | 40      | from supplier |
| PhytoComm | Ma Huang  | G097HS255TK2 | 62939     | 40      | from supplier |
| PhytoComm | Ma Huang  | G097HS255TK2 | 62940     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G097HS255SL1 | 62693 <sup>†</sup> | 20      |
| PhytoComm | Ma Huang  | G097HS255SL1 | 62694 <sup>†</sup> | 20      |
| PhytoComm | Ma Huang  | G097HS255TK2 | 62939 <sup>†</sup> | 20      |
| PhytoComm | Ma Huang  | G097HS255TK2 | 62940 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jin Yin Hua     | 7.31                      | —                                 |
| Fu Pen Zi       | 11.41                     | —                                 |
| Bai Shao Yao    | 11.61                     | —                                 |
| Zhi Ke          | 11.96                     | —                                 |
| Ye Jiao Teng    | 12.07                     | —                                 |
| Lu Gen          | 14.21                     | —                                 |
| Hou Po          | 14.73                     | —                                 |
| Gan Cao         | 15.60                     | —                                 |
| Guang Huo Xiang | 15.81                     | —                                 |
| Ji Xue Teng     | 16.03                     | —                                 |
| Hong Jing Tian  | 16.14                     | —                                 |
| Ze Xie          | 16.35                     | —                                 |
| Tian Hua Fen    | 16.41                     | —                                 |
| Mu Zei          | 16.45                     | —                                 |
| Zi Hua Di Ding  | 16.84                     | —                                 |
| Dan Dou Chi     | 17.12                     | —                                 |
| Ren Dong Teng   | 17.14                     | —                                 |
| Yin Yang Huo    | 17.47                     | —                                 |
| Huang Bai       | 17.67                     | —                                 |
| Yan Hu Suo      | 17.72                     | —                                 |
| Tao Ren         | 17.79                     | —                                 |
| Ban Lan Gen     | 17.82                     | —                                 |
| Fu Zi           | 17.88                     | —                                 |
| Pi Pa Ye        | 18.00                     | —                                 |
| He Huan Pi      | 18.42                     | —                                 |
| Cang Zhu        | 18.81                     | —                                 |
| Huang Qin       | 18.88                     | —                                 |
| Hong Hua        | 18.93                     | —                                 |
| Lian Qiao       | 19.46                     | —                                 |
| Rou Gui         | 19.54                     | —                                 |
| Dan Shen        | 19.61                     | —                                 |
| Zhi Gan Cao     | 19.73                     | —                                 |
| Suan Zao Ren    | 20.05                     | —                                 |
| Gu Sui Bu       | 20.95                     | —                                 |
| Gui Zhi         | 21.29                     | —                                 |
| Dang Gui        | 22.00                     | —                                 |
| Bo He           | 22.81                     | —                                 |
| Zhe Bei Mu      | 23.06                     | —                                 |
| Jiao Gu Lan     | 23.08                     | —                                 |
| Huo Ma Ren      | 23.47                     | —                                 |
| Lai Fu Zi       | 23.52                     | —                                 |
| Lian Zi         | 23.68                     | —                                 |
| (Fen) Bi Xie    | 24.22                     | —                                 |
| She Gan         | 24.29                     | —                                 |
| Bai Xian Pi     | 24.41                     | —                                 |
| Gua Lou         | 24.41                     | —                                 |
| Sheng Jiang     | 24.55                     | —                                 |
| Ci Wu Jia       | 24.67                     | —                                 |

*continued on the next page*

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Shan Yao        | 24.71                     | —                                 |
| Huang Lian      | 24.82                     | —                                 |
| Gou Teng        | 25.09                     | —                                 |
| Shen Qu         | 25.28                     | —                                 |
| Di Gu Pi        | 25.34                     | —                                 |
| Gou Qi Zi       | 26.38                     | —                                 |
| Qiang Huo       | 26.72                     | —                                 |
| Chuang Mu Xiang | 26.90                     | —                                 |
| Ren Shen        | 26.95                     | —                                 |
| Tu Fu Ling      | 27.24                     | —                                 |
| Jie Geng        | 27.36                     | —                                 |
| Ling Zhi        | 27.93                     | —                                 |
| Yu Jin          | 27.98                     | —                                 |
| Zhi Mu          | 28.20                     | —                                 |
| Ji Li           | 28.28                     | —                                 |
| Ce Bai Ye       | 28.57                     | —                                 |
| Mang Xiao       | 28.63                     | —                                 |
| Che Qian Zi     | 28.90                     | —                                 |
| Chai Hu         | 29.05                     | —                                 |
| Jing Jie        | 29.17                     | —                                 |
| Chi Shao (Yao)  | 29.38                     | —                                 |
| Fo Shou         | 29.65                     | —                                 |
| Ku Shen         | 29.87                     | —                                 |
| Long Yan Rou    | 30.01                     | —                                 |
| Ban Xia (Jiang) | 30.20                     | —                                 |
| Ma Huang Gen    | 30.24                     | —                                 |
| Sha Ren         | 30.40                     | —                                 |
| Bai Zi Ren      | 30.41                     | —                                 |
| Fu Ling         | 30.78                     | —                                 |
| San Qi          | 30.82                     | —                                 |
| Mao Dong Qing   | 33.10                     | —                                 |
| Zhu Ling        | 33.27                     | —                                 |
| Qing Pi         | 33.79                     | —                                 |
| Fu Shen         | 34.38                     | —                                 |
| Sang Ye         | 35.07                     | —                                 |
| Mu Gua          | 35.50                     | —                                 |
| Yi Yi Ren       | 36.58                     | —                                 |
| Bai Jiang Cao   | 36.90                     | —                                 |
| Du Zhong        | 37.13                     | —                                 |
| Fu Xiao Mai     | 38.08                     | —                                 |
| Zhu Ru          | 39.04                     | —                                 |
| Ban Zhi Lian    | 39.12                     | —                                 |
| Sang Zhi        | 40.39                     | —                                 |
| Cang Er Zi      | 41.63                     | —                                 |
| Xie Bai         | 42.11                     | —                                 |
| Pu Gong Ying    | 43.18                     | —                                 |
| Ze Lan          | 43.19                     | —                                 |
| Yuan Zhi        | 44.64                     | —                                 |
| Qing Hao        | 46.95                     | —                                 |
| Huang Qi        | 48.74                     | —                                 |

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                         | 7.90                            |
| 62694     | 62694               | 0.00                         | 7.31                            |
| 62939     | 62939               | 0.00                         | 11.96                           |
| 62940     | 62940               | 0.00                         | 12.53                           |

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 2.4-2022-02

Validated substance/substance group **Ma Huang Gen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60063-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ma Huang Gen | G278HS393RN1 | 62262 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 78            | 2              | 22 359        |
| <b>Type B</b> | 6              | 35            | 5              | 11 351        |
| <b>Type C</b> | 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        |
|---------------|-------------------------|-------------------------|
| <b>Type A</b> | 99.9975 % (> 99.9812 %) | 97.5000 % (> 93.7500 %) |
| <b>Type B</b> | 99.9702 % (> 99.9382 %) | 87.5000 % (> 80.0000 %) |
| <b>Type C</b> | 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.

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

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Rou Gui         | 3.15                      | —                                 |
| He Huan Pi      | 3.67                      | —                                 |
| Gou Teng        | 6.12                      | —                                 |
| Fu Shen         | 8.33                      | —                                 |
| Gui Zhi         | 10.61                     | —                                 |
| Yi Yi Ren       | 11.03                     | —                                 |
| Ji Xue Teng     | 11.24                     | —                                 |
| Fu Ling         | 11.71                     | —                                 |
| Sheng Jiang     | 14.10                     | —                                 |
| Mu Zei          | 17.26                     | —                                 |
| Ban Xia (Jiang) | 17.70                     | —                                 |
| Fo Shou         | 18.34                     | —                                 |
| Fu Xiao Mai     | 19.69                     | —                                 |
| Ye Jiao Teng    | 19.98                     | —                                 |
| Lu Gen          | 20.50                     | —                                 |
| Bai Xian Pi     | 20.91                     | —                                 |
| Di Gu Pi        | 21.34                     | —                                 |
| Huo Ma Ren      | 21.70                     | —                                 |
| Bai Shao Yao    | 23.25                     | —                                 |
| Lai Fu Zi       | 23.28                     | —                                 |
| Lian Zi         | 23.38                     | —                                 |
| Ren Dong Teng   | 23.79                     | —                                 |
| Ci Wu Jia       | 24.18                     | —                                 |
| Ling Zhi        | 24.36                     | —                                 |
| Tao Ren         | 24.48                     | —                                 |
| Gu Sui Bu       | 25.87                     | —                                 |
| Zhu Ling        | 26.51                     | —                                 |
| Zhu Ru          | 27.36                     | —                                 |
| Bai Zi Ren      | 27.38                     | —                                 |
| Tu Fu Ling      | 28.02                     | —                                 |
| Zhe Bei Mu      | 28.30                     | —                                 |
| Dan Dou Chi     | 28.37                     | —                                 |
| Suan Zao Ren    | 28.47                     | —                                 |
| She Gan         | 28.84                     | —                                 |
| Shen Qu         | 29.03                     | —                                 |
| (Fen) Bi Xie    | 29.83                     | —                                 |
| Ji Li           | 30.35                     | —                                 |
| Mang Xiao       | 32.03                     | —                                 |
| Ze Xie          | 32.13                     | —                                 |
| Dan Shen        | 32.20                     | —                                 |
| Yu Jin          | 32.45                     | —                                 |
| Lian Qiao       | 33.83                     | —                                 |
| Tian Hua Fen    | 34.25                     | —                                 |
| Yan Hu Suo      | 34.30                     | —                                 |
| Shan Yao        | 37.43                     | —                                 |
| Pi Pa Ye        | 37.89                     | —                                 |
| Yin Yang Huo    | 38.31                     | —                                 |
| Zhi Ke          | 38.69                     | —                                 |
| Jiao Gu Lan     | 38.85                     | —                                 |
| Hong Jing Tian  | 41.15                     | —                                 |
| Ren Shen        | 41.15                     | —                                 |
| Jin Yin Hua     | 41.33                     | —                                 |
| Mao Dong Qing   | 42.25                     | —                                 |
| Dang Gui        | 42.62                     | —                                 |
| Chai Hu         | 43.22                     | —                                 |
| Ce Bai Ye       | 43.64                     | —                                 |
| Guang Huo Xiang | 43.66                     | —                                 |
| Ma Huang        | 43.69                     | —                                 |
| Huang Qin       | 43.74                     | —                                 |

*continued on the next page*



continued from previous page

| Substanz    | Distance in<br>main model | Distance in<br>second-stage model |
|-------------|---------------------------|-----------------------------------|
| Cang Zhu    | 43.97                     | —                                 |
| Zhi Mu      | 44.27                     | —                                 |
| Jie Geng    | 45.88                     | —                                 |
| Gua Lou     | 45.92                     | —                                 |
| Fu Pen Zi   | 46.55                     | —                                 |
| Fu Zi       | 48.18                     | —                                 |
| Ban Lan Gen | 48.20                     | —                                 |
| Huang Lian  | 48.85                     | —                                 |
| Qiang Huo   | 49.44                     | —                                 |
| Gan Cao     | 49.90                     | —                                 |
| Hou Po      | 50.07                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62261     | 62261                  | 0.00                            | 3.15                               |
| 62262     | 62262                  | 0.00                            | 6.00                               |

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 2.4-2022-02

Validated substance/substance group **Man Jing Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60025-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Man Jing Zi | G250H1505822 | 62502 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------|---------------------------|-----------------------------------|
| Hua Shi   | 30.75                     | —                                 |
| Mang Xiao | 56.08                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62501     | 62501                  | 0.00                            | 30.79                              |
| 62502     | 62502                  | 0.00                            | 30.75                              |

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 2.4-2022-02

Validated substance/substance group **Mang Xiao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50387-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Mang Xiao                 | 2      | 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 |
| PhytoComm | Mang Xiao | G160HS137TH1 | 62873     | 40      | from supplier |
| PhytoComm | Mang Xiao | G160HS137TH1 | 62874     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Mang Xiao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Mang Xiao | G160H0627821 | 62470 <sup>†</sup> | 20      |
| PhytoComm | Mang Xiao | G160HS137TH1 | 62873 <sup>†</sup> | 20      |
| PhytoComm | Mang Xiao | G160HS137TH1 | 62874 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 150           | 10             | 22 280        |
| <b>Type B</b> | 0              | 77            | 3              | 11 317        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 93.7500 % (> 91.8750 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 96.2500 % (> 92.5000 %) |
| <b>Type C</b> | 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.

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

### 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.

| Substance | Distance in<br>main model | Distance in<br>second-stage model |
|-----------|---------------------------|-----------------------------------|
| Hua Shi   | 43.91                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62469     | 62469                  | 0.00                            | 44.69                              |
| 62470     | 62470                  | 0.00                            | 44.92                              |
| 62873     | 62873                  | 0.00                            | 44.20                              |
| 62874     | 62874                  | 0.00                            | 43.91                              |

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 2.4-2022-02

Validated substance/substance group **Mao Dong Qing**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60028-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Mao Dong Qing | G319HS063RN1 | 62418 <sup>†</sup> | 20      |
| PhytoComm | Mao Dong Qing | G319HS063SK1 | 62619 <sup>†</sup> | 20      |
| PhytoComm | Mao Dong Qing | G319HS063SK1 | 62620 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 3              | 79            | 1              | 11 314        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 99.9653 % (> 99.9331 %)  | 98.7500 % (> 95.0000 %)  |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Du Zhong        | 6.60                      | —                                 |
| Bai Xian Pi     | 7.09                      | —                                 |
| Yin Yang Huo    | 7.79                      | —                                 |
| Ling Zhi        | 7.86                      | —                                 |
| Sha Ren         | 9.17                      | —                                 |
| Ye Jiao Teng    | 9.26                      | —                                 |
| Yu Jin          | 9.47                      | —                                 |
| Che Qian Zi     | 10.01                     | —                                 |
| Hou Po          | 10.95                     | —                                 |
| Qing Hao        | 11.86                     | —                                 |
| Qiang Huo       | 12.30                     | —                                 |
| Bo He           | 12.35                     | —                                 |
| Dan Dou Chi     | 12.50                     | —                                 |
| Chai Hu         | 13.07                     | —                                 |
| Zi Hua Di Ding  | 14.29                     | —                                 |
| Jiao Gu Lan     | 15.03                     | —                                 |
| Jing Jie        | 15.46                     | —                                 |
| Fu Zi           | 16.25                     | —                                 |
| Shen Qu         | 16.31                     | —                                 |
| Ren Dong Teng   | 16.94                     | —                                 |
| Xi Xian Cao     | 17.31                     | —                                 |
| Ce Bai Ye       | 17.79                     | —                                 |
| Tu Fu Ling      | 17.85                     | —                                 |
| Qing Pi         | 18.16                     | —                                 |
| Yan Hu Suo      | 18.29                     | —                                 |
| Ji Li           | 18.42                     | —                                 |
| Bai Jiang Cao   | 18.46                     | —                                 |
| Lian Zi         | 18.53                     | —                                 |
| Huang Bai       | 18.87                     | —                                 |
| Shan Yao        | 19.71                     | —                                 |
| Zhu Ling        | 20.10                     | —                                 |
| Ji Xue Teng     | 20.52                     | —                                 |
| Rou Gui         | 20.55                     | —                                 |
| Dan Shen        | 21.54                     | —                                 |
| Guang Huo Xiang | 21.87                     | —                                 |
| Pi Pa Ye        | 21.92                     | —                                 |
| Tian Hua Fen    | 22.92                     | —                                 |
| Nü Zhen Zi      | 23.22                     | —                                 |
| He Huan Pi      | 23.55                     | —                                 |
| Hong Jing Tian  | 23.59                     | —                                 |
| Fu Pen Zi       | 23.62                     | —                                 |
| Ma Huang        | 23.68                     | —                                 |
| Zhi Ke          | 23.75                     | —                                 |
| Huang Lian      | 24.22                     | —                                 |
| Pu Gong Ying    | 24.67                     | —                                 |
| Gou Teng        | 25.67                     | —                                 |
| Lian Qiao       | 26.03                     | —                                 |
| Ze Lan          | 26.29                     | —                                 |
| Ma Huang Gen    | 26.35                     | —                                 |
| Di Gu Pi        | 27.18                     | —                                 |
| Jin Yin Hua     | 28.12                     | —                                 |
| (Fen) Bi Xie    | 28.22                     | —                                 |

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| Substanz         | Distance in<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Gu Sui Bu        | 28.64                     | —                                 |
| Suan Zao Ren     | 28.85                     | —                                 |
| Sang Ye          | 28.93                     | —                                 |
| Yi Yi Ren        | 29.77                     | —                                 |
| Sheng Jiang      | 29.96                     | —                                 |
| Ban Lan Gen      | 30.96                     | —                                 |
| Bai Shao Yao     | 31.21                     | —                                 |
| Zhi Shi          | 31.72                     | —                                 |
| Ren Shen         | 32.09                     | —                                 |
| Lu Gen           | 32.17                     | —                                 |
| Mang Xiao        | 32.19                     | —                                 |
| Ban Zhi Lian     | 32.41                     | —                                 |
| Gui Zhi          | 32.81                     | —                                 |
| Cang Er Zi       | 33.39                     | —                                 |
| Huo Ma Ren       | 33.43                     | —                                 |
| Chuang Mu Xiang  | 34.38                     | —                                 |
| Xin Yi           | 34.86                     | —                                 |
| Mu Zei           | 35.10                     | —                                 |
| Gan Cao          | 35.37                     | —                                 |
| Zhe Bei Mu       | 35.39                     | —                                 |
| E Zhu            | 35.51                     | —                                 |
| Fu Ling          | 36.38                     | —                                 |
| Jiang Huang      | 37.47                     | —                                 |
| She Gan          | 38.65                     | —                                 |
| Yin Chen Hao     | 39.25                     | —                                 |
| Tao Ren          | 39.45                     | —                                 |
| Fu Shen          | 39.98                     | —                                 |
| Hong Hua         | 41.19                     | —                                 |
| Wang Bu Liu Xing | 41.25                     | —                                 |
| Wu Wei Zi        | 42.80                     | —                                 |
| Chi Shao (Yao)   | 43.02                     | —                                 |
| Cang Zhu         | 43.48                     | —                                 |
| Sang Zhi         | 43.91                     | —                                 |
| Zhi Gan Cao      | 44.00                     | —                                 |
| Fo Shou          | 45.16                     | —                                 |
| Ci Wu Jia        | 45.72                     | —                                 |
| Ban Xia (Jiang)  | 45.90                     | —                                 |
| Niu Bang Zi      | 45.91                     | —                                 |
| Fu Xiao Mai      | 45.95                     | —                                 |
| Yi Mu Cao        | 46.22                     | —                                 |
| Xie Bai          | 46.71                     | —                                 |
| Jie Geng         | 47.39                     | —                                 |
| Zi Su Zi         | 47.77                     | —                                 |
| Huang Qin        | 49.14                     | —                                 |
| Yu Xing Cao      | 49.16                     | —                                 |
| Zhu Ru           | 49.24                     | —                                 |
| Bai Zi Ren       | 49.46                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62417     | 62417               | 0.00                         | 6.60                            |
| 62418     | 62418               | 0.00                         | 7.09                            |
| 62619     | 62619               | 0.00                         | 9.99                            |
| 62620     | 62620               | 0.00                         | 9.97                            |

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 2.4-2022-02

Validated substance/substance group **Mi Huan Jun**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60556-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Mi Huan Jun; Armillariella mellea rhizoma

### Special notes

When selecting the *Mi Huan Jun* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Mi Huan Jun               | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Mi Huan Jun* 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 *Mi Huan Jun*:

| Supplier  | Substance   | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-------------|--------------|-----------|---------|---------------|
| PhytoComm | Mi Huan Jun | G510H0418021 | 62983     | 40      | from supplier |
| PhytoComm | Mi Huan Jun | G510H0418021 | 62984     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Mi Huan Jun*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Mi Huan Jun*.
- 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 | Mi Huan Jun | G510H0418021 | 62983 <sup>†</sup> | 20      |
| PhytoComm | Mi Huan Jun | G510H0418021 | 62984 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Mi Huan Jun*.
- 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 | Mi Huan Jun | G510H0418221 | 1       |
| Phytocomm | Mi Huan Jun | G510H0418422 | 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 *Mi Huan Jun* 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 *Mi Huan Jun* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 79            | 1              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 1              | 0             | 2              | 854           |

The substance/substance group *Mi Huan Jun* 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 98.7500 % (> 95.0000 %)  |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 99.9070 % (> 99.3221 %)  | n/a (n/a)                |

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

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

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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mi Huan Jun* 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Chuan Mu Tong  | 5.98                      | —                                 |
| Sang Zhi       | 9.13                      | —                                 |
| Di Gu Pi       | 10.00                     | —                                 |
| Chuan Lian Zi  | 11.64                     | —                                 |
| E Zhu          | 14.74                     | —                                 |
| Bai He         | 14.89                     | —                                 |
| Gan Jiang      | 15.29                     | —                                 |
| Dang Gui       | 16.51                     | —                                 |
| Sha Shen (Bei) | 18.25                     | —                                 |
| Long Dan (Cao) | 20.91                     | —                                 |
| Qin Jiao       | 21.15                     | —                                 |
| Tian Hua Fen   | 21.89                     | —                                 |
| Lai Fu Zi      | 22.67                     | —                                 |
| Ban Zhi Lian   | 23.68                     | —                                 |
| Mang Xiao      | 24.08                     | —                                 |
| (Huai) Niu Xi  | 25.55                     | —                                 |
| Zi Su Zi       | 27.22                     | —                                 |
| Jiang Huang    | 27.85                     | —                                 |
| Cang Er Zi     | 28.53                     | —                                 |
| Huang Qi       | 30.19                     | —                                 |
| Zhi Gan Cao    | 30.30                     | —                                 |
| Yan Hu Suo     | 30.53                     | —                                 |
| Da Zao         | 30.61                     | —                                 |
| Chuan Niu Xi   | 30.63                     | —                                 |
| Shan Yao       | 30.77                     | —                                 |
| Jie Geng       | 31.29                     | —                                 |
| Bai Zhi        | 31.69                     | —                                 |
| Bai Zhu        | 32.44                     | —                                 |
| (Bai) Dou Kou  | 33.31                     | —                                 |
| Niu Bang Zi    | 35.10                     | —                                 |
| Sha Ren        | 36.27                     | —                                 |
| Fu Ling        | 36.30                     | —                                 |
| Chen Pi        | 37.09                     | —                                 |
| He Huan Pi     | 37.35                     | —                                 |
| Lian Qiao      | 38.21                     | —                                 |
| Lian Zi        | 38.69                     | —                                 |
| Rou Gui        | 38.88                     | —                                 |
| Ji Li          | 41.10                     | —                                 |
| Bai Xian Pi    | 41.99                     | —                                 |
| Bing Lang      | 42.54                     | —                                 |
| (Shi) Chang Pu | 42.92                     | —                                 |
| Yi Yi Ren      | 42.97                     | —                                 |
| Suan Zao Ren   | 42.98                     | —                                 |
| Bai Shao Yao   | 43.70                     | —                                 |
| Xiao Hui Xiang | 44.68                     | —                                 |
| Xiang Fu       | 45.51                     | —                                 |
| Huang Lian     | 45.61                     | —                                 |
| Tu Fu Ling     | 46.16                     | —                                 |
| Chi Shao (Yao) | 47.11                     | —                                 |
| Zi Hua Di Ding | 47.19                     | —                                 |
| Jin Yin Hua    | 47.35                     | —                                 |
| Mu Dan Pi      | 47.46                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Ku Shen             | 47.64                     | —                                 |
| Ye Jiao Teng        | 47.97                     | —                                 |
| Sheng Jiang         | 48.55                     | —                                 |
| Bai Hua She She Cao | 48.56                     | —                                 |
| Ji Xue Teng         | 48.88                     | —                                 |
| Mao Dong Qing       | 49.19                     | —                                 |
| Qiang Huo           | 49.23                     | —                                 |
| Shan Yu Rou         | 49.29                     | —                                 |
| Yuan Zhi            | 49.32                     | —                                 |
| Mu Gua              | 49.36                     | —                                 |
| Zhi Ke              | 49.41                     | —                                 |
| Du Zhong            | 49.55                     | —                                 |
| Chai Hu             | 49.68                     | —                                 |
| Bo He               | 49.71                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mi Huan Jun* 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62983     | 62983                  | 0.00                            | 6.14                               |
| 62984     | 62984                  | 0.00                            | 5.98                               |

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 2.4-2022-02

Validated substance/substance group **Mu Dan Pi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60113-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Mu Dan Pi                 | 1      | 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 | G166H0741021 | 62825     | 40      | from supplier |
| PhytoComm | Mu Dan Pi | G166H0741021 | 62826     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Mu Dan Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G166H0741021 | 62825 <sup>†</sup> | 20      |
| PhytoComm | Mu Dan Pi | G166H0741021 | 62826 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 | G166H0741321 | 2       |
| PhytoComm | Mu Dan Pi | G166H0741321 | 1       |
| Phytocomm | Mu Dan Pi | G166H0741421 | 4       |
| Phytocomm | Mu Dan Pi | g166j074122  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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 new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

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

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

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Chen Pi             | 11.63                     | —                                 |
| Shan Yu Rou         | 17.45                     | —                                 |
| Gu Sui Bu           | 18.71                     | —                                 |
| He Huan Pi          | 20.31                     | —                                 |
| Wu Yao              | 20.75                     | —                                 |
| He Shou Wu          | 21.36                     | —                                 |
| Dang Gui            | 23.10                     | —                                 |
| (Shi) Chang Pu      | 24.26                     | —                                 |
| Ju Hua              | 24.79                     | —                                 |
| Chuan Lian Zi       | 24.97                     | —                                 |
| Fang Feng           | 26.07                     | —                                 |
| Hong Jing Tian      | 26.52                     | —                                 |
| Mang Xiao           | 26.64                     | —                                 |
| Ba Ji Tian          | 26.90                     | —                                 |
| Sha Ren             | 27.76                     | —                                 |
| Jiang Huang         | 28.24                     | —                                 |
| Sang Ji Shend       | 29.07                     | —                                 |
| Huang Qi            | 31.59                     | —                                 |
| Chuan Niu Xi        | 32.03                     | —                                 |
| Bing Lang           | 33.21                     | —                                 |
| E Zhu               | 34.50                     | —                                 |
| Yin Chen Hao        | 34.56                     | —                                 |
| Sang Zhi            | 34.64                     | —                                 |
| Xiang Fu            | 34.90                     | —                                 |
| Du Huo              | 35.18                     | —                                 |
| Wu Zhu Yu           | 35.31                     | —                                 |
| Tu Si Zi            | 35.95                     | —                                 |
| Shan Yao            | 37.01                     | —                                 |
| Sang Bai Pi         | 38.47                     | —                                 |
| Ge Gen              | 39.75                     | —                                 |
| (Bai) Dou Kou       | 40.70                     | —                                 |
| Zhi Gan Cao         | 40.90                     | —                                 |
| Tian Hua Fen        | 42.32                     | —                                 |
| Zhi Ke              | 42.80                     | —                                 |
| Bai Hua She She Cao | 43.02                     | —                                 |
| Xiao Hui Xiang      | 44.42                     | —                                 |
| Ku Shen             | 44.72                     | —                                 |
| Lai Fu Zi           | 45.26                     | —                                 |
| Di Gu Pi            | 45.30                     | —                                 |
| (Huai) Niu Xi       | 45.39                     | —                                 |
| Da Zao              | 45.61                     | —                                 |
| Zi Su Zi            | 45.79                     | —                                 |
| Yi Mu Cao           | 45.86                     | —                                 |
| Bai Zhi             | 46.24                     | —                                 |
| Xin Yi              | 47.08                     | —                                 |
| Xu Duan             | 48.06                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62825     | 62825               | 0.00                         | 11.63                           |
| 62826     | 62826               | 0.00                         | 11.82                           |

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 2.4-2022-02

Validated substance/substance group **Mu Gua**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10003578-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Mu Gua; Chaenomelis lagenariae fructus

### Special notes

When selecting the *Mu Gua* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Mu Gua                    | 2      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Mu Gua* 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 Gua*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Mu Gua    | G063HS043TK1 | 62929     | 40      | from supplier |
| PhytoComm | Mu Gua    | G063HS043TK1 | 62930     | 40      | from supplier |
| PhytoComm | Mu Gua    | G063H0424922 | 63017     | 40      | from supplier |
| PhytoComm | Mu Gua    | G063H0424922 | 63018     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Gua*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 Gua*.
- 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 Gua    | G063HS043TK1 | 62929 <sup>†</sup> | 20      |
| PhytoComm | Mu Gua    | G063HS043TK1 | 62930 <sup>†</sup> | 20      |
| PhytoComm | Mu Gua    | G063H0424922 | 63017 <sup>†</sup> | 20      |
| PhytoComm | Mu Gua    | G063H0424922 | 63018 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 2 batches from the substance/substance group *Mu Gua*.
- 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 | Mu Gua    | G063H0424221 | 1       |
| PhytoComm | Mu Gua    | G063H0424221 | 1       |
| Phytocomm | Mu Gua    | G063H0424521 | 4       |

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

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 1              | 0             | 6              | 850           |

The substance/substance group *Mu Gua* 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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 new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 Gua* 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Huang Qi        | 7.99                      | —                                 |
| Zhi Mu          | 11.42                     | —                                 |
| Bai Shao Yao    | 11.68                     | —                                 |
| Zhi Gan Cao     | 11.78                     | —                                 |
| Gou Qi Zi       | 13.36                     | —                                 |
| Bai Zhu         | 13.45                     | —                                 |
| San Qi          | 14.26                     | —                                 |
| Yuan Zhi        | 14.29                     | —                                 |
| Chi Shao (Yao)  | 14.33                     | —                                 |
| Ren Shen        | 14.69                     | —                                 |
| Jie Geng        | 15.70                     | —                                 |
| Pi Pa Ye        | 15.76                     | —                                 |
| Xie Bai         | 15.98                     | —                                 |
| Shan Yao        | 17.90                     | —                                 |
| Ku Shen         | 18.27                     | —                                 |
| Cang Zhu        | 18.55                     | —                                 |
| Lian Qiao       | 19.06                     | —                                 |
| Gua Lou         | 19.36                     | —                                 |
| Chuan Lian Zi   | 20.34                     | —                                 |
| Sang Zhi        | 21.53                     | —                                 |
| Jiao Gu Lan     | 21.56                     | —                                 |
| Dang Gui        | 21.57                     | —                                 |
| Zhe Bei Mu      | 21.70                     | —                                 |
| Bai Zi Ren      | 22.44                     | —                                 |
| Di Gu Pi        | 22.58                     | —                                 |
| Ji Li           | 23.14                     | —                                 |
| Suan Zao Ren    | 23.31                     | —                                 |
| Fo Shou         | 23.73                     | —                                 |
| Chuang Mu Xiang | 23.78                     | —                                 |
| Mu Zei          | 24.19                     | —                                 |
| (Huai) Niu Xi   | 24.32                     | —                                 |
| Gan Cao         | 24.40                     | —                                 |
| Lian Zi         | 24.43                     | —                                 |
| Ye Jiao Teng    | 24.80                     | —                                 |
| Long Dan (Cao)  | 24.86                     | —                                 |
| Ban Lan Gen     | 24.95                     | —                                 |
| Ren Dong Teng   | 25.11                     | —                                 |
| Jin Yin Hua     | 25.32                     | —                                 |
| Zhu Ru          | 25.87                     | —                                 |
| Tian Hua Fen    | 25.88                     | —                                 |
| Tu Fu Ling      | 26.05                     | —                                 |
| Ling Zhi        | 26.11                     | —                                 |
| Long Yan Rou    | 26.19                     | —                                 |
| Shen Qu         | 26.91                     | —                                 |
| Lai Fu Zi       | 26.98                     | —                                 |

*continued on the next page*



*continued from previous page*

| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Zhi Ke          | 27.01                             | —                                         |
| He Huan Pi      | 27.24                             | —                                         |
| Qin Jiao        | 27.47                             | —                                         |
| Dan Dou Chi     | 27.62                             | —                                         |
| Mao Dong Qing   | 27.89                             | —                                         |
| Fu Zi           | 28.00                             | —                                         |
| Fu Ling         | 28.39                             | —                                         |
| Mang Xiao       | 28.72                             | —                                         |
| Hou Po          | 28.93                             | —                                         |
| Sheng Jiang     | 28.99                             | —                                         |
| Dan Shen        | 29.31                             | —                                         |
| Huo Ma Ren      | 29.31                             | —                                         |
| Bai He          | 29.71                             | —                                         |
| Ze Xie          | 31.60                             | —                                         |
| Lu Gen          | 32.20                             | —                                         |
| Fu Pen Zi       | 32.37                             | —                                         |
| Ci Wu Jia       | 32.71                             | —                                         |
| Tao Ren         | 33.44                             | —                                         |
| Chai Hu         | 33.48                             | —                                         |
| Hong Jing Tian  | 33.82                             | —                                         |
| Huang Qin       | 33.94                             | —                                         |
| Rou Gui         | 34.13                             | —                                         |
| Fu Xiao Mai     | 34.47                             | —                                         |
| Bing Lang       | 34.85                             | —                                         |
| Ban Xia (Jiang) | 36.06                             | —                                         |
| Gou Teng        | 36.48                             | —                                         |
| Ji Xue Teng     | 36.52                             | —                                         |
| Zi Su Zi        | 37.09                             | —                                         |
| Che Qian Zi     | 37.27                             | —                                         |
| Gui Zhi         | 38.33                             | —                                         |
| Chuan Mu Tong   | 38.54                             | —                                         |
| Bai Xian Pi     | 39.37                             | —                                         |
| Yin Yang Huo    | 39.44                             | —                                         |
| Qing Pi         | 40.28                             | —                                         |
| Hong Hua        | 40.36                             | —                                         |
| Gan Jiang       | 40.45                             | —                                         |
| Yi Yi Ren       | 40.46                             | —                                         |
| Yan Hu Suo      | 40.53                             | —                                         |
| Sha Shen (Bei)  | 40.55                             | —                                         |
| Ma Huang        | 40.93                             | —                                         |
| Qiang Huo       | 41.09                             | —                                         |
| Gu Sui Bu       | 41.35                             | —                                         |
| Cang Er Zi      | 41.44                             | —                                         |
| Zi Hua Di Ding  | 41.60                             | —                                         |
| Ban Zhi Lian    | 41.81                             | —                                         |
| Bai Zhi         | 42.67                             | —                                         |
| She Gan         | 42.68                             | —                                         |
| Chuan Niu Xi    | 43.18                             | —                                         |
| Ce Bai Ye       | 43.19                             | —                                         |
| E Zhu           | 44.19                             | —                                         |
| (Fen) Bi Xie    | 44.73                             | —                                         |
| Bo He           | 45.36                             | —                                         |
| Zhu Ling        | 45.49                             | —                                         |
| Yu Jin          | 45.86                             | —                                         |
| Huang Lian      | 47.91                             | —                                         |
| Huang Bai       | 47.93                             | —                                         |
| Guang Huo Xiang | 48.33                             | —                                         |
| Ma Huang Gen    | 48.38                             | —                                         |
| Niu Bang Zi     | 50.55                             | —                                         |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mu Gua* 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62929     | 62929               | 0.00                         | 11.70                           |
| 62930     | 62930               | 0.00                         | 11.42                           |
| 63017     | 63017               | 0.00                         | 8.56                            |
| 63018     | 63018               | 0.00                         | 7.99                            |

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 2.4-2022-02

Validated substance/substance group **Mu Zei**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60123-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Mu Zei; Equiseti hiemalis herba

### Special notes

When selecting the *Mu Zei* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Mu Zei                    | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Mu Zei* 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 Zei*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Mu Zei    | G265HS045TK1 | 62811     | 40      | from supplier |
| PhytoComm | Mu Zei    | G265HS045TK1 | 62812     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Mu Zei*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Mu Zei*.
- 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 Zei    | G265HS045TK1 | 62811 <sup>†</sup> | 20      |
| PhytoComm | Mu Zei    | G265HS045TK1 | 62812 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Mu Zei*.
- 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 | Mu Zei    | G265H0427421 | 1       |
| PhytoComm | Mu Zei    | G265H0427823 | 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 *Mu Zei* 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 Zei* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 3              | 76            | 4              | 22 357        |
| <b>Type B</b> | 2              | 18            | 22             | 11 355        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Mu Zei* 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9907 % (> 99.9744 %)  | 95.0000 % (> 91.2500 %) |
| <b>Type B</b> | 99.9702 % (> 99.9382 %)  | 45.0000 % (> 37.5000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mu Zei* 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Shen Qu         | 3.98                      | —                                 |
| Huo Ma Ren      | 4.16                      | —                                 |
| He Huan Pi      | 4.60                      | —                                 |
| Bai Shao Yao    | 5.23                      | —                                 |
| Lai Fu Zi       | 6.34                      | —                                 |
| Lu Gen          | 6.42                      | —                                 |
| Tao Ren         | 6.77                      | —                                 |
| Gui Zhi         | 7.24                      | —                                 |
| Gou Teng        | 7.44                      | —                                 |
| Ye Jiao Teng    | 7.58                      | —                                 |
| Zhe Bei Mu      | 7.60                      | —                                 |
| Gu Sui Bu       | 7.72                      | —                                 |
| Ji Li           | 8.25                      | —                                 |
| Ji Xue Teng     | 8.36                      | —                                 |
| Tian Hua Fen    | 8.82                      | —                                 |
| Ci Wu Jia       | 8.88                      | —                                 |
| Sheng Jiang     | 9.25                      | —                                 |
| Bai Zi Ren      | 9.87                      | —                                 |
| Ling Zhi        | 9.98                      | —                                 |
| Lian Zi         | 10.89                     | —                                 |
| Rou Gui         | 10.93                     | —                                 |
| Ze Xie          | 11.03                     | —                                 |
| Ren Dong Teng   | 11.33                     | —                                 |
| Fo Shou         | 11.38                     | —                                 |
| Fu Ling         | 11.57                     | —                                 |
| Ban Xia (Jiang) | 11.85                     | —                                 |
| Di Gu Pi        | 12.06                     | —                                 |
| (Fen) Bi Xie    | 12.49                     | —                                 |
| Bai Xian Pi     | 12.61                     | —                                 |
| Lian Qiao       | 13.07                     | —                                 |
| Pi Pa Ye        | 13.36                     | —                                 |
| Zhu Ru          | 13.84                     | —                                 |
| Shan Yao        | 14.09                     | —                                 |
| Ma Huang Gen    | 14.09                     | —                                 |
| Suan Zao Ren    | 14.51                     | —                                 |
| Fu Xiao Mai     | 16.03                     | —                                 |
| She Gan         | 16.20                     | —                                 |
| Yi Yi Ren       | 16.56                     | —                                 |
| Tu Fu Ling      | 16.94                     | —                                 |
| Jin Yin Hua     | 17.20                     | —                                 |
| Zhu Ling        | 17.35                     | —                                 |
| Fu Zi           | 17.38                     | —                                 |
| Gua Lou         | 17.54                     | —                                 |
| Fu Pen Zi       | 17.79                     | —                                 |
| Ce Bai Ye       | 17.84                     | —                                 |
| Yan Hu Suo      | 18.19                     | —                                 |
| Yu Jin          | 18.72                     | —                                 |
| Dan Shen        | 19.23                     | —                                 |
| Dan Dou Chi     | 19.64                     | —                                 |
| Ban Lan Gen     | 20.80                     | —                                 |
| Yin Yang Huo    | 21.14                     | —                                 |
| Ma Huang        | 21.73                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Hou Po          | 21.73                     | —                                 |
| Jiao Gu Lan     | 21.99                     | —                                 |
| Jie Geng        | 23.17                     | —                                 |
| Hong Jing Tian  | 23.32                     | —                                 |
| Cang Zhu        | 23.48                     | —                                 |
| Chai Hu         | 23.94                     | —                                 |
| Guang Huo Xiang | 23.96                     | —                                 |
| Dang Gui        | 24.02                     | —                                 |
| Mao Dong Qing   | 24.40                     | —                                 |
| Che Qian Zi     | 24.51                     | —                                 |
| Ren Shen        | 24.78                     | —                                 |
| Fu Shen         | 25.02                     | —                                 |
| San Qi          | 25.71                     | —                                 |
| Zhi Ke          | 26.05                     | —                                 |
| Zhi Mu          | 27.69                     | —                                 |
| Gan Cao         | 28.02                     | —                                 |
| Qiang Huo       | 28.74                     | —                                 |
| Huang Qin       | 29.70                     | —                                 |
| Mang Xiao       | 32.42                     | —                                 |
| Gou Qi Zi       | 32.54                     | —                                 |
| Mu Gua          | 33.36                     | —                                 |
| Jing Jie        | 33.65                     | —                                 |
| Long Yan Rou    | 33.92                     | —                                 |
| Ku Shen         | 33.99                     | —                                 |
| Yuan Zhi        | 35.83                     | —                                 |
| Huang Lian      | 36.01                     | —                                 |
| Zi Hua Di Ding  | 36.43                     | —                                 |
| Sang Zhi        | 37.58                     | —                                 |
| Qing Pi         | 38.06                     | —                                 |
| Chuang Mu Xiang | 38.10                     | —                                 |
| Sha Ren         | 38.54                     | —                                 |
| Zhi Gan Cao     | 38.81                     | —                                 |
| Xie Bai         | 39.70                     | —                                 |
| Chi Shao (Yao)  | 41.48                     | —                                 |
| Du Zhong        | 42.17                     | —                                 |
| Bo He           | 42.83                     | —                                 |
| Huang Bai       | 47.46                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mu Zei* 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62811     | 62811                  | 0.00                            | 4.72                               |
| 62812     | 62812                  | 0.00                            | 3.98                               |

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 2.4-2022-02

Validated substance/substance group **Niu Bang Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002261-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Niu Bang Zi               | 2      | 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 |
| PhytoComm | Niu Bang Zi | G026H0433921 | 62967     | 40      | from supplier |
| PhytoComm | Niu Bang Zi | G026H0433921 | 62968     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Niu Bang Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Niu Bang Zi | G026H0433822 | 62766 <sup>†</sup> | 20      |
| PhytoComm | Niu Bang Zi | G026H0433921 | 62967 <sup>†</sup> | 20      |
| PhytoComm | Niu Bang Zi | G026H0433921 | 62968 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G026H0433321 | 2       |
| Phytocomm | Niu Bang Zi | G026H0433521 | 3       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 0              | 2             | 6              | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Lian Qiao      | 11.47                     | —                                 |
| Ku Shen        | 13.43                     | —                                 |
| Zi Su Zi       | 18.95                     | —                                 |
| Cang Er Zi     | 20.60                     | —                                 |
| Yi Mu Cao      | 21.61                     | —                                 |
| Xiao Hui Xiang | 22.42                     | —                                 |
| Shan Yao       | 25.17                     | —                                 |
| Di Gu Pi       | 25.71                     | —                                 |
| Xiang Fu       | 26.35                     | —                                 |
| (Huai) Niu Xi  | 28.02                     | —                                 |
| Jiang Huang    | 31.07                     | —                                 |
| Mang Xiao      | 31.09                     | —                                 |
| Yan Hu Suo     | 32.04                     | —                                 |
| Gan Cao        | 32.12                     | —                                 |
| Gan Jiang      | 32.33                     | —                                 |
| Tian Hua Fen   | 33.69                     | —                                 |
| Sang Zhi       | 33.89                     | —                                 |
| Zhi Ke         | 33.94                     | —                                 |
| Dong Gua Zi    | 35.54                     | —                                 |
| Chuan Lian Zi  | 36.40                     | —                                 |
| Shen Qu        | 36.95                     | —                                 |
| (Bai) Dou Kou  | 37.11                     | —                                 |
| Jin Yin Hua    | 37.26                     | —                                 |
| Suan Zao Ren   | 37.29                     | —                                 |
| Chi Shao (Yao) | 37.58                     | —                                 |
| Sha Ren        | 37.61                     | —                                 |
| Jie Geng       | 37.65                     | —                                 |
| E Zhu          | 38.62                     | —                                 |
| Qiang Huo      | 39.24                     | —                                 |
| Yuan Zhi       | 39.66                     | —                                 |
| Pu Gong Ying   | 39.68                     | —                                 |
| Huang Qi       | 40.03                     | —                                 |
| Ze Lan         | 40.59                     | —                                 |
| Chen Pi        | 41.56                     | —                                 |
| Zi Hua Di Ding | 42.02                     | —                                 |
| Shan Yu Rou    | 42.55                     | —                                 |
| Zhi Gan Cao    | 42.88                     | —                                 |
| Huang Lian     | 42.92                     | —                                 |
| Du Huo         | 43.58                     | —                                 |
| Ju Hua         | 43.76                     | —                                 |
| Qing Pi        | 44.38                     | —                                 |
| Wu Yao         | 44.78                     | —                                 |
| Sang Ye        | 44.88                     | —                                 |
| (Shi) Chang Pu | 45.23                     | —                                 |
| Bai Zhi        | 45.40                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Dang Gui            | 46.10                     | —                                 |
| Sha Shen (Bei)      | 46.25                     | —                                 |
| Huang Bai           | 47.29                     | —                                 |
| Chuan Niu Xi        | 48.42                     | —                                 |
| Chuan Mu Tong       | 48.76                     | —                                 |
| Fu Zi               | 49.18                     | —                                 |
| Xie Bai             | 49.55                     | —                                 |
| Wang Bu Liu Xing    | 49.59                     | —                                 |
| Bai Hua She She Cao | 49.77                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62765     | 62765                  | 0.00                            | 11.47                              |
| 62766     | 62766                  | 0.00                            | 11.69                              |
| 62967     | 62967                  | 0.00                            | 13.32                              |
| 62968     | 62968                  | 0.00                            | 13.63                              |

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 2.4-2022-02

Validated substance/substance group **Nü Zhen Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60065-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Nü Zhen Zi                | 2      | 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 | 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 34 694 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 *Nü Zhen Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G138H0345821 | 62343 <sup>†</sup> | 20      |
| PhytoComm | Nü Zhen Zi | G138H0345821 | 62344 <sup>†</sup> | 20      |
| PhytoComm | Nü Zhen Zi | G138HS010SK1 | 62569 <sup>†</sup> | 20      |
| PhytoComm | Nü Zhen Zi | G138HS010SK1 | 62570 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 | 420319901    | 1       |
| Phytocomm | Nü Zhen Zi | G138H0345421 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Shan Yao       | 16.68                     | —                                 |
| Yin Chen Hao   | 16.97                     | —                                 |
| Xi Xian Cao    | 17.14                     | —                                 |
| Sang Ye        | 17.70                     | —                                 |
| Yi Mu Cao      | 18.22                     | —                                 |
| Du Zhong       | 19.56                     | —                                 |
| Xin Yi         | 20.39                     | —                                 |
| Zhi Shi        | 20.91                     | —                                 |
| Sang Bai Pi    | 21.14                     | —                                 |
| Qiang Huo      | 22.60                     | —                                 |
| Pu Gong Ying   | 23.50                     | —                                 |
| Jing Jie       | 23.84                     | —                                 |
| Qing Pi        | 23.99                     | —                                 |
| Sha Ren        | 24.11                     | —                                 |
| Wu Zhu Yu      | 24.15                     | —                                 |
| Gou Teng       | 24.30                     | —                                 |
| Mao Dong Qing  | 24.34                     | —                                 |
| Zi Hua Di Ding | 25.25                     | —                                 |
| Mang Xiao      | 26.26                     | —                                 |
| Jiang Huang    | 26.57                     | —                                 |
| Ce Bai Ye      | 26.71                     | —                                 |
| Dan Shen       | 28.24                     | —                                 |
| Ze Lan         | 28.28                     | —                                 |
| Huang Lian     | 28.46                     | —                                 |
| Tu Fu Ling     | 28.85                     | —                                 |
| Yu Jin         | 28.89                     | —                                 |
| Sang Ji Shend  | 29.19                     | —                                 |
| Hou Po         | 29.49                     | —                                 |
| Chai Hu        | 29.60                     | —                                 |
| Fu Zi          | 29.69                     | —                                 |
| Bai Jiang Cao  | 29.85                     | —                                 |
| Dan Dou Chi    | 29.99                     | —                                 |
| Zhi Ke         | 30.58                     | —                                 |
| Qing Hao       | 31.34                     | —                                 |
| Hu Zhang       | 31.79                     | —                                 |
| Ling Zhi       | 31.79                     | —                                 |
| Hong Jing Tian | 31.84                     | —                                 |
| He Huan Pi     | 32.07                     | —                                 |
| Xiao Hui Xiang | 32.36                     | —                                 |
| Cang Er Zi     | 32.41                     | —                                 |
| Jiao Gu Lan    | 32.49                     | —                                 |
| Huang Bai      | 32.58                     | —                                 |
| Xuan Fu Hua    | 32.80                     | —                                 |
| Yu Xing Cao    | 33.15                     | —                                 |
| Bo He          | 33.20                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Jin Yin Hua         | 33.99                     | —                                 |
| Di Gu Pi            | 34.15                     | —                                 |
| Ye Jiao Teng        | 34.45                     | —                                 |
| Yin Yang Huo        | 34.89                     | —                                 |
| Wang Bu Liu Xing    | 35.23                     | —                                 |
| Bu Gu Zhi           | 36.90                     | —                                 |
| Bai Hua She She Cao | 36.92                     | —                                 |
| Fu Pen Zi           | 37.80                     | —                                 |
| Han Lian Cao        | 37.95                     | —                                 |
| Ma Huang            | 38.14                     | —                                 |
| Gu Sui Bu           | 38.40                     | —                                 |
| Bai Xian Pi         | 38.85                     | —                                 |
| Zi Su Zi            | 39.51                     | —                                 |
| He Shou Wu          | 40.21                     | —                                 |
| Lian Qiao           | 40.44                     | —                                 |
| Xia Ku Cao          | 40.66                     | —                                 |
| Ku Shen             | 41.30                     | —                                 |
| Chuang Mu Xiang     | 41.45                     | —                                 |
| Zhe Bei Mu          | 42.54                     | —                                 |
| Hong Hua            | 43.16                     | —                                 |
| Pi Pa Ye            | 43.36                     | —                                 |
| Chen Pi             | 43.50                     | —                                 |
| Wu Wei Zi           | 43.99                     | —                                 |
| Ban Lan Gen         | 44.10                     | —                                 |
| Che Qian Zi         | 44.22                     | —                                 |
| Yan Hu Suo          | 45.00                     | —                                 |
| Wu Jia Pi           | 45.60                     | —                                 |
| Ji Li               | 45.62                     | —                                 |
| (Shi) Chang Pu      | 45.86                     | —                                 |
| Ge Gen              | 46.63                     | —                                 |
| Ding Xiang          | 47.10                     | —                                 |
| Ren Dong Teng       | 47.38                     | —                                 |
| E Zhu               | 47.46                     | —                                 |
| Bai Shao Yao        | 47.46                     | —                                 |
| Tian Hua Fen        | 47.60                     | —                                 |
| Shen Qu             | 48.41                     | —                                 |
| Guang Huo Xiang     | 48.55                     | —                                 |
| Lian Zi             | 48.66                     | —                                 |
| Jin Qian Cao        | 48.69                     | —                                 |
| Fang Feng           | 49.20                     | —                                 |
| Gan Cao             | 49.50                     | —                                 |
| Jie Geng            | 49.62                     | —                                 |
| Niu Bang Zi         | 49.97                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62343     | 62343               | 0.00                         | 18.22                           |
| 62344     | 62344               | 0.00                         | 18.37                           |
| 62569     | 62569               | 0.00                         | 16.81                           |
| 62570     | 62570               | 0.00                         | 16.68                           |

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 2.4-2022-02

Validated substance/substance group **Pi Pa Ye**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60201-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Pi Pa Ye  | G099HS166RP1 | 62452 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 4              | 78            | 2              | 22 356        |
| <b>Type B</b> | 6              | 32            | 8              | 11 351        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9814 % (> 99.9651 %)  | 97.5000 % (> 93.7500 %) |
| <b>Type B</b> | 99.9182 % (> 99.8861 %)  | 80.0000 % (> 72.5000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Shan Yao       | 3.94                      | —                                 |
| Lian Qiao      | 5.72                      | —                                 |
| Ze Xie         | 6.28                      | —                                 |
| Fu Zi          | 6.88                      | —                                 |
| Tian Hua Fen   | 7.61                      | —                                 |
| Ji Li          | 8.06                      | —                                 |
| Ling Zhi       | 8.24                      | —                                 |
| Ren Dong Teng  | 8.43                      | —                                 |
| Zhe Bei Mu     | 8.65                      | —                                 |
| Bai Zi Ren     | 9.47                      | —                                 |
| Mu Zei         | 9.50                      | —                                 |
| Shen Qu        | 9.80                      | —                                 |
| Huo Ma Ren     | 10.19                     | —                                 |
| Bai Shao Yao   | 11.15                     | —                                 |
| Jin Yin Hua    | 11.87                     | —                                 |
| Ban Lan Gen    | 11.94                     | —                                 |
| Gua Lou        | 12.14                     | —                                 |
| San Qi         | 12.52                     | —                                 |
| Hou Po         | 12.57                     | —                                 |
| Lai Fu Zi      | 12.87                     | —                                 |
| Lian Zi        | 13.25                     | —                                 |
| He Huan Pi     | 13.41                     | —                                 |
| Jiao Gu Lan    | 13.70                     | —                                 |
| Sheng Jiang    | 14.08                     | —                                 |
| Fu Ling        | 14.36                     | —                                 |
| Dan Dou Chi    | 14.54                     | —                                 |
| Gu Sui Bu      | 14.69                     | —                                 |
| Fu Pen Zi      | 15.07                     | —                                 |
| Dan Shen       | 16.14                     | —                                 |
| Ku Shen        | 16.23                     | —                                 |
| Zhu Ru         | 16.36                     | —                                 |
| Suan Zao Ren   | 16.44                     | —                                 |
| Dang Gui       | 16.71                     | —                                 |
| Mao Dong Qing  | 17.03                     | —                                 |
| Ren Shen       | 17.32                     | —                                 |
| Ye Jiao Teng   | 17.43                     | —                                 |
| Che Qian Zi    | 17.54                     | —                                 |
| Chai Hu        | 17.72                     | —                                 |
| Tu Fu Ling     | 18.27                     | —                                 |
| Di Gu Pi       | 18.43                     | —                                 |
| Ji Xue Teng    | 18.44                     | —                                 |
| Jie Geng       | 18.48                     | —                                 |
| Cang Zhu       | 18.57                     | —                                 |
| Ci Wu Jia      | 18.58                     | —                                 |
| Gui Zhi        | 18.73                     | —                                 |
| Lu Gen         | 18.81                     | —                                 |
| Hong Jing Tian | 18.94                     | —                                 |
| Gou Teng       | 19.67                     | —                                 |
| Yan Hu Suo     | 19.80                     | —                                 |
| Tao Ren        | 20.07                     | —                                 |
| Ce Bai Ye      | 20.11                     | —                                 |
| Zhi Gan Cao    | 20.27                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Yu Jin          | 20.83                     | —                                 |
| Xie Bai         | 20.95                     | —                                 |
| She Gan         | 21.74                     | —                                 |
| Zhi Mu          | 21.84                     | —                                 |
| Zhu Ling        | 21.98                     | —                                 |
| Yin Yang Huo    | 22.27                     | —                                 |
| Guang Huo Xiang | 22.31                     | —                                 |
| Bai Xian Pi     | 22.47                     | —                                 |
| Fu Xiao Mai     | 22.91                     | —                                 |
| Qiang Huo       | 23.12                     | —                                 |
| Yi Yi Ren       | 23.87                     | —                                 |
| (Fen) Bi Xie    | 24.39                     | —                                 |
| Ban Xia (Jiang) | 24.41                     | —                                 |
| Fo Shou         | 24.41                     | —                                 |
| Gou Qi Zi       | 24.53                     | —                                 |
| Zhi Ke          | 24.77                     | —                                 |
| Ma Huang        | 24.84                     | —                                 |
| Rou Gui         | 25.05                     | —                                 |
| Gan Cao         | 25.31                     | —                                 |
| Qing Pi         | 26.03                     | —                                 |
| Mu Gua          | 26.18                     | —                                 |
| Long Yan Rou    | 27.86                     | —                                 |
| Chuang Mu Xiang | 28.65                     | —                                 |
| Huang Qin       | 28.70                     | —                                 |
| Ma Huang Gen    | 28.74                     | —                                 |
| Yuan Zhi        | 30.17                     | —                                 |
| Zi Hua Di Ding  | 30.26                     | —                                 |
| Bo He           | 32.79                     | —                                 |
| Mang Xiao       | 32.95                     | —                                 |
| Huang Lian      | 33.11                     | —                                 |
| Sang Zhi        | 33.26                     | —                                 |
| Jing Jie        | 33.28                     | —                                 |
| Du Zhong        | 33.93                     | —                                 |
| Chi Shao (Yao)  | 35.25                     | —                                 |
| Sha Ren         | 35.89                     | —                                 |
| Huang Bai       | 37.45                     | —                                 |
| Cang Er Zi      | 38.46                     | —                                 |
| Hong Hua        | 39.23                     | —                                 |
| Fu Shen         | 42.23                     | —                                 |
| Sang Ye         | 46.89                     | —                                 |
| Bai Jiang Cao   | 48.29                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62451     | 62451               | 0.00                         | 4.17                            |
| 62452     | 62452               | 0.00                         | 3.94                            |

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 2.4-2022-02

Validated substance/substance group **Pu Gong Ying**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50358-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Pu Gong Ying              | 2      | 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 | 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 34 694 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 *Pu Gong Ying*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G239HS308RN1 | 62263 <sup>†</sup> | 20      |
| PhytoComm | Pu Gong Ying | G239HS308RN1 | 62264 <sup>†</sup> | 20      |
| PhytoComm | Pu Gong Ying | G239HS308SH1 | 62635 <sup>†</sup> | 20      |
| PhytoComm | Pu Gong Ying | G239HS308SH1 | 62636 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 0              | 0             | 6              | 851           |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Yin Chen Hao        | 7.25                      | —                                 |
| Sang Ye             | 7.56                      | —                                 |
| Ze Lan              | 7.83                      | —                                 |
| Huang Lian          | 8.31                      | —                                 |
| Xin Yi              | 8.79                      | —                                 |
| Tu Fu Ling          | 9.30                      | —                                 |
| Xi Xian Cao         | 11.33                     | —                                 |
| Nü Zhen Zi          | 14.19                     | —                                 |
| Shan Yao            | 14.41                     | —                                 |
| Bai Jiang Cao       | 14.81                     | —                                 |
| Zhi Shi             | 15.86                     | —                                 |
| Sha Ren             | 16.82                     | —                                 |
| Dan Shen            | 18.47                     | —                                 |
| Han Lian Cao        | 19.63                     | —                                 |
| Hu Zhang            | 20.38                     | —                                 |
| Jiang Huang         | 20.81                     | —                                 |
| Zhi Ke              | 21.01                     | —                                 |
| Bo He               | 21.10                     | —                                 |
| Fu Zi               | 21.23                     | —                                 |
| Yu Xing Cao         | 22.00                     | —                                 |
| Du Zhong            | 22.26                     | —                                 |
| Huang Bai           | 23.73                     | —                                 |
| Che Qian Zi         | 23.77                     | —                                 |
| Bai Hua She She Cao | 23.98                     | —                                 |
| Qiang Huo           | 24.03                     | —                                 |
| Jiao Gu Lan         | 25.51                     | —                                 |
| Yu Jin              | 25.58                     | —                                 |
| Mao Dong Qing       | 25.86                     | —                                 |
| Chai Hu             | 28.36                     | —                                 |
| Mang Xiao           | 28.79                     | —                                 |
| Xiang Fu            | 29.31                     | —                                 |
| Hou Po              | 29.54                     | —                                 |
| Qing Hao            | 30.22                     | —                                 |
| Yi Mu Cao           | 31.57                     | —                                 |
| Zi Hua Di Ding      | 31.82                     | —                                 |
| Hong Jing Tian      | 31.84                     | —                                 |
| Ye Jiao Teng        | 32.10                     | —                                 |
| Yin Yang Huo        | 32.44                     | —                                 |
| Qing Pi             | 32.67                     | —                                 |
| Jing Jie            | 33.23                     | —                                 |
| Dan Dou Chi         | 33.52                     | —                                 |
| Cang Er Zi          | 34.09                     | —                                 |
| Fu Pen Zi           | 35.45                     | —                                 |
| Jin Yin Hua         | 36.32                     | —                                 |
| Chuang Mu Xiang     | 36.43                     | —                                 |
| Zi Su Zi            | 36.64                     | —                                 |
| Di Gu Pi            | 36.87                     | —                                 |
| Ma Huang            | 37.13                     | —                                 |

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| Substanz         | Distance in<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Bai Xian Pi      | 37.63                     | —                                 |
| Ce Bai Ye        | 38.22                     | —                                 |
| Suan Zao Ren     | 38.54                     | —                                 |
| Wang Bu Liu Xing | 38.80                     | —                                 |
| Xia Ku Cao       | 39.17                     | —                                 |
| He Huan Pi       | 40.00                     | —                                 |
| Chi Shao (Yao)   | 40.34                     | —                                 |
| Yan Hu Suo       | 40.95                     | —                                 |
| E Zhu            | 41.28                     | —                                 |
| Pi Pa Ye         | 41.92                     | —                                 |
| Niu Bang Zi      | 42.54                     | —                                 |
| Gu Sui Bu        | 42.87                     | —                                 |
| Gan Cao          | 43.41                     | —                                 |
| Lian Zi          | 43.91                     | —                                 |
| Bai Shao Yao     | 44.53                     | —                                 |
| (Bai) Dou Kou    | 45.78                     | —                                 |
| Ling Zhi         | 46.04                     | —                                 |
| Lian Qiao        | 46.17                     | —                                 |
| Ren Dong Teng    | 47.11                     | —                                 |
| Huang Qin        | 48.64                     | —                                 |
| Tian Hua Fen     | 49.08                     | —                                 |
| Cang Zhu         | 49.66                     | —                                 |
| Ji Xue Teng      | 49.80                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62263     | 62263                  | 0.00                            | 7.95                               |
| 62264     | 62264                  | 0.00                            | 7.83                               |
| 62635     | 62635                  | 0.00                            | 7.25                               |
| 62636     | 62636                  | 0.00                            | 7.54                               |

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





# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Qiang Huo**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60109-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Qiang Huo                 | 1      | 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 | G172HS154SL1 | 62719     | 40      | from supplier |
| PhytoComm | Qiang Huo | G172HS154SL1 | 62720     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Qiang Huo*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G172HS154SL1 | 62719 <sup>†</sup> | 20      |
| PhytoComm | Qiang Huo | G172HS154SL1 | 62720 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G172H0840321 | 1       |
| Phytocomm | Qiang Huo | g172h0841321 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 1              | 38            | 2              | 11 356        |
| <b>Type C</b> | 0              | 0             | 3              | 854           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9926 % (> 99.9605 %)  | 95.0000 % (> 87.5000 %)  |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mao Dong Qing   | 6.14                      | —                                 |
| Zi Hua Di Ding  | 6.95                      | —                                 |
| Hou Po          | 7.49                      | —                                 |
| Jing Jie        | 7.60                      | —                                 |
| Chai Hu         | 7.80                      | —                                 |
| Yu Jin          | 7.84                      | —                                 |
| Ling Zhi        | 8.18                      | —                                 |
| Bo He           | 8.39                      | —                                 |
| Du Zhong        | 8.50                      | —                                 |
| Qing Hao        | 9.78                      | —                                 |
| Yin Yang Huo    | 10.04                     | —                                 |
| Bai Xian Pi     | 10.17                     | —                                 |
| Dan Dou Chi     | 10.29                     | —                                 |
| Ce Bai Ye       | 11.56                     | —                                 |
| Qing Pi         | 11.61                     | —                                 |
| Fu Zi           | 11.83                     | —                                 |
| Sha Ren         | 13.36                     | —                                 |
| Ye Jiao Teng    | 13.83                     | —                                 |
| Dan Shen        | 14.95                     | —                                 |
| Shen Qu         | 15.50                     | —                                 |
| Lian Zi         | 15.64                     | —                                 |
| Jiao Gu Lan     | 15.71                     | —                                 |
| Ji Li           | 16.41                     | —                                 |
| Hong Jing Tian  | 16.84                     | —                                 |
| Shan Yao        | 16.85                     | —                                 |
| Guang Huo Xiang | 17.13                     | —                                 |
| Bai Jiang Cao   | 17.19                     | —                                 |
| Pi Pa Ye        | 17.24                     | —                                 |
| Che Qian Zi     | 17.26                     | —                                 |
| Fu Pen Zi       | 17.45                     | —                                 |
| Huang Bai       | 18.34                     | —                                 |
| Yan Hu Suo      | 18.44                     | —                                 |
| Ren Dong Teng   | 18.44                     | —                                 |
| Tian Hua Fen    | 19.03                     | —                                 |
| Zhu Ling        | 19.60                     | —                                 |
| Lian Qiao       | 19.68                     | —                                 |
| Jin Yin Hua     | 21.22                     | —                                 |
| Gu Sui Bu       | 22.21                     | —                                 |
| Ma Huang        | 23.15                     | —                                 |
| Di Gu Pi        | 23.18                     | —                                 |
| Zhi Ke          | 23.33                     | —                                 |
| Huang Lian      | 23.54                     | —                                 |
| Ji Xue Teng     | 23.91                     | —                                 |
| Ban Lan Gen     | 24.02                     | —                                 |
| He Huan Pi      | 24.62                     | —                                 |
| Suan Zao Ren    | 25.15                     | —                                 |
| Bai Shao Yao    | 25.17                     | —                                 |
| Gou Teng        | 26.43                     | —                                 |
| Tu Fu Ling      | 26.57                     | —                                 |
| Chuang Mu Xiang | 26.92                     | —                                 |
| Gan Cao         | 27.12                     | —                                 |
| Sheng Jiang     | 27.82                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zhe Bei Mu      | 28.65                     | —                                 |
| (Fen) Bi Xie    | 29.21                     | —                                 |
| Ren Shen        | 30.12                     | —                                 |
| Fu Ling         | 30.31                     | —                                 |
| Rou Gui         | 30.47                     | —                                 |
| Pu Gong Ying    | 30.48                     | —                                 |
| Lu Gen          | 30.58                     | —                                 |
| She Gan         | 30.65                     | —                                 |
| Ma Huang Gen    | 30.66                     | —                                 |
| Ze Lan          | 32.32                     | —                                 |
| Mang Xiao       | 32.77                     | —                                 |
| Zhi Gan Cao     | 33.12                     | —                                 |
| Huo Ma Ren      | 33.18                     | —                                 |
| Mu Zei          | 33.49                     | —                                 |
| Xi Xian Cao     | 34.73                     | —                                 |
| Sang Ye         | 34.99                     | —                                 |
| Cang Er Zi      | 35.02                     | —                                 |
| Gui Zhi         | 35.26                     | —                                 |
| Yi Yi Ren       | 36.02                     | —                                 |
| Tao Ren         | 36.79                     | —                                 |
| Hong Hua        | 36.90                     | —                                 |
| Cang Zhu        | 37.54                     | —                                 |
| Chi Shao (Yao)  | 37.81                     | —                                 |
| Sang Zhi        | 38.10                     | —                                 |
| Ban Zhi Lian    | 38.70                     | —                                 |
| Xie Bai         | 39.04                     | —                                 |
| Nü Zhen Zi      | 40.66                     | —                                 |
| Bai Zi Ren      | 41.17                     | —                                 |
| E Zhu           | 41.54                     | —                                 |
| Jiang Huang     | 42.05                     | —                                 |
| Jie Geng        | 42.20                     | —                                 |
| Zhu Ru          | 42.97                     | —                                 |
| Ci Wu Jia       | 43.16                     | —                                 |
| Ze Xie          | 43.25                     | —                                 |
| Huang Qin       | 44.21                     | —                                 |
| Wu Wei Zi       | 45.81                     | —                                 |
| Gua Lou         | 45.84                     | —                                 |
| San Qi          | 45.86                     | —                                 |
| Ban Xia (Jiang) | 46.19                     | —                                 |
| Dang Gui        | 47.18                     | —                                 |
| Niu Bang Zi     | 47.47                     | —                                 |
| Fu Xiao Mai     | 47.99                     | —                                 |
| Xin Yi          | 49.60                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62719     | 62719               | 0.00                         | 6.87                            |
| 62720     | 62720               | 0.00                         | 6.14                            |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Qin Jiao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60222-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Qin Jiao  | G113H1059921 | 62736 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Long Dan (Cao) | 7.21                      | —                                 |
| Bai Zhu        | 12.42                     | —                                 |
| Zhi Gan Cao    | 12.53                     | —                                 |
| Huang Qi       | 13.11                     | —                                 |
| Jie Geng       | 14.82                     | —                                 |
| Sang Zhi       | 18.70                     | —                                 |
| Bai He         | 19.65                     | —                                 |
| Chuan Mu Tong  | 20.25                     | —                                 |
| (Huai) Niu Xi  | 20.96                     | —                                 |
| Chuan Lian Zi  | 23.15                     | —                                 |
| Tian Hua Fen   | 23.44                     | —                                 |
| Dang Gui       | 23.74                     | —                                 |
| Chuan Niu Xi   | 25.08                     | —                                 |
| Chi Shao (Yao) | 26.10                     | —                                 |
| Di Gu Pi       | 26.33                     | —                                 |
| Yuan Zhi       | 26.93                     | —                                 |
| Mu Gua         | 27.55                     | —                                 |
| Bai Zhi        | 27.98                     | —                                 |
| Mang Xiao      | 29.41                     | —                                 |
| Lai Fu Zi      | 29.55                     | —                                 |
| Sha Shen (Bei) | 30.11                     | —                                 |
| Mi Huan Jun    | 30.27                     | —                                 |
| Zi Su Zi       | 30.37                     | —                                 |
| Bing Lang      | 31.18                     | —                                 |
| Gan Jiang      | 34.75                     | —                                 |
| E Zhu          | 35.22                     | —                                 |
| Lian Qiao      | 35.71                     | —                                 |
| Da Zao         | 36.30                     | —                                 |
| (Shi) Chang Pu | 36.56                     | —                                 |
| Shan Yao       | 37.51                     | —                                 |
| Chen Pi        | 39.15                     | —                                 |
| Cang Er Zi     | 42.02                     | —                                 |
| Ban Zhi Lian   | 42.06                     | —                                 |
| Fang Feng      | 42.96                     | —                                 |
| Ku Shen        | 43.08                     | —                                 |
| Niu Bang Zi    | 44.35                     | —                                 |
| Tu Fu Ling     | 45.39                     | —                                 |
| Zhi Ke         | 45.51                     | —                                 |
| Bai Shao Yao   | 46.11                     | —                                 |
| Yan Hu Suo     | 46.22                     | —                                 |
| Lian Zi        | 46.68                     | —                                 |
| Jiang Huang    | 48.40                     | —                                 |
| Gan Cao        | 48.83                     | —                                 |
| Bai Xian Pi    | 49.22                     | —                                 |
| Ju Hua         | 49.61                     | —                                 |
| Chai Hu        | 50.15                     | —                                 |

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                         | 8.72                            |
| 62736     | 62736               | 0.00                         | 7.21                            |

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 2.4-2022-02

Validated substance/substance group **Qing Hao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60198-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | G031HS145TR1 | 63023     | 40      | from supplier |
| PhytoComm | Qing Hao  | G031HS145TR1 | 63024     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G031HS145TR1 | 63023 <sup>†</sup> | 20      |
| PhytoComm | Qing Hao  | G031HS145TR1 | 63024 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 2              | 40            | 0              | 11 355        |
| <b>Type C</b> | 0              | 0             | 0              | 857           |

The substance/substance group *Qing 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9851 % (> 99.9531 %)  | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Qiang Huo       | 6.41                      | —                                 |
| Qing Pi         | 7.86                      | —                                 |
| Du Zhong        | 7.96                      | —                                 |
| Zi Hua Di Ding  | 8.09                      | —                                 |
| Jiao Gu Lan     | 8.76                      | —                                 |
| Mao Dong Qing   | 9.44                      | —                                 |
| Huang Bai       | 10.30                     | —                                 |
| Dan Shen        | 10.66                     | —                                 |
| Chai Hu         | 10.84                     | —                                 |
| Jing Jie        | 10.97                     | —                                 |
| Bo He           | 12.41                     | —                                 |
| Yu Jin          | 12.84                     | —                                 |
| Fu Zi           | 13.27                     | —                                 |
| Ce Bai Ye       | 14.06                     | —                                 |
| Yan Hu Suo      | 14.26                     | —                                 |
| Sha Ren         | 14.59                     | —                                 |
| Hou Po          | 14.61                     | —                                 |
| Shan Yao        | 15.13                     | —                                 |
| Hong Jing Tian  | 15.25                     | —                                 |
| Fu Pen Zi       | 15.46                     | —                                 |
| Pi Pa Ye        | 16.01                     | —                                 |
| Ling Zhi        | 16.84                     | —                                 |
| Bai Jiang Cao   | 16.86                     | —                                 |
| Dan Dou Chi     | 16.91                     | —                                 |
| Yin Yang Huo    | 17.55                     | —                                 |
| Jin Yin Hua     | 18.33                     | —                                 |
| Tian Hua Fen    | 18.42                     | —                                 |
| Bai Xian Pi     | 19.15                     | —                                 |
| Huang Lian      | 19.18                     | —                                 |
| Gu Sui Bu       | 19.20                     | —                                 |
| Sang Ye         | 19.87                     | —                                 |
| Zhi Ke          | 20.27                     | —                                 |
| Ye Jiao Teng    | 20.32                     | —                                 |
| Ren Dong Teng   | 20.51                     | —                                 |
| Ji Li           | 20.53                     | —                                 |
| Ma Huang        | 20.77                     | —                                 |
| Ban Lan Gen     | 21.11                     | —                                 |
| Guang Huo Xiang | 21.78                     | —                                 |
| Che Qian Zi     | 21.78                     | —                                 |
| Gan Cao         | 21.91                     | —                                 |
| Zhu Ling        | 22.29                     | —                                 |
| Tu Fu Ling      | 23.28                     | —                                 |
| Shen Qu         | 23.52                     | —                                 |
| She Gan         | 23.84                     | —                                 |
| Zhe Bei Mu      | 24.21                     | —                                 |
| Bai Shao Yao    | 24.27                     | —                                 |
| Ren Shen        | 24.50                     | —                                 |
| Lian Qiao       | 24.53                     | —                                 |
| Di Gu Pi        | 25.03                     | —                                 |
| Xi Xian Cao     | 25.19                     | —                                 |
| Lian Zi         | 25.20                     | —                                 |
| Ji Xue Teng     | 25.89                     | —                                 |
| Pu Gong Ying    | 26.58                     | —                                 |
| Hong Hua        | 26.72                     | —                                 |
| He Huan Pi      | 27.89                     | —                                 |
| Mu Zei          | 28.83                     | —                                 |
| Zhi Gan Cao     | 29.22                     | —                                 |
| Chuang Mu Xiang | 29.49                     | —                                 |
| Ze Lan          | 29.99                     | —                                 |

*continued on the next page*



continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Sheng Jiang     | 31.08                     | —                                 |
| Lu Gen          | 31.22                     | —                                 |
| Suan Zao Ren    | 31.39                     | —                                 |
| Cang Er Zi      | 31.68                     | —                                 |
| (Fen) Bi Xie    | 31.79                     | —                                 |
| Mang Xiao       | 32.27                     | —                                 |
| Gou Teng        | 33.13                     | —                                 |
| Fu Ling         | 33.37                     | —                                 |
| Nü Zhen Zi      | 33.45                     | —                                 |
| Cang Zhu        | 34.87                     | —                                 |
| Ze Xie          | 35.33                     | —                                 |
| Xie Bai         | 35.80                     | —                                 |
| Huo Ma Ren      | 36.40                     | —                                 |
| Jie Geng        | 36.51                     | —                                 |
| Tao Ren         | 38.62                     | —                                 |
| Gua Lou         | 38.92                     | —                                 |
| Chi Shao (Yao)  | 38.94                     | —                                 |
| Zhi Shi         | 39.21                     | —                                 |
| Huang Qin       | 39.82                     | —                                 |
| Wu Wei Zi       | 40.06                     | —                                 |
| Bai Zi Ren      | 40.13                     | —                                 |
| Ma Huang Gen    | 40.63                     | —                                 |
| Jiang Huang     | 41.15                     | —                                 |
| Ku Shen         | 41.31                     | —                                 |
| Gui Zhi         | 41.76                     | —                                 |
| Sang Zhi        | 43.29                     | —                                 |
| Rou Gui         | 43.69                     | —                                 |
| San Qi          | 43.75                     | —                                 |
| Dang Gui        | 44.02                     | —                                 |
| Xin Yi          | 44.07                     | —                                 |
| E Zhu           | 44.57                     | —                                 |
| Ban Zhi Lian    | 45.78                     | —                                 |
| Yi Yi Ren       | 46.16                     | —                                 |
| Yi Mu Cao       | 46.20                     | —                                 |
| Zhu Ru          | 47.19                     | —                                 |
| Yin Chen Hao    | 47.87                     | —                                 |
| Ban Xia (Jiang) | 48.75                     | —                                 |
| Ci Wu Jia       | 49.10                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 63023     | 63023                  | 0.00                            | 6.41                               |
| 63024     | 63024                  | 0.00                            | 7.07                               |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Qing Pi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50371-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Qing Pi                   | 1      | 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   | G074HS361SK1 | 62671     | 40      | from supplier |
| PhytoComm | Qing Pi   | G074HS361SK1 | 62672     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Pi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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   | G074HS361SK1 | 62671 <sup>†</sup> | 20      |
| PhytoComm | Qing Pi   | G074HS361SK1 | 62672 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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   | G074H0809621 | 1       |
| Phytocomm | Qing Pi   | g074h100713  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Qing Hao        | 5.41                      | —                                 |
| Huang Bai       | 9.74                      | —                                 |
| Zi Hua Di Ding  | 12.02                     | —                                 |
| Zhi Ke          | 12.91                     | —                                 |
| Gan Cao         | 14.10                     | —                                 |
| Sang Ye         | 14.43                     | —                                 |
| Shan Yao        | 14.63                     | —                                 |
| Jiao Gu Lan     | 15.78                     | —                                 |
| Du Zhong        | 16.65                     | —                                 |
| Qiang Huo       | 16.89                     | —                                 |
| Mao Dong Qing   | 17.20                     | —                                 |
| Fu Zi           | 18.06                     | —                                 |
| Chai Hu         | 18.49                     | —                                 |
| Dan Dou Chi     | 18.74                     | —                                 |
| Jin Yin Hua     | 18.90                     | —                                 |
| Sha Ren         | 19.99                     | —                                 |
| Dan Shen        | 20.31                     | —                                 |
| Huang Lian      | 20.89                     | —                                 |
| Hou Po          | 21.04                     | —                                 |
| Fu Pen Zi       | 21.14                     | —                                 |
| Zhe Bei Mu      | 21.24                     | —                                 |
| Jing Jie        | 21.44                     | —                                 |
| Hong Hua        | 21.52                     | —                                 |
| Bo He           | 22.35                     | —                                 |
| Ma Huang        | 22.49                     | —                                 |
| Ce Bai Ye       | 23.26                     | —                                 |
| Hong Jing Tian  | 23.36                     | —                                 |
| Yan Hu Suo      | 23.58                     | —                                 |
| Ban Lan Gen     | 23.66                     | —                                 |
| Yin Yang Huo    | 24.58                     | —                                 |
| She Gan         | 24.97                     | —                                 |
| Ye Jiao Teng    | 25.08                     | —                                 |
| Bai Jiang Cao   | 25.17                     | —                                 |
| Zhi Gan Cao     | 25.31                     | —                                 |
| Suan Zao Ren    | 26.06                     | —                                 |
| Lian Qiao       | 26.34                     | —                                 |
| Guang Huo Xiang | 26.53                     | —                                 |
| Pi Pa Ye        | 26.59                     | —                                 |
| Chuang Mu Xiang | 26.63                     | —                                 |
| Ren Dong Teng   | 28.48                     | —                                 |
| Tian Hua Fen    | 29.26                     | —                                 |
| Gu Sui Bu       | 29.50                     | —                                 |
| Cang Er Zi      | 29.63                     | —                                 |
| Ren Shen        | 30.10                     | —                                 |
| Ji Li           | 30.12                     | —                                 |
| Xi Xian Cao     | 30.17                     | —                                 |
| Xie Bai         | 30.31                     | —                                 |
| Bai Shao Yao    | 31.13                     | —                                 |
| Ku Shen         | 31.17                     | —                                 |
| Che Qian Zi     | 31.37                     | —                                 |
| Tu Fu Ling      | 31.54                     | —                                 |
| Wu Wei Zi       | 31.68                     | —                                 |

*continued on the next page*

continued from previous page

| Substanz         | Distance in<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| He Huan Pi       | 31.79                     | —                                 |
| Mang Xiao        | 32.01                     | —                                 |
| Mu Zei           | 32.39                     | —                                 |
| Di Gu Pi         | 32.71                     | —                                 |
| Ling Zhi         | 32.91                     | —                                 |
| Yu Jin           | 32.96                     | —                                 |
| Bai Xian Pi      | 33.34                     | —                                 |
| Jie Geng         | 33.46                     | —                                 |
| Lu Gen           | 33.48                     | —                                 |
| Ze Xie           | 34.86                     | —                                 |
| Cang Zhu         | 35.24                     | —                                 |
| Ze Lan           | 35.24                     | —                                 |
| Zhu Ling         | 35.39                     | —                                 |
| Nü Zhen Zi       | 35.62                     | —                                 |
| Lian Zi          | 35.95                     | —                                 |
| Pu Gong Ying     | 36.09                     | —                                 |
| Gua Lou          | 36.87                     | —                                 |
| Sheng Jiang      | 37.20                     | —                                 |
| Gou Qi Zi        | 37.70                     | —                                 |
| Huang Qin        | 38.32                     | —                                 |
| San Qi           | 40.58                     | —                                 |
| Tao Ren          | 41.07                     | —                                 |
| Ji Xue Teng      | 41.95                     | —                                 |
| Huo Ma Ren       | 42.13                     | —                                 |
| Bai Zi Ren       | 43.08                     | —                                 |
| Shen Qu          | 43.11                     | —                                 |
| (Fen) Bi Xie     | 43.42                     | —                                 |
| Zhi Shi          | 43.51                     | —                                 |
| Chi Shao (Yao)   | 43.63                     | —                                 |
| Xin Yi           | 43.66                     | —                                 |
| Dang Gui         | 43.68                     | —                                 |
| Gou Teng         | 45.00                     | —                                 |
| Jiang Huang      | 45.07                     | —                                 |
| Fu Ling          | 46.37                     | —                                 |
| Yin Chen Hao     | 46.62                     | —                                 |
| Yi Mu Cao        | 47.93                     | —                                 |
| Gui Zhi          | 48.67                     | —                                 |
| Zhu Ru           | 49.60                     | —                                 |
| Wang Bu Liu Xing | 49.80                     | —                                 |
| Rou Gui          | 49.95                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62671     | 62671               | 0.00                         | 5.94                            |
| 62672     | 62672               | 0.00                         | 5.41                            |

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 2.4-2022-02

Validated substance/substance group **Ren Dong Teng**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60104-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ren Dong Teng | G297HS144SK1 | 62696 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 3              | 79            | 1              | 22 357        |
| <b>Type B</b> | 3              | 39            | 1              | 11 354        |
| <b>Type C</b> | 0              | 0             | 0              | 857           |

The substance/substance group *Ren Dong 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9777 % (> 99.9614 %)  | 98.7500 % (> 95.0000 %) |
| <b>Type B</b> | 99.9554 % (> 99.9233 %)  | 97.5000 % (> 90.0000 %) |
| <b>Type C</b> | 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.

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

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ling Zhi        | 5.15                      | —                                 |
| Ce Bai Ye       | 5.82                      | —                                 |
| Shen Qu         | 5.87                      | —                                 |
| (Fen) Bi Xie    | 5.99                      | —                                 |
| Bai Xian Pi     | 6.65                      | —                                 |
| She Gan         | 6.99                      | —                                 |
| Gu Sui Bu       | 8.32                      | —                                 |
| Lu Gen          | 8.40                      | —                                 |
| Ye Jiao Teng    | 8.51                      | —                                 |
| Dan Dou Chi     | 8.57                      | —                                 |
| Zhu Ling        | 8.66                      | —                                 |
| Lian Zi         | 9.06                      | —                                 |
| Ji Xue Teng     | 9.51                      | —                                 |
| Yu Jin          | 9.51                      | —                                 |
| Ji Li           | 9.69                      | —                                 |
| Guang Huo Xiang | 9.73                      | —                                 |
| Rou Gui         | 9.95                      | —                                 |
| Chai Hu         | 10.06                     | —                                 |
| Hou Po          | 10.97                     | —                                 |
| Huo Ma Ren      | 11.02                     | —                                 |
| Che Qian Zi     | 11.34                     | —                                 |
| Gou Teng        | 11.34                     | —                                 |
| Shan Yao        | 11.63                     | —                                 |
| Ma Huang Gen    | 11.86                     | —                                 |
| Lian Qiao       | 11.92                     | —                                 |
| Mao Dong Qing   | 12.00                     | —                                 |
| Pi Pa Ye        | 12.10                     | —                                 |
| Suan Zao Ren    | 12.24                     | —                                 |
| He Huan Pi      | 12.24                     | —                                 |
| Bai Shao Yao    | 12.33                     | —                                 |
| Fu Pen Zi       | 12.41                     | —                                 |
| Tu Fu Ling      | 12.72                     | —                                 |
| Fu Ling         | 13.13                     | —                                 |
| Dan Shen        | 13.48                     | —                                 |
| Yin Yang Huo    | 13.55                     | —                                 |
| Yan Hu Suo      | 13.73                     | —                                 |
| Mu Zei          | 13.77                     | —                                 |
| Tian Hua Fen    | 14.11                     | —                                 |
| Fu Zi           | 14.29                     | —                                 |
| Sheng Jiang     | 14.60                     | —                                 |
| Gui Zhi         | 15.52                     | —                                 |
| Yi Yi Ren       | 17.01                     | —                                 |
| Qiang Huo       | 17.70                     | —                                 |
| Zhe Bei Mu      | 17.87                     | —                                 |
| Tao Ren         | 18.48                     | —                                 |
| Jiao Gu Lan     | 18.53                     | —                                 |
| Fo Shou         | 18.53                     | —                                 |
| Gan Cao         | 18.70                     | —                                 |
| Jin Yin Hua     | 18.87                     | —                                 |
| Bai Zi Ren      | 19.06                     | —                                 |
| Ze Xie          | 19.76                     | —                                 |
| Ma Huang        | 19.81                     | —                                 |
| Hong Jing Tian  | 20.05                     | —                                 |
| Ban Lan Gen     | 20.75                     | —                                 |
| Jing Jie        | 20.93                     | —                                 |
| Ci Wu Jia       | 21.56                     | —                                 |
| Di Gu Pi        | 21.90                     | —                                 |
| Ban Xia (Jiang) | 23.34                     | —                                 |
| Fu Xiao Mai     | 23.37                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zi Hua Di Ding  | 23.42                     | —                                 |
| Zhu Ru          | 24.54                     | —                                 |
| Zhi Gan Cao     | 25.46                     | —                                 |
| Qing Pi         | 25.68                     | —                                 |
| Fu Shen         | 25.84                     | —                                 |
| Du Zhong        | 26.61                     | —                                 |
| Sha Ren         | 26.73                     | —                                 |
| Cang Zhu        | 26.85                     | —                                 |
| Ren Shen        | 27.30                     | —                                 |
| Zhi Ke          | 27.64                     | —                                 |
| Lai Fu Zi       | 27.81                     | —                                 |
| Bo He           | 28.89                     | —                                 |
| Gua Lou         | 29.27                     | —                                 |
| Huang Lian      | 29.96                     | —                                 |
| Huang Bai       | 31.06                     | —                                 |
| San Qi          | 31.43                     | —                                 |
| Chuang Mu Xiang | 31.85                     | —                                 |
| Mang Xiao       | 32.17                     | —                                 |
| Dang Gui        | 32.46                     | —                                 |
| Jie Geng        | 32.76                     | —                                 |
| Huang Qin       | 36.43                     | —                                 |
| Xie Bai         | 36.62                     | —                                 |
| Sang Zhi        | 37.47                     | —                                 |
| Ku Shen         | 38.58                     | —                                 |
| Qing Hao        | 39.95                     | —                                 |
| Chi Shao (Yao)  | 40.31                     | —                                 |
| Long Yan Rou    | 42.22                     | —                                 |
| Bai Jiang Cao   | 42.37                     | —                                 |
| Zhi Mu          | 43.38                     | —                                 |
| Gou Qi Zi       | 45.15                     | —                                 |
| Cang Er Zi      | 46.65                     | —                                 |
| Ban Zhi Lian    | 47.27                     | —                                 |
| Mu Gua          | 47.34                     | —                                 |
| Hong Hua        | 47.41                     | —                                 |
| Bai Zhu         | 49.94                     | —                                 |
| Yuan Zhi        | 50.07                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62695     | 62695                  | 0.00                            | 5.99                               |
| 62696     | 62696                  | 0.00                            | 5.15                               |

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Ren Shen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60984-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Ren Shen; Ginseng radix et rhizoma

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ren Shen                  | 2      | 0      | 1      |

### Second-stage model

For differentiation of the substance/substance group *Ren 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 *Ren Shen*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Ren Shen  | G115HS003TG1 | 62881     | 40      | from supplier |
| PhytoComm | Ren Shen  | G115HS003TG1 | 62882     | 40      | from supplier |
| PhytoComm | Ren Shen  | G115H0562922 | 63001     | 40      | from supplier |
| PhytoComm | Ren Shen  | G115H0562922 | 63002     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Ren Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ren 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 | Ren Shen  | G115HS003TG1 | 62881 <sup>†</sup> | 20      |
| PhytoComm | Ren Shen  | G115HS003TG1 | 62882 <sup>†</sup> | 20      |
| PhytoComm | Ren Shen  | G115H0562922 | 63001 <sup>†</sup> | 20      |
| PhytoComm | Ren Shen  | G115H0562922 | 63002 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 *Ren Shen*.
- 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 | Ren Shen  | g115ho562121 | 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 *Ren 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 *Ren 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

The substance/substance group *Ren 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Long Yan Rou    | 13.65                     | —                                 |
| Ye Jiao Teng    | 16.01                     | —                                 |
| Gou Teng        | 16.28                     | —                                 |
| Bai Shao Yao    | 16.74                     | —                                 |
| Gui Zhi         | 17.18                     | —                                 |
| Ma Huang        | 17.31                     | —                                 |
| Zhe Bei Mu      | 17.97                     | —                                 |
| Jin Yin Hua     | 18.02                     | —                                 |
| Dang Gui        | 19.14                     | —                                 |
| Fo Shou         | 19.45                     | —                                 |
| Lian Qiao       | 19.45                     | —                                 |
| Tian Hua Fen    | 19.65                     | —                                 |
| Jiao Gu Lan     | 19.96                     | —                                 |
| Rou Gui         | 20.17                     | —                                 |
| Lu Gen          | 20.78                     | —                                 |
| Di Gu Pi        | 20.82                     | —                                 |
| Cang Zhu        | 21.02                     | —                                 |
| Yuan Zhi        | 21.11                     | —                                 |
| Tao Ren         | 21.28                     | —                                 |
| Jie Geng        | 21.41                     | —                                 |
| Ban Xia (Jiang) | 21.92                     | —                                 |
| Zhi Ke          | 22.12                     | —                                 |
| Ji Xue Teng     | 22.34                     | —                                 |
| San Qi          | 22.53                     | —                                 |
| He Huan Pi      | 23.01                     | —                                 |
| Mu Zei          | 23.48                     | —                                 |
| Pi Pa Ye        | 23.77                     | —                                 |
| Fu Shen         | 24.04                     | —                                 |
| Ze Xie          | 24.13                     | —                                 |
| Ren Dong Teng   | 24.35                     | —                                 |
| Huang Qin       | 24.38                     | —                                 |
| Ji Li           | 24.75                     | —                                 |
| Shen Qu         | 25.31                     | —                                 |
| Zhi Mu          | 25.33                     | —                                 |
| Zhu Ru          | 25.44                     | —                                 |
| Yin Yang Huo    | 25.49                     | —                                 |
| Bai Xian Pi     | 25.79                     | —                                 |
| Gu Sui Bu       | 26.13                     | —                                 |
| Ci Wu Jia       | 26.40                     | —                                 |
| Tu Fu Ling      | 26.41                     | —                                 |
| Ma Huang Gen    | 26.44                     | —                                 |
| Hou Po          | 26.60                     | —                                 |
| Ling Zhi        | 26.88                     | —                                 |
| Bai Zi Ren      | 26.92                     | —                                 |
| Yan Hu Suo      | 27.15                     | —                                 |
| Dan Shen        | 27.47                     | —                                 |
| Gou Qi Zi       | 27.57                     | —                                 |
| Huo Ma Ren      | 27.77                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ku Shen         | 27.98                     | —                                 |
| Hong Jing Tian  | 28.09                     | —                                 |
| Ban Lan Gen     | 28.42                     | —                                 |
| Fu Ling         | 28.43                     | —                                 |
| Fu Xiao Mai     | 28.55                     | —                                 |
| Fu Zi           | 28.77                     | —                                 |
| Gua Lou         | 29.04                     | —                                 |
| Sheng Jiang     | 29.08                     | —                                 |
| Lian Zi         | 29.21                     | —                                 |
| Mang Xiao       | 29.29                     | —                                 |
| Lai Fu Zi       | 29.66                     | —                                 |
| Gan Cao         | 29.67                     | —                                 |
| Fu Pen Zi       | 29.77                     | —                                 |
| Shan Yao        | 30.17                     | —                                 |
| (Fen) Bi Xie    | 30.81                     | —                                 |
| Mu Gua          | 31.36                     | —                                 |
| Dan Dou Chi     | 31.74                     | —                                 |
| Che Qian Zi     | 32.26                     | —                                 |
| Yi Yi Ren       | 32.45                     | —                                 |
| Sang Zhi        | 32.98                     | —                                 |
| Guang Huo Xiang | 33.86                     | —                                 |
| Suan Zao Ren    | 34.18                     | —                                 |
| Yu Jin          | 34.75                     | —                                 |
| She Gan         | 34.95                     | —                                 |
| Chi Shao (Yao)  | 35.23                     | —                                 |
| Chai Hu         | 35.46                     | —                                 |
| Hong Hua        | 35.62                     | —                                 |
| Xie Bai         | 36.88                     | —                                 |
| Huang Lian      | 36.98                     | —                                 |
| Huang Qi        | 37.64                     | —                                 |
| Qing Pi         | 38.08                     | —                                 |
| Chuan Lian Zi   | 39.66                     | —                                 |
| Qiang Huo       | 39.66                     | —                                 |
| Ce Bai Ye       | 40.09                     | —                                 |
| Jing Jie        | 40.66                     | —                                 |
| Zi Hua Di Ding  | 40.86                     | —                                 |
| Zhu Ling        | 41.74                     | —                                 |
| Mao Dong Qing   | 42.12                     | —                                 |
| Chuang Mu Xiang | 42.18                     | —                                 |
| Zhi Gan Cao     | 44.93                     | —                                 |
| Sha Ren         | 45.32                     | —                                 |
| Bo He           | 46.68                     | —                                 |
| Sang Ye         | 47.30                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ren 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62881     | 62881               | 0.00                         | 13.65                           |
| 62882     | 62882               | 0.00                         | 15.01                           |
| 63001     | 63001               | 0.00                         | 18.51                           |
| 63002     | 63002               | 0.00                         | 16.74                           |

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 2.4-2022-02

Validated substance/substance group **Rou Gui**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60169-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Rou Gui                   | 3      | 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 |
| PhytoComm | Rou Gui   | G069HS204TH1 | 62917     | 40      | from supplier |
| PhytoComm | Rou Gui   | G069HS204TH1 | 62918     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Rou Gui*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Rou Gui   | G069HS204RN1 | 62272 <sup>†</sup> | 20      |
| PhytoComm | Rou Gui   | G069HS204RM1 | 62443 <sup>†</sup> | 20      |
| PhytoComm | Rou Gui   | G069HS204RM1 | 62444 <sup>†</sup> | 20      |
| PhytoComm | Rou Gui   | G069HS204TH1 | 62917 <sup>†</sup> | 20      |
| PhytoComm | Rou Gui   | G069HS204TH1 | 62918 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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   | g069h0617123 | 1       |
| PhytoComm | Rou Gui   | G069H0617123 | 2       |
| Phytocomm | Rou Gui   | G069H0617323 | 1       |
| PhytoComm | Rou Gui   | G069H0617323 | 1       |
| Phytocomm | Rou Gui   | H0617022     | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 9              | 239           | 1              | 22 191        |
| <b>Type B</b> | 23             | 116           | 4              | 11 254        |
| <b>Type C</b> | 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        |
|---------------|-------------------------|-------------------------|
| <b>Type A</b> | 99.9715 % (> 99.9551 %) | 99.5833 % (> 98.3333 %) |
| <b>Type B</b> | 99.8450 % (> 99.8128 %) | 96.6667 % (> 94.1667 %) |
| <b>Type C</b> | 99.7674 % (> 99.1804 %) | n/a (n/a)               |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Gui Zhi         | 6.71                      | —                                 |
| Ma Huang Gen    | 6.86                      | —                                 |
| Sheng Jiang     | 7.66                      | —                                 |
| He Huan Pi      | 8.29                      | —                                 |
| Yi Yi Ren       | 8.33                      | —                                 |
| Fu Ling         | 8.64                      | —                                 |
| Ban Xia (Jiang) | 9.41                      | —                                 |
| Gou Teng        | 9.45                      | —                                 |
| Ji Xue Teng     | 10.36                     | —                                 |
| Fu Shen         | 10.42                     | —                                 |
| Mu Zei          | 10.60                     | —                                 |
| Di Gu Pi        | 11.68                     | —                                 |
| Fu Xiao Mai     | 11.72                     | —                                 |
| Fo Shou         | 13.22                     | —                                 |
| Tao Ren         | 13.47                     | —                                 |
| Zhu Ru          | 15.49                     | —                                 |
| Ye Jiao Teng    | 15.58                     | —                                 |
| Bai Xian Pi     | 15.60                     | —                                 |
| Lai Fu Zi       | 15.67                     | —                                 |
| Ci Wu Jia       | 15.78                     | —                                 |
| Bai Shao Yao    | 16.19                     | —                                 |
| Huo Ma Ren      | 16.72                     | —                                 |
| Lian Zi         | 17.43                     | —                                 |
| Lu Gen          | 17.67                     | —                                 |
| Bai Zi Ren      | 18.53                     | —                                 |
| Gu Sui Bu       | 18.80                     | —                                 |
| Ling Zhi        | 19.19                     | —                                 |
| Shen Qu         | 19.73                     | —                                 |
| Ji Li           | 19.91                     | —                                 |
| Zhe Bei Mu      | 22.36                     | —                                 |
| Ren Dong Teng   | 23.28                     | —                                 |
| Ze Xie          | 23.85                     | —                                 |
| Tu Fu Ling      | 24.59                     | —                                 |
| Tian Hua Fen    | 25.59                     | —                                 |
| Suan Zao Ren    | 25.64                     | —                                 |
| Zhu Ling        | 26.03                     | —                                 |
| (Fen) Bi Xie    | 26.96                     | —                                 |
| She Gan         | 28.24                     | —                                 |
| Pi Pa Ye        | 28.70                     | —                                 |
| Dan Dou Chi     | 28.83                     | —                                 |
| Lian Qiao       | 29.26                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Yu Jin          | 29.44                     | —                                 |
| Dan Shen        | 31.17                     | —                                 |
| Yan Hu Suo      | 31.46                     | —                                 |
| Mang Xiao       | 32.43                     | —                                 |
| Jin Yin Hua     | 32.86                     | —                                 |
| Shan Yao        | 33.74                     | —                                 |
| Gua Lou         | 34.01                     | —                                 |
| Zhi Mu          | 34.19                     | —                                 |
| Ren Shen        | 34.40                     | —                                 |
| Jiao Gu Lan     | 34.74                     | —                                 |
| Zhi Ke          | 34.77                     | —                                 |
| Jie Geng        | 35.30                     | —                                 |
| Yin Yang Huo    | 35.35                     | —                                 |
| Cang Zhu        | 35.69                     | —                                 |
| Dang Gui        | 35.81                     | —                                 |
| Ce Bai Ye       | 36.49                     | —                                 |
| Hong Jing Tian  | 36.62                     | —                                 |
| Huang Qin       | 37.36                     | —                                 |
| Fu Pen Zi       | 38.06                     | —                                 |
| Ma Huang        | 38.16                     | —                                 |
| Ban Lan Gen     | 38.21                     | —                                 |
| Chai Hu         | 38.88                     | —                                 |
| Mao Dong Qing   | 38.93                     | —                                 |
| Fu Zi           | 39.83                     | —                                 |
| Guang Huo Xiang | 40.10                     | —                                 |
| San Qi          | 42.08                     | —                                 |
| Hou Po          | 43.95                     | —                                 |
| Yuan Zhi        | 45.10                     | —                                 |
| Gan Cao         | 45.23                     | —                                 |
| Qiang Huo       | 45.56                     | —                                 |
| Mu Gua          | 45.98                     | —                                 |
| Sang Zhi        | 47.48                     | —                                 |
| Huang Lian      | 48.05                     | —                                 |
| Long Yan Rou    | 48.37                     | —                                 |
| Gou Qi Zi       | 48.61                     | —                                 |
| Jing Jie        | 48.98                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62271     | 62271                  | 0.00                            | 6.96                               |
| 62272     | 62272                  | 0.00                            | 6.82                               |
| 62443     | 62443                  | 0.00                            | 6.71                               |
| 62444     | 62444                  | 0.00                            | 6.86                               |
| 62917     | 62917                  | 0.00                            | 8.57                               |
| 62918     | 62918                  | 0.00                            | 7.54                               |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **San Qi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60415-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| San Qi                    | 1      | 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    | G203HS030SL1 | 62701     | 40      | from supplier |
| PhytoComm | San Qi    | G203HS030SL1 | 62702     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *San Qi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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    | G203HS030SL1 | 62701 <sup>†</sup> | 20      |
| PhytoComm | San Qi    | G203HS030SL1 | 62702 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 1              | 0             | 1              | 855           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| Ku Shen       | 5.07                      | —                                 |
| Lian Qiao     | 8.98                      | —                                 |
| Shan Yao      | 9.08                      | —                                 |
| Pi Pa Ye      | 9.55                      | —                                 |
| Bai Shao Yao  | 10.66                     | —                                 |
| Zhi Mu        | 10.76                     | —                                 |
| Ji Li         | 11.59                     | —                                 |
| Bai Zi Ren    | 11.94                     | —                                 |
| Zhu Ru        | 14.25                     | —                                 |
| Suan Zao Ren  | 14.31                     | —                                 |
| Lai Fu Zi     | 14.33                     | —                                 |
| Ren Shen      | 14.69                     | —                                 |
| Zhe Bei Mu    | 14.70                     | —                                 |
| Jiao Gu Lan   | 15.41                     | —                                 |
| Huo Ma Ren    | 15.71                     | —                                 |
| Jie Geng      | 15.87                     | —                                 |
| Ling Zhi      | 15.88                     | —                                 |
| Tian Hua Fen  | 16.25                     | —                                 |
| Xie Bai       | 16.77                     | —                                 |
| Jin Yin Hua   | 16.87                     | —                                 |
| Lian Zi       | 16.88                     | —                                 |
| Mu Gua        | 17.57                     | —                                 |
| Gua Lou       | 18.52                     | —                                 |
| Sheng Jiang   | 18.73                     | —                                 |
| Shen Qu       | 18.76                     | —                                 |
| Mu Zei        | 19.08                     | —                                 |
| Cang Zhu      | 19.50                     | —                                 |
| Ren Dong Teng | 19.53                     | —                                 |
| Gou Qi Zi     | 19.55                     | —                                 |
| Dang Gui      | 19.59                     | —                                 |
| Di Gu Pi      | 19.62                     | —                                 |
| Fu Zi         | 19.78                     | —                                 |
| Hou Po        | 20.06                     | —                                 |
| Fu Ling       | 20.34                     | —                                 |
| Mao Dong Qing | 20.50                     | —                                 |
| He Huan Pi    | 21.21                     | —                                 |
| Yuan Zhi      | 21.38                     | —                                 |
| Ye Jiao Teng  | 21.96                     | —                                 |
| Ze Xie        | 22.80                     | —                                 |
| Ban Lan Gen   | 24.77                     | —                                 |
| Gui Zhi       | 24.85                     | —                                 |
| Dan Dou Chi   | 24.96                     | —                                 |
| Ci Wu Jia     | 25.09                     | —                                 |
| Zhi Ke        | 26.10                     | —                                 |
| Dan Shen      | 26.42                     | —                                 |
| Ji Xue Teng   | 26.76                     | —                                 |
| Fu Xiao Mai   | 26.81                     | —                                 |
| Yi Yi Ren     | 27.35                     | —                                 |
| Tu Fu Ling    | 27.39                     | —                                 |
| Che Qian Zi   | 28.04                     | —                                 |
| Lu Gen        | 28.12                     | —                                 |
| Gou Teng      | 28.18                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Gu Sui Bu       | 28.51                     | —                                 |
| Fu Pen Zi       | 28.98                     | —                                 |
| Yan Hu Suo      | 29.30                     | —                                 |
| Tao Ren         | 29.48                     | —                                 |
| Chai Hu         | 30.15                     | —                                 |
| Ban Xia (Jiang) | 30.55                     | —                                 |
| Rou Gui         | 30.60                     | —                                 |
| Fo Shou         | 30.83                     | —                                 |
| Chuang Mu Xiang | 30.92                     | —                                 |
| Guang Huo Xiang | 30.98                     | —                                 |
| Yu Jin          | 31.26                     | —                                 |
| Bai Xian Pi     | 32.03                     | —                                 |
| Gan Cao         | 32.07                     | —                                 |
| Huang Qin       | 32.24                     | —                                 |
| Long Yan Rou    | 33.84                     | —                                 |
| Mang Xiao       | 34.01                     | —                                 |
| Ce Bai Ye       | 34.61                     | —                                 |
| Zhi Gan Cao     | 34.78                     | —                                 |
| Yin Yang Huo    | 35.00                     | —                                 |
| Zhu Ling        | 35.24                     | —                                 |
| Qing Pi         | 35.27                     | —                                 |
| Hong Jing Tian  | 35.28                     | —                                 |
| Qiang Huo       | 35.70                     | —                                 |
| She Gan         | 38.26                     | —                                 |
| Ma Huang        | 38.58                     | —                                 |
| Cang Er Zi      | 39.68                     | —                                 |
| (Fen) Bi Xie    | 40.38                     | —                                 |
| Sang Zhi        | 40.65                     | —                                 |
| Ma Huang Gen    | 41.03                     | —                                 |
| Chi Shao (Yao)  | 41.78                     | —                                 |
| Du Zhong        | 42.75                     | —                                 |
| Huang Lian      | 43.03                     | —                                 |
| Zi Hua Di Ding  | 43.11                     | —                                 |
| Bo He           | 44.26                     | —                                 |
| Hong Hua        | 46.36                     | —                                 |
| Sha Ren         | 48.20                     | —                                 |
| Huang Bai       | 50.36                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62701     | 62701                  | 0.00                            | 5.07                               |
| 62702     | 62702                  | 0.00                            | 5.13                               |

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 2.4-2022-02

Validated substance/substance group **Sang Bai Pi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50287-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G161H1042921 | 62883     | 40      | from supplier |
| PhytoComm | Sang Bai Pi | G161H1042921 | 62884     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G161H1042921 | 62883 <sup>†</sup> | 20      |
| PhytoComm | Sang Bai Pi | G161H1042921 | 62884 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Yin Chen Hao   | 11.03                     | —                                 |
| Gu Sui Bu      | 11.89                     | —                                 |
| Xuan Fu Hua    | 15.58                     | —                                 |
| He Huan Pi     | 15.79                     | —                                 |
| Sang Ji Shend  | 18.37                     | —                                 |
| Bu Gu Zhi      | 18.59                     | —                                 |
| Chen Pi        | 19.62                     | —                                 |
| He Shou Wu     | 19.80                     | —                                 |
| Wu Zhu Yu      | 20.73                     | —                                 |
| Tu Si Zi       | 24.15                     | —                                 |
| Sha Ren        | 24.17                     | —                                 |
| Mang Xiao      | 26.81                     | —                                 |
| Jiang Huang    | 27.19                     | —                                 |
| Jing Jie       | 27.71                     | —                                 |
| Nü Zhen Zi     | 27.94                     | —                                 |
| (Shi) Chang Pu | 28.95                     | —                                 |
| Dan Zhu Ye     | 32.49                     | —                                 |
| (Bai) Dou Kou  | 33.55                     | —                                 |
| Wu Yao         | 33.83                     | —                                 |
| Yi Mu Cao      | 34.01                     | —                                 |
| Jin Qian Cao   | 35.44                     | —                                 |
| Du Zhong       | 35.94                     | —                                 |
| Ge Gen         | 36.11                     | —                                 |
| Hong Jing Tian | 39.90                     | —                                 |
| Mu Dan Pi      | 40.35                     | —                                 |
| Shan Yao       | 40.52                     | —                                 |
| Gou Teng       | 41.18                     | —                                 |
| Xiao Hui Xiang | 41.40                     | —                                 |
| Hu Zhang       | 42.48                     | —                                 |
| Sang Ye        | 44.83                     | —                                 |
| Shan Yu Rou    | 45.41                     | —                                 |
| Ju Hua         | 45.58                     | —                                 |
| Fang Feng      | 45.87                     | —                                 |
| Wu Jia Pi      | 45.99                     | —                                 |
| E Zhu          | 48.02                     | —                                 |
| Ku Shen        | 48.25                     | —                                 |
| Yu Xing Cao    | 49.30                     | —                                 |
| Hua Shi        | 50.18                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62883     | 62883               | 0.00                         | 11.42                           |
| 62884     | 62884               | 0.00                         | 11.03                           |

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 2.4-2022-02

Validated substance/substance group **Sang Ji Shend**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60142-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G146H1045822 | 62543     | 40      | from supplier |
| PhytoComm | Sang Ji Shend | G146H1045822 | 62544     | 40      | from supplier |
| PhytoComm | Sang Ji Shend | G146H1045922 | 62865     | 40      | from supplier |
| PhytoComm | Sang Ji Shend | G146H1045922 | 62866     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G146H1045822 | 62543 <sup>†</sup> | 20      |
| PhytoComm | Sang Ji Shend | G146H1045822 | 62544 <sup>†</sup> | 20      |
| PhytoComm | Sang Ji Shend | G146H1045922 | 62865 <sup>†</sup> | 20      |
| PhytoComm | Sang Ji Shend | G146H1045922 | 62866 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 | G146H1045322 | 1       |
| Phytocomm | Sang Ji Shend | G146H1045522 | 4       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| He Shou Wu          | 10.51                     | —                                 |
| Gu Sui Bu           | 11.59                     | —                                 |
| Xuan Fu Hua         | 13.79                     | —                                 |
| Yin Chen Hao        | 17.29                     | —                                 |
| Sang Bai Pi         | 22.23                     | —                                 |
| Mang Xiao           | 23.42                     | —                                 |
| He Huan Pi          | 23.83                     | —                                 |
| Ge Gen              | 24.85                     | —                                 |
| Hong Jing Tian      | 26.90                     | —                                 |
| Jing Jie            | 27.00                     | —                                 |
| Wu Zhu Yu           | 29.51                     | —                                 |
| Bu Gu Zhi           | 31.56                     | —                                 |
| Chen Pi             | 31.63                     | —                                 |
| Dan Zhu Ye          | 32.98                     | —                                 |
| Nü Zhen Zi          | 33.11                     | —                                 |
| Sha Ren             | 34.16                     | —                                 |
| Gou Teng            | 36.29                     | —                                 |
| Jin Qian Cao        | 38.32                     | —                                 |
| Du Zhong            | 38.78                     | —                                 |
| Yi Mu Cao           | 38.93                     | —                                 |
| Hu Zhang            | 40.80                     | —                                 |
| Tu Si Zi            | 43.17                     | —                                 |
| Jiang Huang         | 44.12                     | —                                 |
| Wu Yao              | 44.71                     | —                                 |
| Mu Dan Pi           | 45.78                     | —                                 |
| Sang Ye             | 45.99                     | —                                 |
| Bai Hua She She Cao | 46.66                     | —                                 |
| Shan Yu Rou         | 47.49                     | —                                 |
| (Shi) Chang Pu      | 47.55                     | —                                 |
| Xia Ku Cao          | 48.47                     | —                                 |
| (Bai) Dou Kou       | 48.60                     | —                                 |
| Wu Jia Pi           | 48.99                     | —                                 |
| Fang Feng           | 49.31                     | —                                 |
| Hua Shi             | 49.63                     | —                                 |
| Xiao Hui Xiang      | 49.97                     | —                                 |

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                         | 20.10                           |
| 62544     | 62544               | 0.00                         | 20.62                           |
| 62865     | 62865               | 0.00                         | 11.38                           |
| 62866     | 62866               | 0.00                         | 10.51                           |

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 2.4-2022-02

Validated substance/substance group **Sang Ye**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60079-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Sang Ye                   | 2      | 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 |
| PhytoComm | Sang Ye   | G162H1043021 | 62993     | 40      | from supplier |
| PhytoComm | Sang Ye   | G162H1043021 | 62994     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Ye*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Sang Ye   | G162HS206RQ1 | 62462 <sup>†</sup> | 20      |
| PhytoComm | Sang Ye   | G162H1043021 | 62993 <sup>†</sup> | 20      |
| PhytoComm | Sang Ye   | G162H1043021 | 62994 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 0              | 0             | 5              | 852           |

The substance/substance group *Sang 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Zhi Shi          | 9.01                      | —                                 |
| Yin Chen Hao     | 9.20                      | —                                 |
| Ze Lan           | 12.13                     | —                                 |
| Bai Jiang Cao    | 12.32                     | —                                 |
| Shan Yao         | 12.86                     | —                                 |
| Pu Gong Ying     | 13.04                     | —                                 |
| Huang Lian       | 13.74                     | —                                 |
| Sha Ren          | 14.95                     | —                                 |
| Nü Zhen Zi       | 15.67                     | —                                 |
| Tu Fu Ling       | 17.02                     | —                                 |
| Wu Jia Pi        | 18.08                     | —                                 |
| Xin Yi           | 18.09                     | —                                 |
| Jing Jie         | 18.53                     | —                                 |
| Xi Xian Cao      | 18.67                     | —                                 |
| Yu Xing Cao      | 18.80                     | —                                 |
| Qiang Huo        | 20.01                     | —                                 |
| Qing Pi          | 21.18                     | —                                 |
| Du Zhong         | 21.86                     | —                                 |
| Zi Hua Di Ding   | 22.20                     | —                                 |
| Dan Shen         | 22.22                     | —                                 |
| Huang Bai        | 22.26                     | —                                 |
| Mang Xiao        | 23.22                     | —                                 |
| Bo He            | 23.32                     | —                                 |
| Fu Zi            | 23.33                     | —                                 |
| Xian Mao         | 24.60                     | —                                 |
| Mao Dong Qing    | 24.61                     | —                                 |
| Zhi Ke           | 24.68                     | —                                 |
| Qing Hao         | 24.70                     | —                                 |
| Hong Jing Tian   | 25.43                     | —                                 |
| Jin Qian Cao     | 25.84                     | —                                 |
| (Sheng) Di Huang | 26.56                     | —                                 |
| Chai Hu          | 27.43                     | —                                 |
| Hou Po           | 28.15                     | —                                 |
| Ding Xiang       | 28.62                     | —                                 |
| Jiang Huang      | 28.90                     | —                                 |
| Dan Dou Chi      | 29.75                     | —                                 |
| Dan Zhu Ye       | 30.01                     | —                                 |
| Ma Huang         | 30.45                     | —                                 |
| Yin Yang Huo     | 30.74                     | —                                 |
| Han Lian Cao     | 30.74                     | —                                 |
| Yu Jin           | 30.76                     | —                                 |
| Hu Zhang         | 31.10                     | —                                 |
| Jiao Gu Lan      | 31.67                     | —                                 |
| Ce Bai Ye        | 31.78                     | —                                 |
| Fu Pen Zi        | 31.81                     | —                                 |
| Cang Er Zi       | 32.26                     | —                                 |
| Che Qian Zi      | 32.66                     | —                                 |
| Ye Jiao Teng     | 33.90                     | —                                 |

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| Substanz            | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Sang Ji Shend       | 34.01                     | —                                 |
| Yi Mu Cao           | 34.63                     | —                                 |
| Chuang Mu Xiang     | 35.06                     | —                                 |
| Hong Hua            | 35.27                     | —                                 |
| Jin Yin Hua         | 35.44                     | —                                 |
| Zi Su Zi            | 37.89                     | —                                 |
| Gan Cao             | 38.83                     | —                                 |
| Bai Hua She She Cao | 39.09                     | —                                 |
| Wang Bu Liu Xing    | 39.38                     | —                                 |
| Gou Teng            | 40.25                     | —                                 |
| Di Gu Pi            | 40.29                     | —                                 |
| Xiang Fu            | 40.81                     | —                                 |
| He Huan Pi          | 41.05                     | —                                 |
| Suan Zao Ren        | 41.22                     | —                                 |
| Ge Gen              | 41.52                     | —                                 |
| Wu Wei Zi           | 41.89                     | —                                 |
| Bai Xian Pi         | 41.91                     | —                                 |
| Niu Bang Zi         | 42.00                     | —                                 |
| Zhe Bei Mu          | 42.24                     | —                                 |
| Lian Qiao           | 42.47                     | —                                 |
| Yan Hu Suo          | 43.05                     | —                                 |
| Ban Lan Gen         | 43.51                     | —                                 |
| Pi Pa Ye            | 43.97                     | —                                 |
| Jie Geng            | 45.19                     | —                                 |
| Bai Shao Yao        | 45.35                     | —                                 |
| Bu Gu Zhi           | 45.50                     | —                                 |
| Chi Shao (Yao)      | 45.93                     | —                                 |
| Shu Di (Huang)      | 45.97                     | —                                 |
| Ren Dong Teng       | 46.22                     | —                                 |
| Zhi Gan Cao         | 46.49                     | —                                 |
| E Zhu               | 47.66                     | —                                 |
| Hua Shi             | 47.79                     | —                                 |
| Lian Zi             | 47.96                     | —                                 |
| Ling Zhi            | 48.13                     | —                                 |
| Huang Qin           | 48.61                     | —                                 |
| Gu Sui Bu           | 49.25                     | —                                 |
| Ren Shen            | 49.46                     | —                                 |
| Tian Hua Fen        | 49.74                     | —                                 |
| Xia Ku Cao          | 49.75                     | —                                 |
| He Shou Wu          | 49.80                     | —                                 |
| Guang Huo Xiang     | 50.01                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62461     | 62461               | 0.00                         | 9.01                            |
| 62462     | 62462               | 0.00                         | 9.11                            |
| 62993     | 62993               | 0.00                         | 18.10                           |
| 62994     | 62994               | 0.00                         | 18.08                           |

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 2.4-2022-02

Validated substance/substance group **Sang Zhi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60091-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | G164H1044821 | 62473     | 40      | from supplier |
| PhytoComm | Sang Zhi  | G164H1044821 | 62474     | 40      | from supplier |
| PhytoComm | Sang Zhi  | G164H1044921 | 62895     | 40      | from supplier |
| PhytoComm | Sang Zhi  | G164H1044921 | 62896     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G164H1044821 | 62473 <sup>†</sup> | 20      |
| PhytoComm | Sang Zhi  | G164H1044821 | 62474 <sup>†</sup> | 20      |
| PhytoComm | Sang Zhi  | G164H1044921 | 62895 <sup>†</sup> | 20      |
| PhytoComm | Sang Zhi  | G164H1044921 | 62896 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 5              | 0             | 0              | 852           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 99.3981 % (> 98.8154 %)  | n/a (n/a)                |

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

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

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

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

### 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Chuan Lian Zi  | 7.64                      | —                                 |
| Tian Hua Fen   | 10.05                     | —                                 |
| Mi Huan Jun    | 10.92                     | —                                 |
| Jie Geng       | 12.10                     | —                                 |
| Di Gu Pi       | 13.13                     | —                                 |
| Gan Jiang      | 13.35                     | —                                 |
| Bai He         | 13.93                     | —                                 |
| E Zhu          | 13.93                     | —                                 |
| Lai Fu Zi      | 15.49                     | —                                 |
| Sha Shen (Bei) | 15.56                     | —                                 |
| Chuan Mu Tong  | 15.75                     | —                                 |
| Bai Zhu        | 18.22                     | —                                 |
| Huang Qi       | 19.16                     | —                                 |
| Dang Gui       | 20.88                     | —                                 |
| Zhi Gan Cao    | 20.91                     | —                                 |
| Qin Jiao       | 21.06                     | —                                 |
| Zi Su Zi       | 21.49                     | —                                 |
| Long Dan (Cao) | 23.24                     | —                                 |
| Cang Er Zi     | 23.56                     | —                                 |
| Mang Xiao      | 24.56                     | —                                 |
| Ban Zhi Lian   | 25.18                     | —                                 |
| Shan Yao       | 26.34                     | —                                 |
| (Huai) Niu Xi  | 26.68                     | —                                 |
| Jiang Huang    | 28.21                     | —                                 |
| Chi Shao (Yao) | 28.34                     | —                                 |
| Bai Zhi        | 30.19                     | —                                 |
| Mu Gua         | 30.21                     | —                                 |
| Da Zao         | 30.91                     | —                                 |
| Lian Zi        | 32.81                     | —                                 |
| Chuan Niu Xi   | 33.78                     | —                                 |
| Niu Bang Zi    | 34.03                     | —                                 |
| Tu Fu Ling     | 34.23                     | —                                 |
| Bai Xian Pi    | 34.31                     | —                                 |
| Lian Qiao      | 34.54                     | —                                 |
| Suan Zao Ren   | 35.14                     | —                                 |
| Fu Ling        | 35.42                     | —                                 |
| Yan Hu Suo     | 35.54                     | —                                 |
| (Bai) Dou Kou  | 35.54                     | —                                 |
| Bai Shao Yao   | 36.74                     | —                                 |
| Jin Yin Hua    | 37.03                     | —                                 |
| Yuan Zhi       | 37.25                     | —                                 |
| Ji Li          | 37.70                     | —                                 |
| Chai Hu        | 37.84                     | —                                 |
| Sha Ren        | 38.39                     | —                                 |
| Bing Lang      | 38.78                     | —                                 |
| Ku Shen        | 39.40                     | —                                 |
| Zhi Ke         | 39.40                     | —                                 |
| Bo He          | 39.67                     | —                                 |
| Qiang Huo      | 40.14                     | —                                 |
| Rou Gui        | 40.30                     | —                                 |
| Gou Teng       | 40.93                     | —                                 |
| Pu Gong Ying   | 41.02                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Chen Pi        | 41.30                     | —                                 |
| Xiao Hui Xiang | 41.43                     | —                                 |
| Huang Lian     | 41.70                     | —                                 |
| Yi Yi Ren      | 41.75                     | —                                 |
| He Huan Pi     | 42.16                     | —                                 |
| Ye Jiao Teng   | 42.28                     | —                                 |
| Zi Hua Di Ding | 42.34                     | —                                 |
| Fo Shou        | 42.71                     | —                                 |
| Ren Dong Teng  | 42.93                     | —                                 |
| Shen Qu        | 43.37                     | —                                 |
| Ji Xue Teng    | 44.16                     | —                                 |
| Dan Dou Chi    | 44.36                     | —                                 |
| Ce Bai Ye      | 44.77                     | —                                 |
| Zhe Bei Mu     | 44.90                     | —                                 |
| Zhu Ling       | 45.56                     | —                                 |
| Yu Jin         | 45.72                     | —                                 |
| Cang Zhu       | 45.72                     | —                                 |
| Gan Cao        | 45.84                     | —                                 |
| (Shi) Chang Pu | 45.99                     | —                                 |
| Mao Dong Qing  | 46.02                     | —                                 |
| Du Zhong       | 46.08                     | —                                 |
| Jing Jie       | 46.99                     | —                                 |
| Sheng Jiang    | 47.17                     | —                                 |
| Fu Zi          | 48.40                     | —                                 |
| Xiang Fu       | 49.13                     | —                                 |
| Ma Huang Gen   | 49.19                     | —                                 |
| Gu Sui Bu      | 49.21                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62473     | 62473                  | 0.00                            | 9.49                               |
| 62474     | 62474                  | 0.00                            | 9.32                               |
| 62895     | 62895                  | 0.00                            | 8.21                               |
| 62896     | 62896                  | 0.00                            | 7.64                               |

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 2.4-2022-02

Validated substance/substance group **Sha Ren**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60184-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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   | 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 |
| PhytoComm | Sha Ren   | G018HS179TH1 | 62957     | 40      | from supplier |
| PhytoComm | Sha Ren   | G018HS179TH1 | 62958     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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   | G018H0939821 | 62401 <sup>†</sup> | 20      |
| PhytoComm | Sha Ren   | G018H0939821 | 62404 <sup>†</sup> | 20      |
| PhytoComm | Sha Ren   | G018H0939922 | 62763 <sup>†</sup> | 20      |
| PhytoComm | Sha Ren   | G018H0939922 | 62764 <sup>†</sup> | 20      |
| PhytoComm | Sha Ren   | G018HS179TH1 | 62957 <sup>†</sup> | 20      |
| PhytoComm | Sha Ren   | G018HS179TH1 | 62958 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 2              | 120           | 0              | 11 275        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 99.9702 % (> 99.9380 %)  | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 99.7674 % (> 99.1806 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Bai Jiang Cao  | 7.88                      | —                                 |
| Bo He          | 8.38                      | —                                 |
| Qing Hao       | 9.58                      | —                                 |
| Chai Hu        | 10.29                     | —                                 |
| Yu Jin         | 10.30                     | —                                 |
| Du Zhong       | 10.71                     | —                                 |
| Dan Shen       | 11.97                     | —                                 |
| Fu Zi          | 12.54                     | —                                 |
| Jiao Gu Lan    | 12.71                     | —                                 |
| Qiang Huo      | 12.79                     | —                                 |
| Zi Hua Di Ding | 12.86                     | —                                 |
| Huang Bai      | 13.19                     | —                                 |
| Mao Dong Qing  | 13.46                     | —                                 |
| Jing Jie       | 13.95                     | —                                 |
| Gu Sui Bu      | 14.84                     | —                                 |
| Pu Gong Ying   | 15.04                     | —                                 |
| Huang Lian     | 15.23                     | —                                 |
| Zhi Ke         | 15.31                     | —                                 |
| Yin Chen Hao   | 16.08                     | —                                 |
| Tu Si Zi       | 16.65                     | —                                 |
| Hou Po         | 16.68                     | —                                 |
| Dan Dou Chi    | 17.20                     | —                                 |
| Ye Jiao Teng   | 17.60                     | —                                 |
| Tu Fu Ling     | 17.69                     | —                                 |
| Yin Yang Huo   | 17.77                     | —                                 |
| Chen Pi        | 18.25                     | —                                 |
| Fu Pen Zi      | 18.58                     | —                                 |
| Ce Bai Ye      | 18.63                     | —                                 |
| He Shou Wu     | 18.73                     | —                                 |
| Shan Yao       | 18.89                     | —                                 |
| Hong Jing Tian | 19.12                     | —                                 |
| Che Qian Zi    | 19.19                     | —                                 |
| Jiang Huang    | 19.24                     | —                                 |
| Ze Lan         | 19.55                     | —                                 |
| Qing Pi        | 19.85                     | —                                 |
| Bu Gu Zhi      | 20.00                     | —                                 |
| Bai Xian Pi    | 20.04                     | —                                 |
| (Bai) Dou Kou  | 20.76                     | —                                 |
| Wu Zhu Yu      | 21.12                     | —                                 |
| Pi Pa Ye       | 21.22                     | —                                 |
| Sang Ye        | 21.41                     | —                                 |

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| <b>Substanz</b>     | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|---------------------|-----------------------------------|-------------------------------------------|
| Ling Zhi            | 21.94                             | —                                         |
| Yan Hu Suo          | 22.47                             | —                                         |
| Sang Bai Pi         | 22.52                             | —                                         |
| Ma Huang            | 23.13                             | —                                         |
| Xi Xian Cao         | 23.26                             | —                                         |
| Sang Ji Shend       | 23.61                             | —                                         |
| Guang Huo Xiang     | 23.79                             | —                                         |
| Jin Yin Hua         | 23.90                             | —                                         |
| Ji Xue Teng         | 24.86                             | —                                         |
| Xuan Fu Hua         | 25.12                             | —                                         |
| Ren Dong Teng       | 25.28                             | —                                         |
| He Huan Pi          | 25.74                             | —                                         |
| Di Gu Pi            | 26.44                             | —                                         |
| Yi Mu Cao           | 26.97                             | —                                         |
| Bai Hua She She Cao | 27.67                             | —                                         |
| Mang Xiao           | 27.73                             | —                                         |
| Tian Hua Fen        | 27.76                             | —                                         |
| Bai Shao Yao        | 28.61                             | —                                         |
| Shen Qu             | 28.66                             | —                                         |
| Lian Zi             | 28.69                             | —                                         |
| Suan Zao Ren        | 28.89                             | —                                         |
| Yu Xing Cao         | 30.08                             | —                                         |
| Nü Zhen Zi          | 30.95                             | —                                         |
| Gan Cao             | 31.76                             | —                                         |
| Ren Shen            | 31.89                             | —                                         |
| Zhu Ling            | 31.92                             | —                                         |
| (Fen) Bi Xie        | 31.93                             | —                                         |
| Chuang Mu Xiang     | 32.21                             | —                                         |
| Lian Qiao           | 32.34                             | —                                         |
| Ji Li               | 32.61                             | —                                         |
| She Gan             | 32.93                             | —                                         |
| Ban Lan Gen         | 32.99                             | —                                         |
| Zhi Shi             | 33.08                             | —                                         |
| Xiao Hui Xiang      | 33.49                             | —                                         |
| Mu Zei              | 33.67                             | —                                         |
| Gou Teng            | 34.28                             | —                                         |
| Lu Gen              | 34.38                             | —                                         |
| Jin Qian Cao        | 34.44                             | —                                         |
| Wu Yao              | 34.72                             | —                                         |
| Gan Jiang           | 34.92                             | —                                         |
| Hong Hua            | 34.95                             | —                                         |
| Zhe Bei Mu          | 35.11                             | —                                         |
| Wang Bu Liu Xing    | 35.97                             | —                                         |
| Cang Zhu            | 36.71                             | —                                         |
| Cang Er Zi          | 37.11                             | —                                         |
| Sheng Jiang         | 37.45                             | —                                         |
| Tao Ren             | 37.69                             | —                                         |
| E Zhu               | 37.77                             | —                                         |
| Xin Yi              | 37.91                             | —                                         |
| Ban Zhi Lian        | 38.61                             | —                                         |
| Chi Shao (Yao)      | 39.60                             | —                                         |
| (Shi) Chang Pu      | 39.89                             | —                                         |
| Mu Dan Pi           | 39.96                             | —                                         |
| Jie Geng            | 40.16                             | —                                         |
| Zhi Gan Cao         | 40.56                             | —                                         |
| Ge Gen              | 40.58                             | —                                         |
| Dan Zhu Ye          | 40.61                             | —                                         |
| Hu Zhang            | 40.93                             | —                                         |
| Sha Shen (Bei)      | 41.31                             | —                                         |

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| Substanz     | Distance in<br>main model | Distance in<br>second-stage model |
|--------------|---------------------------|-----------------------------------|
| Shan Yu Rou  | 41.38                     | —                                 |
| Huo Ma Ren   | 41.48                     | —                                 |
| Chuan Niu Xi | 42.09                     | —                                 |
| Xiang Fu     | 42.41                     | —                                 |
| Ma Huang Gen | 43.27                     | —                                 |
| Rou Gui      | 43.38                     | —                                 |
| Du Huo       | 43.60                     | —                                 |
| Huang Qin    | 43.70                     | —                                 |
| Niu Bang Zi  | 44.04                     | —                                 |
| Ku Shen      | 44.34                     | —                                 |
| Wu Jia Pi    | 44.53                     | —                                 |
| Zi Su Zi     | 45.31                     | —                                 |
| Dang Gui     | 46.07                     | —                                 |
| Sang Zhi     | 47.13                     | —                                 |
| Fu Ling      | 47.14                     | —                                 |
| Mi Huan Jun  | 48.37                     | —                                 |
| Xie Bai      | 48.52                     | —                                 |
| Bai Zhi      | 48.92                     | —                                 |
| Yi Yi Ren    | 49.07                     | —                                 |
| Hua Shi      | 49.15                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62401     | 62401                  | 0.00                            | 19.24                              |
| 62404     | 62404                  | 0.00                            | 20.58                              |
| 62763     | 62763                  | 0.00                            | 15.13                              |
| 62764     | 62764                  | 0.00                            | 14.84                              |
| 62957     | 62957                  | 0.00                            | 8.29                               |
| 62958     | 62958                  | 0.00                            | 7.88                               |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Sha Shen (Bei)**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60200-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Sha Shen (Bei)            | 2      | 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 |
| PhytoComm | Sha Shen (Bei) | G117H0754921 | 62891     | 40      | from supplier |
| PhytoComm | Sha Shen (Bei) | G117H0754921 | 62892     | 40      | from supplier |

## Validation samples

A total of 34 694 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

**Type A** All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Sha Shen (Bei)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 320 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 119 spectra of 4 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 <sup>†</sup> | 20      |
| PhytoComm | Sha Shen (Bei) | G117H0754821 | 62588              | 59      |
| PhytoComm | Sha Shen (Bei) | G117H0754921 | 62891 <sup>†</sup> | 20      |
| PhytoComm | Sha Shen (Bei) | G117H0754921 | 62892 <sup>†</sup> | 20      |

- 11 278 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the



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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 118           | 2              | 22 320        |
| <b>Type B</b> | 0              | 117           | 2              | 11 278        |
| <b>Type C</b> | 0              | 0             | 4              | 853           |

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

|               | Specificity              | Recognition rate        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 98.3333 % (> 95.8333 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 98.3193 % (> 95.7983 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Tian Hua Fen        | 5.18                      | —                                 |
| Chuan Lian Zi       | 7.67                      | —                                 |
| Di Gu Pi            | 8.12                      | —                                 |
| E Zhu               | 10.16                     | —                                 |
| Sang Zhi            | 11.22                     | —                                 |
| Gan Jiang           | 14.58                     | —                                 |
| Bai He              | 15.89                     | —                                 |
| Jie Geng            | 16.22                     | —                                 |
| Jiang Huang         | 17.35                     | —                                 |
| Yan Hu Suo          | 17.65                     | —                                 |
| Lai Fu Zi           | 17.67                     | —                                 |
| (Bai) Dou Kou       | 18.06                     | —                                 |
| Zi Su Zi            | 18.14                     | —                                 |
| Bai Zhu             | 18.30                     | —                                 |
| Mi Huan Jun         | 19.77                     | —                                 |
| Cang Er Zi          | 20.02                     | —                                 |
| Chuan Mu Tong       | 22.76                     | —                                 |
| Long Dan (Cao)      | 22.91                     | —                                 |
| Sha Ren             | 23.40                     | —                                 |
| Dang Gui            | 23.80                     | —                                 |
| Mang Xiao           | 24.15                     | —                                 |
| Qin Jiao            | 24.22                     | —                                 |
| (Huai) Niu Xi       | 25.25                     | —                                 |
| Niu Bang Zi         | 25.28                     | —                                 |
| Huang Qi            | 25.68                     | —                                 |
| Zhi Gan Cao         | 25.84                     | —                                 |
| Shan Yao            | 26.29                     | —                                 |
| He Huan Pi          | 26.87                     | —                                 |
| Ban Zhi Lian        | 28.44                     | —                                 |
| Chen Pi             | 32.15                     | —                                 |
| Fu Ling             | 32.31                     | —                                 |
| Lian Zi             | 32.58                     | —                                 |
| Xiang Fu            | 33.29                     | —                                 |
| Bai Xian Pi         | 33.53                     | —                                 |
| Ji Li               | 34.47                     | —                                 |
| Chi Shao (Yao)      | 34.85                     | —                                 |
| Huang Lian          | 35.05                     | —                                 |
| Chuan Niu Xi        | 35.38                     | —                                 |
| Bai Hua She She Cao | 35.79                     | —                                 |
| Chai Hu             | 36.79                     | —                                 |
| Ren Dong Teng       | 36.96                     | —                                 |
| Bai Zhi             | 37.23                     | —                                 |
| Xiao Hui Xiang      | 37.50                     | —                                 |
| Bo He               | 37.83                     | —                                 |
| Tu Fu Ling          | 38.30                     | —                                 |
| Rou Gui             | 38.34                     | —                                 |
| Du Huo              | 38.55                     | —                                 |
| Qiang Huo           | 38.60                     | —                                 |
| Ku Shen             | 38.75                     | —                                 |
| Mu Gua              | 39.11                     | —                                 |
| Yi Yi Ren           | 39.14                     | —                                 |
| Suan Zao Ren        | 39.16                     | —                                 |

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| Substanz         | Distance in<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Bai Shao Yao     | 39.28                     | —                                 |
| Lian Qiao        | 39.59                     | —                                 |
| Jin Yin Hua      | 40.05                     | —                                 |
| Da Zao           | 40.85                     | —                                 |
| (Shi) Chang Pu   | 41.66                     | —                                 |
| Ye Jiao Teng     | 42.30                     | —                                 |
| Zhu Ling         | 42.35                     | —                                 |
| Shan Yu Rou      | 42.49                     | —                                 |
| Ce Bai Ye        | 42.62                     | —                                 |
| Pu Gong Ying     | 42.78                     | —                                 |
| Shen Qu          | 42.84                     | —                                 |
| Gou Teng         | 43.52                     | —                                 |
| Zi Hua Di Ding   | 43.54                     | —                                 |
| Dan Dou Chi      | 43.63                     | —                                 |
| Du Zhong         | 43.85                     | —                                 |
| Zhi Ke           | 44.03                     | —                                 |
| Xin Yi           | 44.12                     | —                                 |
| Yuan Zhi         | 44.16                     | —                                 |
| Fo Shou          | 44.44                     | —                                 |
| Ma Huang Gen     | 44.65                     | —                                 |
| Yu Jin           | 44.89                     | —                                 |
| San Qi           | 45.76                     | —                                 |
| Zhu Ru           | 45.95                     | —                                 |
| Sheng Jiang      | 46.05                     | —                                 |
| Wang Bu Liu Xing | 46.85                     | —                                 |
| Mao Dong Qing    | 47.14                     | —                                 |
| Wu Yao           | 47.27                     | —                                 |
| Ji Xue Teng      | 47.53                     | —                                 |
| Xi Xian Cao      | 47.96                     | —                                 |
| Sang Ji Shend    | 48.09                     | —                                 |
| Gan Cao          | 48.49                     | —                                 |
| Hong Jing Tian   | 49.18                     | —                                 |
| Zhe Bei Mu       | 49.39                     | —                                 |
| Ze Lan           | 49.86                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62587     | 62587                  | 0.00                            | 8.12                               |
| 62891     | 62891                  | 0.00                            | 5.38                               |
| 62892     | 62892                  | 0.00                            | 5.18                               |

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 2.4-2022-02

Validated substance/substance group **Shan Yao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60207-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Shan Yao                  | 2      | 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  | 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 34 694 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 Yao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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  | G091HS024RQ1 | 62447 <sup>†</sup> | 20      |
| PhytoComm | Shan Yao  | G091HS024RQ1 | 62448 <sup>†</sup> | 20      |
| PhytoComm | Shan Yao  | G091H0330822 | 62523 <sup>†</sup> | 20      |
| PhytoComm | Shan Yao  | G091H0330822 | 62524 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 3              | 159           | 1              | 22 277        |
| <b>Type B</b> | 13             | 78            | 2              | 11 304        |
| <b>Type C</b> | 2              | 4             | 0              | 851           |

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        |
|---------------|-------------------------|-------------------------|
| <b>Type A</b> | 99.9814 % (> 99.9651 %) | 99.3750 % (> 97.5000 %) |
| <b>Type B</b> | 99.8438 % (> 99.8116 %) | 97.5000 % (> 93.7500 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Pi Pa Ye        | 3.54                      | —                                 |
| Fu Zi           | 4.42                      | —                                 |
| Lian Qiao       | 4.73                      | —                                 |
| Zhe Bei Mu      | 5.67                      | —                                 |
| Ze Xie          | 6.68                      | —                                 |
| Ling Zhi        | 7.47                      | —                                 |
| Ren Dong Teng   | 7.79                      | —                                 |
| Ji Li           | 7.96                      | —                                 |
| Tian Hua Fen    | 8.22                      | —                                 |
| Shen Qu         | 10.02                     | —                                 |
| Bai Zi Ren      | 10.10                     | —                                 |
| Mu Zei          | 10.11                     | —                                 |
| Huo Ma Ren      | 10.22                     | —                                 |
| Gu Sui Bu       | 11.31                     | —                                 |
| Lian Zi         | 11.48                     | —                                 |
| Hou Po          | 11.53                     | —                                 |
| He Huan Pi      | 11.82                     | —                                 |
| Jiao Gu Lan     | 12.16                     | —                                 |
| Jin Yin Hua     | 12.62                     | —                                 |
| Bai Shao Yao    | 13.08                     | —                                 |
| Fu Pen Zi       | 13.09                     | —                                 |
| Suan Zao Ren    | 13.68                     | —                                 |
| Sheng Jiang     | 14.29                     | —                                 |
| Fu Ling         | 14.71                     | —                                 |
| Tu Fu Ling      | 15.36                     | —                                 |
| Gua Lou         | 15.57                     | —                                 |
| Chai Hu         | 15.74                     | —                                 |
| Che Qian Zi     | 15.79                     | —                                 |
| Dan Dou Chi     | 15.80                     | —                                 |
| Yan Hu Suo      | 16.03                     | —                                 |
| Ji Xue Teng     | 16.33                     | —                                 |
| Lai Fu Zi       | 16.59                     | —                                 |
| Dan Shen        | 16.69                     | —                                 |
| Guang Huo Xiang | 16.85                     | —                                 |
| Ce Bai Ye       | 16.99                     | —                                 |
| She Gan         | 17.23                     | —                                 |
| Yu Jin          | 17.34                     | —                                 |
| Ban Lan Gen     | 17.36                     | —                                 |
| San Qi          | 17.46                     | —                                 |
| Lu Gen          | 17.48                     | —                                 |
| Mao Dong Qing   | 18.12                     | —                                 |
| Gui Zhi         | 18.55                     | —                                 |
| Di Gu Pi        | 18.72                     | —                                 |
| Zhu Ling        | 19.04                     | —                                 |
| Tao Ren         | 19.34                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Cang Er Zi      | 19.35                     | —                                 |
| Bai Xian Pi     | 19.80                     | —                                 |
| Ye Jiao Teng    | 19.85                     | —                                 |
| Gou Teng        | 19.91                     | —                                 |
| Ren Shen        | 20.07                     | —                                 |
| Zhu Ru          | 20.08                     | —                                 |
| Yin Yang Huo    | 20.62                     | —                                 |
| Xie Bai         | 21.19                     | —                                 |
| Cang Zhu        | 21.73                     | —                                 |
| Ku Shen         | 21.80                     | —                                 |
| Jie Geng        | 21.98                     | —                                 |
| Ci Wu Jia       | 22.03                     | —                                 |
| Dang Gui        | 22.10                     | —                                 |
| Qiang Huo       | 22.38                     | —                                 |
| Gan Cao         | 22.42                     | —                                 |
| Rou Gui         | 22.76                     | —                                 |
| Hong Jing Tian  | 22.81                     | —                                 |
| Wu Wei Zi       | 22.95                     | —                                 |
| Zhi Gan Cao     | 22.98                     | —                                 |
| (Fen) Bi Xie    | 23.92                     | —                                 |
| Zhi Ke          | 24.46                     | —                                 |
| Ban Xia (Jiang) | 24.87                     | —                                 |
| Ma Huang        | 24.89                     | —                                 |
| Qing Pi         | 25.02                     | —                                 |
| Fu Xiao Mai     | 25.79                     | —                                 |
| Yi Yi Ren       | 26.00                     | —                                 |
| Sang Ye         | 27.53                     | —                                 |
| Gou Qi Zi       | 28.35                     | —                                 |
| Qing Hao        | 28.38                     | —                                 |
| Zi Hua Di Ding  | 28.95                     | —                                 |
| Zhi Mu          | 29.61                     | —                                 |
| Ma Huang Gen    | 29.82                     | —                                 |
| Huang Qin       | 29.94                     | —                                 |
| Chuang Mu Xiang | 30.86                     | —                                 |
| Huang Lian      | 31.38                     | —                                 |
| Fo Shou         | 31.47                     | —                                 |
| Du Zhong        | 31.86                     | —                                 |
| Jing Jie        | 32.21                     | —                                 |
| Hong Hua        | 32.72                     | —                                 |
| Mu Gua          | 32.81                     | —                                 |
| Bo He           | 33.30                     | —                                 |
| Mang Xiao       | 33.32                     | —                                 |
| Sha Ren         | 35.50                     | —                                 |
| Sang Zhi        | 36.16                     | —                                 |
| Long Yan Rou    | 37.03                     | —                                 |
| Chi Shao (Yao)  | 37.09                     | —                                 |
| Huang Bai       | 37.12                     | —                                 |
| Yuan Zhi        | 37.48                     | —                                 |
| Fu Shen         | 42.65                     | —                                 |
| Xi Xian Cao     | 45.23                     | —                                 |
| Bai Jiang Cao   | 47.18                     | —                                 |
| Niu Bang Zi     | 48.67                     | —                                 |
| Nü Zhen Zi      | 48.98                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62447     | 62447               | 0.00                         | 3.54                            |
| 62448     | 62448               | 0.00                         | 3.59                            |
| 62523     | 62523               | 0.00                         | 12.16                           |
| 62524     | 62524               | 0.00                         | 12.92                           |

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 2.4-2022-02

Validated substance/substance group **Shan Yu Rou**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60226-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Shan Yu Rou               | 1      | 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 | G080H0333921 | 63015     | 40      | from supplier |
| PhytoComm | Shan Yu Rou | G080H0333921 | 63016     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Shan Yu Rou*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G080H0333921 | 63015 <sup>†</sup> | 20      |
| PhytoComm | Shan Yu Rou | G080H0333921 | 63016 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G080H0333221 | 1       |
| Phytocomm | Shan Yu Rou | G080H0333421 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 39            | 1              | 11 357        |
| <b>Type C</b> | 0              | 1             | 3              | 853           |

The substance/substance group *Shan Yu 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 97.5000 % (> 90.0000 %)  |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| (Shi) Chang Pu      | 7.39                      | —                                 |
| Chen Pi             | 12.40                     | —                                 |
| Wu Yao              | 13.10                     | —                                 |
| Ju Hua              | 18.32                     | —                                 |
| Chuan Lian Zi       | 18.53                     | —                                 |
| Mu Dan Pi           | 18.81                     | —                                 |
| Dang Gui            | 19.72                     | —                                 |
| Xiang Fu            | 21.32                     | —                                 |
| Chuan Niu Xi        | 21.86                     | —                                 |
| Fang Feng           | 22.18                     | —                                 |
| Sha Ren             | 23.31                     | —                                 |
| Hong Jing Tian      | 23.60                     | —                                 |
| He Huan Pi          | 24.75                     | —                                 |
| Gu Sui Bu           | 25.58                     | —                                 |
| Jiang Huang         | 27.24                     | —                                 |
| Xu Duan             | 27.68                     | —                                 |
| Wu Zhu Yu           | 27.89                     | —                                 |
| Xiao Hui Xiang      | 27.99                     | —                                 |
| Mang Xiao           | 28.07                     | —                                 |
| Ba Ji Tian          | 28.11                     | —                                 |
| Ku Shen             | 29.47                     | —                                 |
| Huang Qi            | 30.80                     | —                                 |
| Bai Zhi             | 31.73                     | —                                 |
| Zhi Gan Cao         | 32.23                     | —                                 |
| Sang Ji Shend       | 32.75                     | —                                 |
| Du Huo              | 32.86                     | —                                 |
| Tian Hua Fen        | 33.02                     | —                                 |
| Yan Hu Suo          | 33.23                     | —                                 |
| Di Gu Pi            | 33.41                     | —                                 |
| (Huai) Niu Xi       | 33.42                     | —                                 |
| Yi Mu Cao           | 33.54                     | —                                 |
| Shan Yao            | 33.91                     | —                                 |
| Sang Bai Pi         | 34.99                     | —                                 |
| Yin Chen Hao        | 35.50                     | —                                 |
| Niu Bang Zi         | 35.55                     | —                                 |
| (Bai) Dou Kou       | 36.15                     | —                                 |
| Sang Zhi            | 36.36                     | —                                 |
| Zi Su Zi            | 36.39                     | —                                 |
| Bai Hua She She Cao | 36.78                     | —                                 |
| He Shou Wu          | 37.03                     | —                                 |
| Gan Jiang           | 38.95                     | —                                 |
| E Zhu               | 39.98                     | —                                 |
| Zhi Ke              | 40.89                     | —                                 |
| Jie Geng            | 41.14                     | —                                 |
| Bai Zhu             | 41.63                     | —                                 |
| Lian Qiao           | 41.91                     | —                                 |
| Da Zao              | 42.01                     | —                                 |
| Ge Gen              | 42.50                     | —                                 |
| Cang Er Zi          | 42.94                     | —                                 |
| Bing Lang           | 43.58                     | —                                 |
| Mi Huan Jun         | 44.21                     | —                                 |
| Xin Yi              | 44.39                     | —                                 |

*continued on the next page*

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| Substanz     | Distance in<br>main model | Distance in<br>second-stage model |
|--------------|---------------------------|-----------------------------------|
| Tu Si Zi     | 44.93                     | —                                 |
| Pu Gong Ying | 46.93                     | —                                 |
| Qin Jiao     | 47.48                     | —                                 |
| Suan Zao Ren | 47.83                     | —                                 |
| Nü Zhen Zi   | 47.94                     | —                                 |
| Sang Ye      | 48.82                     | —                                 |
| Lai Fu Zi    | 49.86                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 63015     | 63015                  | 0.00                            | 7.39                               |
| 63016     | 63016                  | 0.00                            | 8.00                               |

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 2.4-2022-02

Validated substance/substance group **She Gan**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10003577-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

She Gan; Belamcandae rhizoma

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| She Gan                   | 1      | 0      | 1      |

### Second-stage model

For differentiation of the substance/substance group *She Gan* 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 *She Gan*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | She Gan   | G048HS235TL1 | 62923     | 40      | from supplier |
| PhytoComm | She Gan   | G048HS235TL1 | 62924     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *She Gan*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *She Gan*.
- 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 | She Gan   | G048HS235TL1 | 62923 <sup>†</sup> | 20      |
| PhytoComm | She Gan   | G048HS235TL1 | 62924 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *She Gan*.
- 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 | She Gan   | G048H1034422 | 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 *She Gan* 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 *She Gan* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 78            | 2              | 22 360        |
| <b>Type B</b> | 1              | 39            | 1              | 11 356        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

The substance/substance group *She Gan* 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 97.5000 % (> 93.7500 %) |
| <b>Type B</b> | 99.9851 % (> 99.9531 %)  | 97.5000 % (> 90.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *She Gan* 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ren Dong Teng   | 3.80                      | —                                 |
| Shen Qu         | 6.09                      | —                                 |
| (Fen) Bi Xie    | 7.12                      | —                                 |
| Dan Dou Chi     | 8.18                      | —                                 |
| Bai Xian Pi     | 8.31                      | —                                 |
| Gu Sui Bu       | 8.38                      | —                                 |
| Lu Gen          | 8.46                      | —                                 |
| Ce Bai Ye       | 9.06                      | —                                 |
| Ling Zhi        | 9.07                      | —                                 |
| Huo Ma Ren      | 9.61                      | —                                 |
| Ye Jiao Teng    | 10.15                     | —                                 |
| Guang Huo Xiang | 10.31                     | —                                 |
| Lian Zi         | 10.39                     | —                                 |
| Zhu Ling        | 10.40                     | —                                 |
| Mu Zei          | 10.58                     | —                                 |
| He Huan Pi      | 10.87                     | —                                 |
| Gou Teng        | 11.72                     | —                                 |
| Ji Xue Teng     | 12.07                     | —                                 |
| Yin Yang Huo    | 12.11                     | —                                 |
| Yu Jin          | 12.22                     | —                                 |
| Dan Shen        | 12.32                     | —                                 |
| Bai Shao Yao    | 12.98                     | —                                 |
| Suan Zao Ren    | 13.16                     | —                                 |
| Fu Ling         | 13.32                     | —                                 |
| Pi Pa Ye        | 13.47                     | —                                 |
| Fu Pen Zi       | 13.61                     | —                                 |
| Shan Yao        | 13.83                     | —                                 |
| Tu Fu Ling      | 14.25                     | —                                 |
| Fu Zi           | 14.27                     | —                                 |
| Rou Gui         | 14.40                     | —                                 |
| Yan Hu Suo      | 14.47                     | —                                 |
| Ma Huang Gen    | 14.63                     | —                                 |
| Ji Li           | 14.80                     | —                                 |
| Gui Zhi         | 15.08                     | —                                 |
| Hou Po          | 15.09                     | —                                 |
| Lian Qiao       | 15.43                     | —                                 |
| Chai Hu         | 15.77                     | —                                 |
| Tao Ren         | 15.96                     | —                                 |
| Mao Dong Qing   | 16.42                     | —                                 |
| Tian Hua Fen    | 16.45                     | —                                 |
| Sheng Jiang     | 16.52                     | —                                 |
| Gan Cao         | 17.24                     | —                                 |
| Zhe Bei Mu      | 17.25                     | —                                 |
| Ma Huang        | 17.43                     | —                                 |
| Hong Jing Tian  | 17.47                     | —                                 |
| Che Qian Zi     | 17.66                     | —                                 |
| Jin Yin Hua     | 18.09                     | —                                 |
| Qiang Huo       | 19.33                     | —                                 |
| Ban Lan Gen     | 20.06                     | —                                 |
| Ci Wu Jia       | 20.16                     | —                                 |
| Jing Jie        | 20.18                     | —                                 |
| Yi Yi Ren       | 20.23                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jiao Gu Lan     | 20.83                     | —                                 |
| Fo Shou         | 21.00                     | —                                 |
| Bai Zi Ren      | 21.92                     | —                                 |
| Ze Xie          | 22.02                     | —                                 |
| Di Gu Pi        | 22.14                     | —                                 |
| Ban Xia (Jiang) | 22.89                     | —                                 |
| Zi Hua Di Ding  | 23.83                     | —                                 |
| Fu Xiao Mai     | 25.14                     | —                                 |
| Zhi Ke          | 26.06                     | —                                 |
| Cang Zhu        | 26.24                     | —                                 |
| Lai Fu Zi       | 26.39                     | —                                 |
| Sha Ren         | 26.93                     | —                                 |
| Zhu Ru          | 26.99                     | —                                 |
| Zhi Gan Cao     | 27.42                     | —                                 |
| Ren Shen        | 28.10                     | —                                 |
| Huang Lian      | 28.98                     | —                                 |
| Bo He           | 29.92                     | —                                 |
| Gua Lou         | 29.93                     | —                                 |
| Fu Shen         | 30.22                     | —                                 |
| Qing Pi         | 30.33                     | —                                 |
| Jie Geng        | 30.51                     | —                                 |
| Dang Gui        | 31.10                     | —                                 |
| Du Zhong        | 31.18                     | —                                 |
| Chuang Mu Xiang | 31.84                     | —                                 |
| Huang Bai       | 32.10                     | —                                 |
| Mang Xiao       | 32.31                     | —                                 |
| San Qi          | 33.12                     | —                                 |
| Huang Qin       | 33.58                     | —                                 |
| Sang Zhi        | 35.71                     | —                                 |
| Chi Shao (Yao)  | 38.01                     | —                                 |
| Long Yan Rou    | 38.77                     | —                                 |
| Xie Bai         | 40.38                     | —                                 |
| Zhi Mu          | 40.49                     | —                                 |
| Ku Shen         | 42.09                     | —                                 |
| Gou Qi Zi       | 42.67                     | —                                 |
| Hong Hua        | 43.78                     | —                                 |
| Bai Jiang Cao   | 43.91                     | —                                 |
| Mu Gua          | 44.86                     | —                                 |
| Qing Hao        | 46.83                     | —                                 |
| Cang Er Zi      | 49.09                     | —                                 |
| Yuan Zhi        | 49.16                     | —                                 |
| Bai Zhu         | 49.95                     | —                                 |
| Ban Zhi Lian    | 51.18                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *She Gan* 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62923     | 62923               | 0.00                         | 5.00                            |
| 62924     | 62924               | 0.00                         | 3.80                            |

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 2.4-2022-02

Validated substance/substance group **Shen Qu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60020-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Shen Qu   | G156HS222RP1 | 62460 <sup>†</sup> | 20      |
| PhytoComm | Shen Qu   | G156H0935821 | 62467 <sup>†</sup> | 20      |
| PhytoComm | Shen Qu   | G156H0935821 | 62468 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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   | G156H0935121 | 1       |
| phytoComm | Shen Qu   | g156h0935421 | 1       |
| PhytoComm | Shen Qu   | G156H0935521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 158           | 2              | 22 279        |
| <b>Type B</b> | 7              | 79            | 1              | 11 310        |
| <b>Type C</b> | 0              | 0             | 5              | 852           |

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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9926 % (> 99.9762 %)  | 98.7500 % (> 96.8750 %) |
| <b>Type B</b> | 99.8958 % (> 99.8636 %)  | 98.7500 % (> 95.0000 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| Huo Ma Ren    | 4.35                      | —                                 |
| Mu Zei        | 5.59                      | —                                 |
| Ren Dong Teng | 6.07                      | —                                 |
| Gu Sui Bu     | 6.79                      | —                                 |
| He Huan Pi    | 7.20                      | —                                 |
| Lian Zi       | 8.17                      | —                                 |
| Ji Li         | 8.66                      | —                                 |
| Shan Yao      | 8.93                      | —                                 |
| Tian Hua Fen  | 9.04                      | —                                 |
| Ling Zhi      | 9.10                      | —                                 |
| Ze Xie        | 9.45                      | —                                 |
| Bai Shao Yao  | 9.55                      | —                                 |
| Pi Pa Ye      | 9.55                      | —                                 |
| Zhe Bei Mu    | 10.27                     | —                                 |
| Lian Qiao     | 10.37                     | —                                 |
| Tao Ren       | 10.68                     | —                                 |
| Suan Zao Ren  | 10.93                     | —                                 |
| Sheng Jiang   | 11.00                     | —                                 |
| Fu Zi         | 11.35                     | —                                 |
| Lu Gen        | 11.40                     | —                                 |
| Bai Zi Ren    | 11.54                     | —                                 |
| Fu Ling       | 11.98                     | —                                 |
| Ji Xue Teng   | 12.13                     | —                                 |
| Ye Jiao Teng  | 12.43                     | —                                 |
| Gou Teng      | 12.53                     | —                                 |
| She Gan       | 13.50                     | —                                 |
| Ci Wu Jia     | 13.77                     | —                                 |
| Lai Fu Zi     | 13.89                     | —                                 |
| Ce Bai Ye     | 13.90                     | —                                 |
| Gui Zhi       | 13.97                     | —                                 |
| Bai Xian Pi   | 14.03                     | —                                 |
| Fu Pen Zi     | 14.20                     | —                                 |
| Di Gu Pi      | 14.71                     | —                                 |
| Zhu Ling      | 15.37                     | —                                 |
| Yu Jin        | 15.41                     | —                                 |
| (Fen) Bi Xie  | 15.93                     | —                                 |
| Dan Dou Chi   | 16.30                     | —                                 |
| Dan Shen      | 16.62                     | —                                 |
| Yan Hu Suo    | 17.31                     | —                                 |
| Hou Po        | 17.33                     | —                                 |
| Tu Fu Ling    | 17.60                     | —                                 |
| Chai Hu       | 17.65                     | —                                 |
| Jin Yin Hua   | 18.05                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Che Qian Zi     | 18.22                     | —                                 |
| Zhu Ru          | 18.34                     | —                                 |
| Rou Gui         | 18.58                     | —                                 |
| Ban Xia (Jiang) | 18.71                     | —                                 |
| Jiao Gu Lan     | 18.79                     | —                                 |
| Ban Lan Gen     | 19.07                     | —                                 |
| Guang Huo Xiang | 19.14                     | —                                 |
| Yin Yang Huo    | 19.19                     | —                                 |
| Mao Dong Qing   | 19.33                     | —                                 |
| Yi Yi Ren       | 19.76                     | —                                 |
| Gua Lou         | 20.13                     | —                                 |
| Ma Huang Gen    | 20.19                     | —                                 |
| Fu Xiao Mai     | 20.47                     | —                                 |
| Wu Wei Zi       | 21.09                     | —                                 |
| Fo Shou         | 21.34                     | —                                 |
| Cang Zhu        | 21.92                     | —                                 |
| Hong Jing Tian  | 22.55                     | —                                 |
| Gan Cao         | 23.33                     | —                                 |
| San Qi          | 23.58                     | —                                 |
| Ma Huang        | 23.96                     | —                                 |
| Qiang Huo       | 24.21                     | —                                 |
| Jie Geng        | 24.36                     | —                                 |
| Ren Shen        | 24.63                     | —                                 |
| Dang Gui        | 25.38                     | —                                 |
| Zhi Ke          | 25.99                     | —                                 |
| Zhi Gan Cao     | 30.22                     | —                                 |
| Jing Jie        | 30.59                     | —                                 |
| Cang Er Zi      | 31.55                     | —                                 |
| Huang Qin       | 31.63                     | —                                 |
| Zi Hua Di Ding  | 31.93                     | —                                 |
| Qing Pi         | 31.96                     | —                                 |
| Zhi Mu          | 32.07                     | —                                 |
| Fu Shen         | 32.79                     | —                                 |
| Chuang Mu Xiang | 33.13                     | —                                 |
| Mang Xiao       | 33.21                     | —                                 |
| Huang Lian      | 33.35                     | —                                 |
| Ku Shen         | 33.44                     | —                                 |
| Xie Bai         | 34.54                     | —                                 |
| Gou Qi Zi       | 34.71                     | —                                 |
| Sha Ren         | 35.35                     | —                                 |
| Mu Gua          | 35.83                     | —                                 |
| Du Zhong        | 36.09                     | —                                 |
| Bo He           | 36.45                     | —                                 |
| Long Yan Rou    | 36.52                     | —                                 |
| Sang Zhi        | 36.67                     | —                                 |
| Yuan Zhi        | 39.29                     | —                                 |
| Chi Shao (Yao)  | 39.44                     | —                                 |
| Huang Bai       | 40.10                     | —                                 |
| Yi Mu Cao       | 46.62                     | —                                 |

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                         | 5.23                            |
| 62460     | 62460               | 0.00                         | 4.35                            |
| 62467     | 62467               | 0.00                         | 21.09                           |
| 62468     | 62468               | 0.00                         | 21.75                           |

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 2.4-2022-02

Validated substance/substance group **Sheng Jiang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60017-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G253HS085SK1 | 62549     | 40      | from supplier |
| PhytoComm | Sheng Jiang | G253HS085SK1 | 62550     | 40      | from supplier |
| PhytoComm | Sheng Jiang | G253HS085TH2 | 62807     | 40      | from supplier |
| PhytoComm | Sheng Jiang | G253HS085TH2 | 62808     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G253HS085SK1 | 62549 <sup>†</sup> | 20      |
| PhytoComm | Sheng Jiang | G253HS085SK1 | 62550 <sup>†</sup> | 20      |
| PhytoComm | Sheng Jiang | G253HS085TH2 | 62807 <sup>†</sup> | 20      |
| PhytoComm | Sheng Jiang | G253HS085TH2 | 62808 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G253H0534321 | 1       |
| Phytocomm | Sheng Jiang | G253H0534522 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 6              | 156           | 4              | 22 274        |
| <b>Type B</b> | 26             | 71            | 9              | 11 291        |
| <b>Type C</b> | 0              | 0             | 6              | 851           |

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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9640 % (> 99.9477 %)  | 97.5000 % (> 95.6250 %) |
| <b>Type B</b> | 99.7408 % (> 99.7086 %)  | 88.7500 % (> 85.0000 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ci Wu Jia       | 3.22                      | —                                 |
| Di Gu Pi        | 4.05                      | —                                 |
| Fu Xiao Mai     | 4.08                      | —                                 |
| Gui Zhi         | 4.71                      | —                                 |
| He Huan Pi      | 4.87                      | —                                 |
| Yi Yi Ren       | 5.80                      | —                                 |
| Tao Ren         | 6.05                      | —                                 |
| Zhu Ru          | 6.15                      | —                                 |
| Lai Fu Zi       | 7.51                      | —                                 |
| Ban Xia (Jiang) | 7.52                      | —                                 |
| Fu Ling         | 7.55                      | —                                 |
| Ji Li           | 8.95                      | —                                 |
| Bai Zi Ren      | 9.24                      | —                                 |
| Rou Gui         | 10.07                     | —                                 |
| Lian Zi         | 10.14                     | —                                 |
| Mu Zei          | 10.42                     | —                                 |
| Gou Teng        | 10.64                     | —                                 |
| Shen Qu         | 11.31                     | —                                 |
| Bai Shao Yao    | 11.40                     | —                                 |
| Zhe Bei Mu      | 11.78                     | —                                 |
| Huo Ma Ren      | 12.10                     | —                                 |
| Ling Zhi        | 12.77                     | —                                 |
| Gu Sui Bu       | 15.16                     | —                                 |
| Bai Xian Pi     | 15.27                     | —                                 |
| Tian Hua Fen    | 15.61                     | —                                 |
| Lu Gen          | 16.37                     | —                                 |
| Ji Xue Teng     | 16.68                     | —                                 |
| Fo Shou         | 17.21                     | —                                 |
| Ye Jiao Teng    | 17.31                     | —                                 |
| Ma Huang Gen    | 17.42                     | —                                 |
| Ren Dong Teng   | 20.42                     | —                                 |
| Shan Yao        | 21.12                     | —                                 |
| Zhu Ling        | 21.27                     | —                                 |
| Yu Jin          | 21.48                     | —                                 |
| (Fen) Bi Xie    | 21.55                     | —                                 |
| Ze Xie          | 21.82                     | —                                 |
| Fu Shen         | 22.04                     | —                                 |
| Pi Pa Ye        | 22.37                     | —                                 |
| Lian Qiao       | 22.45                     | —                                 |
| Tu Fu Ling      | 22.79                     | —                                 |
| Suan Zao Ren    | 23.64                     | —                                 |
| Yan Hu Suo      | 25.65                     | —                                 |
| Ce Bai Ye       | 26.69                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jin Yin Hua     | 27.97                     | —                                 |
| She Gan         | 28.38                     | —                                 |
| Gua Lou         | 28.52                     | —                                 |
| Dan Shen        | 28.59                     | —                                 |
| Dan Dou Chi     | 28.93                     | —                                 |
| Fu Pen Zi       | 30.40                     | —                                 |
| Fu Zi           | 30.40                     | —                                 |
| Ren Shen        | 30.61                     | —                                 |
| Jiao Gu Lan     | 30.82                     | —                                 |
| Jie Geng        | 31.05                     | —                                 |
| Cang Zhu        | 31.55                     | —                                 |
| Mao Dong Qing   | 31.59                     | —                                 |
| Yin Yang Huo    | 31.95                     | —                                 |
| Chai Hu         | 32.46                     | —                                 |
| Zhi Mu          | 32.54                     | —                                 |
| San Qi          | 33.29                     | —                                 |
| Mang Xiao       | 34.02                     | —                                 |
| Dang Gui        | 34.20                     | —                                 |
| Ban Lan Gen     | 34.69                     | —                                 |
| Zhi Ke          | 34.95                     | —                                 |
| Hou Po          | 35.61                     | —                                 |
| Huang Qin       | 35.85                     | —                                 |
| Che Qian Zi     | 37.06                     | —                                 |
| Yuan Zhi        | 38.04                     | —                                 |
| Hong Jing Tian  | 38.21                     | —                                 |
| Mu Gua          | 39.58                     | —                                 |
| Ma Huang        | 39.75                     | —                                 |
| Qiang Huo       | 39.93                     | —                                 |
| Gan Cao         | 40.50                     | —                                 |
| Guang Huo Xiang | 41.03                     | —                                 |
| Gou Qi Zi       | 42.20                     | —                                 |
| Huang Lian      | 44.18                     | —                                 |
| Long Yan Rou    | 45.21                     | —                                 |
| Sang Zhi        | 45.88                     | —                                 |
| Ku Shen         | 47.12                     | —                                 |
| Jing Jie        | 48.17                     | —                                 |
| Sha Ren         | 49.65                     | —                                 |
| Zi Hua Di Ding  | 49.67                     | —                                 |
| Chuang Mu Xiang | 49.75                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62549     | 62549                  | 0.00                            | 4.20                               |
| 62550     | 62550                  | 0.00                            | 4.05                               |

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| <b>Sample ID</b> | <b>Reference<br/>sample ID</b> | <b>Distance to<br/>reference sample</b> | <b>Distance to<br/>next foreign sample</b> |
|------------------|--------------------------------|-----------------------------------------|--------------------------------------------|
| 62807            | 62807                          | 0.00                                    | 3.88                                       |
| 62808            | 62808                          | 0.00                                    | 3.22                                       |

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 2.4-2022-02

Validated substance/substance group **Shi Gao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50368-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Shi Gao   | G120HS081SH1 | 62562 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------|---------------------------|-----------------------------------|
| Hua Shi   | 53.22                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62561     | 62561                  | 0.00                            | 53.70                              |
| 62562     | 62562                  | 0.00                            | 53.22                              |

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 2.4-2022-02

Validated substance/substance group **Shu Di (Huang)**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60006-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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) | G210H1601921 | 62989     | 40      | from supplier |
| PhytoComm | Shu Di (Huang) | G210H1601921 | 62990     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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) | G210H1601921 | 62989 <sup>†</sup> | 20      |
| PhytoComm | Shu Di (Huang) | G210H1601921 | 62990 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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) | G210H1601121 | 1       |
| Phytocomm | Shu Di (Huang) | G210H1601221 | 1       |
| Phytocomm | Shu Di (Huang) | G210H1601421 | 6       |
| Phytocomm | Shu Di (Huang) | G210H1601521 | 3       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 4              | 1             | 14             | 838           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 99.6705 % (> 99.0828 %)  | n/a (n/a)                |

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

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

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

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

### 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| (Sheng) Di Huang | 13.41                     | —                                 |
| Mang Xiao        | 17.21                     | —                                 |
| Yu Xing Cao      | 23.35                     | —                                 |
| Guang Huo Xiang  | 28.13                     | —                                 |
| Xian Mao         | 43.32                     | —                                 |
| Hua Shi          | 43.99                     | —                                 |
| Jing Jie         | 45.33                     | —                                 |
| Jue Ming Zi      | 45.81                     | —                                 |
| Ding Xiang       | 46.43                     | —                                 |
| Wu Jia Pi        | 54.26                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62989     | 62989                  | 0.00                            | 13.41                              |
| 62990     | 62990                  | 0.00                            | 14.59                              |

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 2.4-2022-02

Validated substance/substance group **Suan Zao Ren**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60059-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Suan Zao Ren              | 3      | 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 |
| PhytoComm | Suan Zao Ren | G254HS310SV1 | 62809     | 40      | from supplier |
| PhytoComm | Suan Zao Ren | G254HS310SV1 | 62810     | 40      | from supplier |
| PhytoComm | Suan Zao Ren | G254H1418021 | 62987     | 40      | from supplier |
| PhytoComm | Suan Zao Ren | G254H1418021 | 62988     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Suan Zao Ren*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Suan Zao Ren | G254HS310SM1 | 62718 <sup>†</sup> | 20      |
| PhytoComm | Suan Zao Ren | G254HS310SV1 | 62809 <sup>†</sup> | 20      |
| PhytoComm | Suan Zao Ren | G254HS310SV1 | 62810 <sup>†</sup> | 20      |
| PhytoComm | Suan Zao Ren | G254H1418021 | 62987 <sup>†</sup> | 20      |
| PhytoComm | Suan Zao Ren | G254H1418021 | 62988 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Lian Zi         | 5.56                      | —                                 |
| Bai Xian Pi     | 8.33                      | —                                 |
| Lian Qiao       | 8.36                      | —                                 |
| She Gan         | 9.11                      | —                                 |
| Lu Gen          | 10.53                     | —                                 |
| Ren Dong Teng   | 11.01                     | —                                 |
| He Huan Pi      | 11.39                     | —                                 |
| Ji Li           | 11.57                     | —                                 |
| Ling Zhi        | 11.94                     | —                                 |
| Bai Zi Ren      | 12.04                     | —                                 |
| Tu Fu Ling      | 12.13                     | —                                 |
| Zhe Bei Mu      | 12.17                     | —                                 |
| Jiao Gu Lan     | 12.34                     | —                                 |
| Tao Ren         | 12.57                     | —                                 |
| Ye Jiao Teng    | 12.59                     | —                                 |
| Dan Dou Chi     | 12.86                     | —                                 |
| Shen Qu         | 12.89                     | —                                 |
| Shan Yao        | 13.27                     | —                                 |
| Xie Bai         | 13.49                     | —                                 |
| Mao Dong Qing   | 13.61                     | —                                 |
| Bai Shao Yao    | 13.79                     | —                                 |
| Gu Sui Bu       | 14.05                     | —                                 |
| San Qi          | 14.17                     | —                                 |
| Rou Gui         | 14.40                     | —                                 |
| Gou Teng        | 14.53                     | —                                 |
| Mu Zei          | 15.13                     | —                                 |
| Huo Ma Ren      | 15.39                     | —                                 |
| Sheng Jiang     | 15.53                     | —                                 |
| Guang Huo Xiang | 15.59                     | —                                 |
| Gui Zhi         | 16.22                     | —                                 |
| Jin Yin Hua     | 16.41                     | —                                 |
| Ji Xue Teng     | 16.44                     | —                                 |
| Ce Bai Ye       | 16.52                     | —                                 |
| Pi Pa Ye        | 16.80                     | —                                 |
| Ku Shen         | 16.95                     | —                                 |
| Fu Ling         | 16.99                     | —                                 |
| Chai Hu         | 17.30                     | —                                 |
| Dan Shen        | 17.62                     | —                                 |
| (Fen) Bi Xie    | 18.01                     | —                                 |
| Fu Zi           | 18.50                     | —                                 |
| Tian Hua Fen    | 18.80                     | —                                 |
| Ci Wu Jia       | 18.85                     | —                                 |
| Fu Pen Zi       | 18.96                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Cang Er Zi      | 19.40                             | —                                         |
| Yu Jin          | 19.47                             | —                                         |
| Hong Jing Tian  | 19.47                             | —                                         |
| Ma Huang Gen    | 20.14                             | —                                         |
| Di Gu Pi        | 20.16                             | —                                         |
| Hou Po          | 20.68                             | —                                         |
| Ban Lan Gen     | 20.78                             | —                                         |
| Gan Cao         | 21.04                             | —                                         |
| Ze Xie          | 21.12                             | —                                         |
| Ma Huang        | 21.33                             | —                                         |
| Fo Shou         | 21.44                             | —                                         |
| Zhu Ling        | 21.56                             | —                                         |
| Yin Yang Huo    | 21.88                             | —                                         |
| Cang Zhu        | 22.21                             | —                                         |
| Zhi Ke          | 23.26                             | —                                         |
| Yi Yi Ren       | 23.56                             | —                                         |
| Gua Lou         | 23.73                             | —                                         |
| Chuang Mu Xiang | 23.78                             | —                                         |
| Zhu Ru          | 23.90                             | —                                         |
| Che Qian Zi     | 25.08                             | —                                         |
| Lai Fu Zi       | 25.73                             | —                                         |
| Jing Jie        | 26.05                             | —                                         |
| Qiang Huo       | 26.32                             | —                                         |
| Ban Xia (Jiang) | 26.36                             | —                                         |
| E Zhu           | 26.48                             | —                                         |
| Fu Xiao Mai     | 26.56                             | —                                         |
| Mang Xiao       | 27.06                             | —                                         |
| Ren Shen        | 27.16                             | —                                         |
| Dang Gui        | 28.10                             | —                                         |
| Yan Hu Suo      | 28.21                             | —                                         |
| Jie Geng        | 29.24                             | —                                         |
| Zi Hua Di Ding  | 29.24                             | —                                         |
| Zhi Gan Cao     | 31.55                             | —                                         |
| Zi Su Zi        | 31.72                             | —                                         |
| Jiang Huang     | 32.62                             | —                                         |
| Dong Gua Zi     | 32.75                             | —                                         |
| Mu Gua          | 32.98                             | —                                         |
| Zhi Mu          | 33.09                             | —                                         |
| Qing Pi         | 33.44                             | —                                         |
| Bo He           | 33.70                             | —                                         |
| Fu Shen         | 33.79                             | —                                         |
| Du Zhong        | 34.04                             | —                                         |
| Huang Bai       | 35.77                             | —                                         |
| Long Yan Rou    | 35.84                             | —                                         |
| Gan Jiang       | 35.97                             | —                                         |
| Sha Ren         | 36.01                             | —                                         |
| Niu Bang Zi     | 36.65                             | —                                         |
| Gou Qi Zi       | 36.65                             | —                                         |
| Sang Zhi        | 36.97                             | —                                         |
| Huang Qin       | 37.23                             | —                                         |
| Huang Lian      | 37.25                             | —                                         |
| Chen Pi         | 37.60                             | —                                         |
| Yuan Zhi        | 39.91                             | —                                         |
| Sha Shen (Bei)  | 40.04                             | —                                         |
| Chi Shao (Yao)  | 40.69                             | —                                         |
| Hong Hua        | 40.80                             | —                                         |
| Qing Hao        | 42.69                             | —                                         |
| Chuan Lian Zi   | 44.94                             | —                                         |
| Long Dan (Cao)  | 45.26                             | —                                         |

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| Substanz      | Distance in<br>main model | Distance in<br>second-stage model |
|---------------|---------------------------|-----------------------------------|
| (Huai) Niu Xi | 46.48                     | —                                 |
| Bai Zhu       | 47.32                     | —                                 |
| Sang Ye       | 48.86                     | —                                 |
| (Bai) Dou Kou | 49.11                     | —                                 |
| Wu Wei Zi     | 49.89                     | —                                 |
| Huang Qi      | 49.97                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62717     | 62717                  | 0.00                            | 8.36                               |
| 62718     | 62718                  | 0.00                            | 9.01                               |
| 62809     | 62809                  | 0.00                            | 5.56                               |
| 62810     | 62810                  | 0.00                            | 6.84                               |
| 62987     | 62987                  | 0.00                            | 19.97                              |
| 62988     | 62988                  | 0.00                            | 19.40                              |

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 2.4-2022-02

Validated substance/substance group **Tao Ren**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60454-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Tao Ren   | G184HS220SK1 | 62610 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 3              | 76            | 4              | 22 357        |
| <b>Type B</b> | 1              | 32            | 8              | 11 356        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9888 % (> 99.9726 %)  | 95.0000 % (> 91.2500 %) |
| <b>Type B</b> | 99.9963 % (> 99.9642 %)  | 80.0000 % (> 72.5000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| He Huan Pi      | 3.77                      | —                                 |
| Gui Zhi         | 5.79                      | —                                 |
| Ci Wu Jia       | 6.14                      | —                                 |
| Lai Fu Zi       | 6.36                      | —                                 |
| Sheng Jiang     | 6.46                      | —                                 |
| Mu Zei          | 7.95                      | —                                 |
| Lian Zi         | 8.75                      | —                                 |
| Rou Gui         | 9.19                      | —                                 |
| Huo Ma Ren      | 9.78                      | —                                 |
| Ling Zhi        | 10.20                     | —                                 |
| Bai Shao Yao    | 10.27                     | —                                 |
| Bai Zi Ren      | 10.34                     | —                                 |
| Fu Xiao Mai     | 10.37                     | —                                 |
| Gou Teng        | 10.76                     | —                                 |
| Di Gu Pi        | 11.05                     | —                                 |
| Ban Xia (Jiang) | 11.56                     | —                                 |
| Bai Xian Pi     | 11.77                     | —                                 |
| Yi Yi Ren       | 11.93                     | —                                 |
| Fu Ling         | 12.38                     | —                                 |
| Ye Jiao Teng    | 12.54                     | —                                 |
| Fo Shou         | 12.86                     | —                                 |
| Gu Sui Bu       | 13.06                     | —                                 |
| Ji Li           | 13.10                     | —                                 |
| Zhu Ru          | 13.19                     | —                                 |
| Shen Qu         | 13.67                     | —                                 |
| Lu Gen          | 13.81                     | —                                 |
| Ji Xue Teng     | 14.92                     | —                                 |
| Zhe Bei Mu      | 15.42                     | —                                 |
| Suan Zao Ren    | 16.09                     | —                                 |
| Ze Xie          | 16.14                     | —                                 |
| Ma Huang Gen    | 16.72                     | —                                 |
| Tu Fu Ling      | 17.73                     | —                                 |
| Ren Dong Teng   | 17.82                     | —                                 |
| Tian Hua Fen    | 18.25                     | —                                 |
| She Gan         | 20.45                     | —                                 |
| (Fen) Bi Xie    | 20.56                     | —                                 |
| Zhu Ling        | 21.75                     | —                                 |
| Pi Pa Ye        | 22.36                     | —                                 |
| Yu Jin          | 22.57                     | —                                 |
| Shan Yao        | 23.04                     | —                                 |
| Fu Shen         | 23.92                     | —                                 |
| Lian Qiao       | 23.97                     | —                                 |
| Jin Yin Hua     | 24.43                     | —                                 |
| Dan Dou Chi     | 24.69                     | —                                 |
| Ce Bai Ye       | 25.06                     | —                                 |
| Gua Lou         | 26.58                     | —                                 |
| Dan Shen        | 26.92                     | —                                 |
| Cang Zhu        | 28.33                     | —                                 |
| Mao Dong Qing   | 28.45                     | —                                 |
| Chai Hu         | 28.91                     | —                                 |
| Fu Pen Zi       | 28.98                     | —                                 |
| Jiao Gu Lan     | 29.31                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Yan Hu Suo      | 29.56                     | —                                 |
| Jie Geng        | 29.64                     | —                                 |
| Ban Lan Gen     | 30.12                     | —                                 |
| Fu Zi           | 30.39                     | —                                 |
| Hong Jing Tian  | 30.40                     | —                                 |
| San Qi          | 30.93                     | —                                 |
| Guang Huo Xiang | 30.93                     | —                                 |
| Yin Yang Huo    | 31.04                     | —                                 |
| Dang Gui        | 31.54                     | —                                 |
| Zhi Ke          | 31.66                     | —                                 |
| Zhi Mu          | 32.18                     | —                                 |
| Mang Xiao       | 33.65                     | —                                 |
| Ma Huang        | 34.08                     | —                                 |
| Hou Po          | 34.55                     | —                                 |
| Ren Shen        | 35.05                     | —                                 |
| Gan Cao         | 36.30                     | —                                 |
| Che Qian Zi     | 37.36                     | —                                 |
| Qiang Huo       | 37.98                     | —                                 |
| Huang Qin       | 38.90                     | —                                 |
| Yuan Zhi        | 39.33                     | —                                 |
| Mu Gua          | 39.34                     | —                                 |
| Chuang Mu Xiang | 41.73                     | —                                 |
| Jing Jie        | 42.14                     | —                                 |
| Long Yan Rou    | 43.70                     | —                                 |
| Gou Qi Zi       | 43.92                     | —                                 |
| Zi Hua Di Ding  | 44.52                     | —                                 |
| Huang Lian      | 44.73                     | —                                 |
| Sang Zhi        | 44.81                     | —                                 |
| Sha Ren         | 47.73                     | —                                 |
| Ku Shen         | 48.42                     | —                                 |
| Xie Bai         | 49.48                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62609     | 62609                  | 0.00                            | 3.77                               |
| 62610     | 62610                  | 0.00                            | 3.98                               |

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 2.4-2022-02

Validated substance/substance group **Tian Hua Fen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60139-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Tian Hua Fen              | 3      | 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 |
| PhytoComm | Tian Hua Fen | G242HS040TK1 | 62799     | 40      | from supplier |
| PhytoComm | Tian Hua Fen | G242HS040TK1 | 62800     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Tian Hua Fen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Tian Hua Fen | G242H0417821 | 62316 <sup>†</sup> | 20      |
| PhytoComm | Tian Hua Fen | G242HS040SG1 | 62633 <sup>†</sup> | 20      |
| PhytoComm | Tian Hua Fen | G242HS040SG1 | 62634 <sup>†</sup> | 20      |
| PhytoComm | Tian Hua Fen | G242HS040TK1 | 62799 <sup>†</sup> | 20      |
| PhytoComm | Tian Hua Fen | G242HS040TK1 | 62800 <sup>†</sup> | 20      |



- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G242H0417423 | 2       |
| Phytocomm | Tian Hua Fen | G242H0417522 | 1       |
| PhytoComm | Tian Hua Fen | G242H0417522 | 1       |
| Phytocomm | Tian Hua Fen | h0417022     | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 2              | 240           | 0              | 22 198        |
| <b>Type B</b> | 6              | 119           | 1              | 11 271        |
| <b>Type C</b> | 0              | 0             | 5              | 852           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 99.9901 % (> 99.9737 %)  | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 99.9528 % (> 99.9206 %)  | 99.1667 % (> 96.6667 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8263 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Lai Fu Zi       | 5.28                      | —                                 |
| Mu Zei          | 5.54                      | —                                 |
| He Huan Pi      | 6.27                      | —                                 |
| Zhe Bei Mu      | 7.07                      | —                                 |
| Huo Ma Ren      | 8.13                      | —                                 |
| Shen Qu         | 8.44                      | —                                 |
| Lian Qiao       | 9.01                      | —                                 |
| Bai Zi Ren      | 9.26                      | —                                 |
| Pi Pa Ye        | 9.27                      | —                                 |
| Ji Li           | 9.40                      | —                                 |
| Bai Shao Yao    | 9.62                      | —                                 |
| Gu Sui Bu       | 9.68                      | —                                 |
| Sha Shen (Bei)  | 9.78                      | —                                 |
| Fu Zi           | 10.09                     | —                                 |
| Ze Xie          | 10.48                     | —                                 |
| Shan Yao        | 10.90                     | —                                 |
| Ji Xue Teng     | 11.51                     | —                                 |
| Gui Zhi         | 11.60                     | —                                 |
| Sheng Jiang     | 11.69                     | —                                 |
| Di Gu Pi        | 11.74                     | —                                 |
| Ren Dong Teng   | 11.78                     | —                                 |
| Jin Yin Hua     | 11.85                     | —                                 |
| Ling Zhi        | 12.15                     | —                                 |
| Tao Ren         | 12.26                     | —                                 |
| Bai He          | 12.41                     | —                                 |
| Sang Zhi        | 12.50                     | —                                 |
| Ban Xia (Jiang) | 13.14                     | —                                 |
| Ye Jiao Teng    | 13.81                     | —                                 |
| Yan Hu Suo      | 13.90                     | —                                 |
| Lu Gen          | 14.03                     | —                                 |
| Lian Zi         | 14.27                     | —                                 |
| Chuan Lian Zi   | 14.34                     | —                                 |
| Rou Gui         | 14.56                     | —                                 |
| Fu Pen Zi       | 14.91                     | —                                 |
| Hou Po          | 15.11                     | —                                 |
| Gou Teng        | 15.40                     | —                                 |
| Zhu Ru          | 16.00                     | —                                 |
| Gan Jiang       | 16.31                     | —                                 |
| Ren Shen        | 16.57                     | —                                 |
| Gua Lou         | 16.87                     | —                                 |
| Ci Wu Jia       | 16.89                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Dang Gui        | 16.97                             | —                                         |
| Ku Shen         | 17.37                             | —                                         |
| Zhu Ling        | 17.92                             | —                                         |
| Ce Bai Ye       | 17.93                             | —                                         |
| Jie Geng        | 17.96                             | —                                         |
| Yi Yi Ren       | 18.29                             | —                                         |
| Yu Jin          | 18.29                             | —                                         |
| Fu Ling         | 18.41                             | —                                         |
| Bai Xian Pi     | 18.51                             | —                                         |
| Fu Xiao Mai     | 18.56                             | —                                         |
| Suan Zao Ren    | 18.69                             | —                                         |
| Che Qian Zi     | 19.07                             | —                                         |
| Jiao Gu Lan     | 19.37                             | —                                         |
| Ban Lan Gen     | 19.58                             | —                                         |
| Dan Shen        | 20.41                             | —                                         |
| Dan Dou Chi     | 20.68                             | —                                         |
| Ma Huang        | 20.80                             | —                                         |
| Zhi Ke          | 21.08                             | —                                         |
| (Fen) Bi Xie    | 21.15                             | —                                         |
| Huang Qin       | 21.30                             | —                                         |
| E Zhu           | 21.53                             | —                                         |
| Cang Zhu        | 21.74                             | —                                         |
| Chuan Mu Tong   | 21.86                             | —                                         |
| San Qi          | 21.90                             | —                                         |
| Yin Yang Huo    | 22.34                             | —                                         |
| Zhi Mu          | 22.60                             | —                                         |
| She Gan         | 23.02                             | —                                         |
| Fo Shou         | 23.10                             | —                                         |
| Cang Er Zi      | 23.20                             | —                                         |
| Zi Su Zi        | 23.37                             | —                                         |
| Ma Huang Gen    | 23.70                             | —                                         |
| Guang Huo Xiang | 23.86                             | —                                         |
| Chai Hu         | 24.15                             | —                                         |
| Gou Qi Zi       | 24.20                             | —                                         |
| Mi Huan Jun     | 25.00                             | —                                         |
| Mao Dong Qing   | 25.18                             | —                                         |
| Tu Fu Ling      | 25.58                             | —                                         |
| Huang Qi        | 26.11                             | —                                         |
| Gan Cao         | 26.52                             | —                                         |
| Qiang Huo       | 27.01                             | —                                         |
| Zhi Gan Cao     | 27.03                             | —                                         |
| Hong Jing Tian  | 27.15                             | —                                         |
| Bai Zhu         | 27.73                             | —                                         |
| Mang Xiao       | 28.32                             | —                                         |
| Niu Bang Zi     | 28.55                             | —                                         |
| Jiang Huang     | 28.57                             | —                                         |
| Qin Jiao        | 28.73                             | —                                         |
| (Huai) Niu Xi   | 29.59                             | —                                         |
| (Bai) Dou Kou   | 30.03                             | —                                         |
| Yuan Zhi        | 30.72                             | —                                         |
| Pu Gong Ying    | 31.33                             | —                                         |
| Mu Gua          | 31.74                             | —                                         |
| Long Yan Rou    | 32.29                             | —                                         |
| Ban Zhi Lian    | 32.35                             | —                                         |
| Long Dan (Cao)  | 32.47                             | —                                         |
| Qing Pi         | 32.98                             | —                                         |
| Fu Shen         | 33.46                             | —                                         |
| Xiao Hui Xiang  | 33.83                             | —                                         |
| Huang Lian      | 33.92                             | —                                         |

*continued on the next page*

continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bo He           | 34.64                     | —                                 |
| Zi Hua Di Ding  | 36.18                     | —                                 |
| Xie Bai         | 37.11                     | —                                 |
| Chi Shao (Yao)  | 37.81                     | —                                 |
| Chuang Mu Xiang | 38.36                     | —                                 |
| Jing Jie        | 38.51                     | —                                 |
| Sha Ren         | 38.89                     | —                                 |
| Du Zhong        | 39.15                     | —                                 |
| Bai Zhi         | 39.50                     | —                                 |
| Yi Mu Cao       | 40.52                     | —                                 |
| Chen Pi         | 41.04                     | —                                 |
| Chuan Niu Xi    | 43.20                     | —                                 |
| Huang Bai       | 45.19                     | —                                 |
| Da Zao          | 46.51                     | —                                 |
| Xiang Fu        | 47.41                     | —                                 |
| (Shi) Chang Pu  | 49.08                     | —                                 |
| Sang Ye         | 49.15                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62315     | 62315                  | 0.00                            | 10.65                              |
| 62316     | 62316                  | 0.00                            | 9.78                               |
| 62633     | 62633                  | 0.00                            | 5.54                               |
| 62634     | 62634                  | 0.00                            | 5.28                               |
| 62799     | 62799                  | 0.00                            | 7.07                               |
| 62800     | 62800                  | 0.00                            | 7.25                               |

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 2.4-2022-02

Validated substance/substance group **Tu Fu Ling**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50885-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Tu Fu Ling                | 3      | 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 |
| PhytoComm | Tu Fu Ling | G231HS009TP1 | 63033     | 40      | from supplier |
| PhytoComm | Tu Fu Ling | G231HS009TP1 | 63034     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Tu Fu Ling*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Tu Fu Ling | G231HS009RK1 | 62428 <sup>†</sup> | 20      |
| PhytoComm | Tu Fu Ling | G231HS009SK1 | 62641 <sup>†</sup> | 20      |
| PhytoComm | Tu Fu Ling | G231HS009SK1 | 62642 <sup>†</sup> | 20      |
| PhytoComm | Tu Fu Ling | G231HS009TP1 | 63033 <sup>†</sup> | 20      |
| PhytoComm | Tu Fu Ling | G231HS009TP1 | 63034 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G231H0325121 | 1       |
| Phytocomm | Tu Fu Ling | G231H0325421 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 117           | 3              | 11 277        |
| <b>Type C</b> | 2              | 0             | 6              | 849           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 97.5000 % (> 95.0000 %)  |
| <b>Type C</b> | 99.4186 % (> 98.8315 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ze Lan          | 5.40                      | —                                 |
| Bai Xian Pi     | 5.63                      | —                                 |
| Ye Jiao Teng    | 8.14                      | —                                 |
| Xi Xian Cao     | 8.67                      | —                                 |
| Chai Hu         | 9.27                      | —                                 |
| Dan Dou Chi     | 9.64                      | —                                 |
| Yin Chen Hao    | 12.01                     | —                                 |
| Ji Xue Teng     | 12.93                     | —                                 |
| Rou Gui         | 13.05                     | —                                 |
| Pu Gong Ying    | 13.17                     | —                                 |
| Mao Dong Qing   | 13.47                     | —                                 |
| Du Zhong        | 13.55                     | —                                 |
| Ling Zhi        | 13.66                     | —                                 |
| Yin Yang Huo    | 14.77                     | —                                 |
| Lian Zi         | 14.91                     | —                                 |
| Dan Shen        | 14.91                     | —                                 |
| Guang Huo Xiang | 15.55                     | —                                 |
| Fu Zi           | 15.83                     | —                                 |
| Ren Dong Teng   | 16.44                     | —                                 |
| Bai Jiang Cao   | 17.45                     | —                                 |
| Xin Yi          | 17.54                     | —                                 |
| Zhi Ke          | 17.56                     | —                                 |
| Ce Bai Ye       | 17.74                     | —                                 |
| Sha Ren         | 18.15                     | —                                 |
| Huang Lian      | 18.49                     | —                                 |
| (Fen) Bi Xie    | 18.62                     | —                                 |
| Jiao Gu Lan     | 18.75                     | —                                 |
| Shan Yao        | 19.09                     | —                                 |
| Jing Jie        | 19.54                     | —                                 |
| Yu Jin          | 19.80                     | —                                 |
| Zhu Ling        | 19.93                     | —                                 |
| Nü Zhen Zi      | 19.94                     | —                                 |
| Bai Shao Yao    | 19.95                     | —                                 |
| Gou Teng        | 19.96                     | —                                 |
| Qiang Huo       | 20.14                     | —                                 |
| Zi Hua Di Ding  | 20.36                     | —                                 |
| Hou Po          | 20.48                     | —                                 |
| Shen Qu         | 20.55                     | —                                 |
| Che Qian Zi     | 20.78                     | —                                 |
| Lu Gen          | 21.04                     | —                                 |
| Fo Shou         | 21.10                     | —                                 |

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| <b>Substanz</b>     | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|---------------------|-----------------------------------|-------------------------------------------|
| Jin Yin Hua         | 21.57                             | —                                         |
| Ma Huang Gen        | 21.64                             | —                                         |
| Bo He               | 21.83                             | —                                         |
| Sang Ye             | 22.03                             | —                                         |
| He Huan Pi          | 22.11                             | —                                         |
| Huang Bai           | 22.96                             | —                                         |
| Zhi Shi             | 23.07                             | —                                         |
| Gan Cao             | 23.65                             | —                                         |
| Huo Ma Ren          | 23.86                             | —                                         |
| Ma Huang            | 24.00                             | —                                         |
| Bai Hua She She Cao | 24.26                             | —                                         |
| Gu Sui Bu           | 24.72                             | —                                         |
| Gui Zhi             | 24.82                             | —                                         |
| Fu Ling             | 25.06                             | —                                         |
| Jiang Huang         | 25.11                             | —                                         |
| Di Gu Pi            | 25.19                             | —                                         |
| Sheng Jiang         | 25.27                             | —                                         |
| Ji Li               | 25.34                             | —                                         |
| Yi Yi Ren           | 25.82                             | —                                         |
| Yu Xing Cao         | 26.38                             | —                                         |
| Ban Zhi Lian        | 26.40                             | —                                         |
| Yan Hu Suo          | 26.97                             | —                                         |
| Pi Pa Ye            | 27.52                             | —                                         |
| She Gan             | 27.91                             | —                                         |
| Mang Xiao           | 28.94                             | —                                         |
| Fu Pen Zi           | 28.96                             | —                                         |
| Lian Qiao           | 28.98                             | —                                         |
| Chuang Mu Xiang     | 29.71                             | —                                         |
| Hu Zhang            | 30.37                             | —                                         |
| Cang Er Zi          | 30.74                             | —                                         |
| Cang Zhu            | 30.87                             | —                                         |
| Suan Zao Ren        | 30.91                             | —                                         |
| Tao Ren             | 31.36                             | —                                         |
| Fu Shen             | 32.11                             | —                                         |
| Qing Pi             | 32.73                             | —                                         |
| Tian Hua Fen        | 32.90                             | —                                         |
| Mu Zei              | 33.03                             | —                                         |
| Zhe Bei Mu          | 33.12                             | —                                         |
| Sang Zhi            | 33.34                             | —                                         |
| Hong Jing Tian      | 33.87                             | —                                         |
| Chi Shao (Yao)      | 34.36                             | —                                         |
| Ban Xia (Jiang)     | 34.43                             | —                                         |
| Ci Wu Jia           | 34.99                             | —                                         |
| Fu Xiao Mai         | 35.09                             | —                                         |
| Wang Bu Liu Xing    | 35.41                             | —                                         |
| Han Lian Cao        | 35.96                             | —                                         |
| Zhi Gan Cao         | 36.02                             | —                                         |
| Qing Hao            | 36.10                             | —                                         |
| Jie Geng            | 36.15                             | —                                         |
| E Zhu               | 37.35                             | —                                         |
| Ban Lan Gen         | 37.55                             | —                                         |
| Xiang Fu            | 37.55                             | —                                         |
| Zi Su Zi            | 37.84                             | —                                         |
| Ren Shen            | 38.89                             | —                                         |
| Yi Mu Cao           | 39.34                             | —                                         |
| Huang Qin           | 40.00                             | —                                         |
| Bai Zhu             | 40.66                             | —                                         |
| Zhu Ru              | 41.08                             | —                                         |
| Hong Hua            | 44.52                             | —                                         |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| (Bai) Dou Kou  | 44.64                     | —                                 |
| Niu Bang Zi    | 44.72                     | —                                 |
| Bai Zi Ren     | 44.91                     | —                                 |
| Dang Gui       | 46.17                     | —                                 |
| Mi Huan Jun    | 46.28                     | —                                 |
| Sha Shen (Bei) | 46.38                     | —                                 |
| Long Yan Rou   | 47.70                     | —                                 |
| Huang Qi       | 48.10                     | —                                 |
| San Qi         | 48.79                     | —                                 |
| Lai Fu Zi      | 50.01                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62427     | 62427                  | 0.00                            | 5.63                               |
| 62428     | 62428                  | 0.00                            | 7.08                               |
| 62641     | 62641                  | 0.00                            | 5.40                               |
| 62642     | 62642                  | 0.00                            | 5.71                               |
| 63033     | 63033                  | 0.00                            | 14.04                              |
| 63034     | 63034                  | 0.00                            | 14.93                              |

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 2.4-2022-02

Validated substance/substance group **Tu Si Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60217-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Tu Si Zi                  | 2      | 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 |
| PhytoComm | Tu Si Zi  | G086H1243924 | 62935     | 40      | from supplier |
| PhytoComm | Tu Si Zi  | G086H1243924 | 62936     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Si Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Tu Si Zi  | G086H1243823 | 62522 <sup>†</sup> | 20      |
| PhytoComm | Tu Si Zi  | G086H1243924 | 62935 <sup>†</sup> | 20      |
| PhytoComm | Tu Si Zi  | G086H1243924 | 62936 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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  | G086H1243521 | 1       |
| Phytocomm | Tu Si Zi  | h1243022     | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Bu Gu Zhi        | 14.29                     | —                                 |
| Wu Yao           | 22.40                     | —                                 |
| Gu Sui Bu        | 22.46                     | —                                 |
| Yin Chen Hao     | 22.90                     | —                                 |
| Mang Xiao        | 23.35                     | —                                 |
| (Bai) Dou Kou    | 25.33                     | —                                 |
| Yu Xing Cao      | 25.36                     | —                                 |
| Sang Bai Pi      | 25.92                     | —                                 |
| Sha Ren          | 28.20                     | —                                 |
| He Huan Pi       | 28.79                     | —                                 |
| Sang Ji Shend    | 31.29                     | —                                 |
| E Zhu            | 34.98                     | —                                 |
| Jiang Huang      | 35.67                     | —                                 |
| Dan Zhu Ye       | 36.65                     | —                                 |
| (Sheng) Di Huang | 39.54                     | —                                 |
| He Shou Wu       | 41.53                     | —                                 |
| Xuan Fu Hua      | 42.85                     | —                                 |
| (Shi) Chang Pu   | 44.65                     | —                                 |
| Jing Jie         | 44.66                     | —                                 |
| Shan Yao         | 45.93                     | —                                 |
| Hua Shi          | 47.18                     | —                                 |
| Wu Zhu Yu        | 48.25                     | —                                 |
| Wu Jia Pi        | 49.41                     | —                                 |
| Chen Pi          | 50.38                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62521     | 62521                  | 0.00                            | 24.32                              |
| 62522     | 62522                  | 0.00                            | 24.00                              |
| 62935     | 62935                  | 0.00                            | 14.29                              |
| 62936     | 62936                  | 0.00                            | 15.14                              |

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





# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Wang Bu Liu Xing**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50390-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Wang Bu Liu Xing          | 1      | 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 | G281H0456921 | 62731     | 40      | from supplier |
| PhytoComm | Wang Bu Liu Xing | G281H0456921 | 62732     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Wang Bu Liu Xing*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G281H0456921 | 62731 <sup>†</sup> | 20      |
| PhytoComm | Wang Bu Liu Xing | G281H0456921 | 62732 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G281H0456221 | 1       |
| PhytoComm | Wang Bu Liu Xing | G281H0456322 | 1       |
| PhytoComm | Wang Bu Liu Xing | G281H0456521 | 1       |
| PhytoComm | Wang Bu Liu Xing | G281H456421  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Cang Er Zi          | 24.31                     | —                                 |
| Mang Xiao           | 25.58                     | —                                 |
| He Huan Pi          | 26.72                     | —                                 |
| E Zhu               | 26.90                     | —                                 |
| Jiang Huang         | 27.36                     | —                                 |
| Zi Su Zi            | 29.44                     | —                                 |
| Sha Ren             | 30.25                     | —                                 |
| Shan Yao            | 32.25                     | —                                 |
| Niu Bang Zi         | 34.06                     | —                                 |
| Qiang Huo           | 36.20                     | —                                 |
| Suan Zao Ren        | 37.30                     | —                                 |
| Yan Hu Suo          | 37.32                     | —                                 |
| (Bai) Dou Kou       | 37.49                     | —                                 |
| Ze Lan              | 37.90                     | —                                 |
| Huang Lian          | 38.16                     | —                                 |
| Du Zhong            | 38.45                     | —                                 |
| Gan Jiang           | 38.55                     | —                                 |
| Chen Pi             | 38.79                     | —                                 |
| Bai Hua She She Cao | 38.92                     | —                                 |
| Yi Mu Cao           | 39.11                     | —                                 |
| Mao Dong Qing       | 42.14                     | —                                 |
| Xin Yi              | 42.18                     | —                                 |
| Sha Shen (Bei)      | 42.35                     | —                                 |
| Nü Zhen Zi          | 42.36                     | —                                 |
| Yin Chen Hao        | 43.61                     | —                                 |
| Dan Dou Chi         | 43.67                     | —                                 |
| Xiang Fu            | 44.88                     | —                                 |
| Xia Ku Cao          | 44.98                     | —                                 |
| Xi Xian Cao         | 45.70                     | —                                 |
| Hu Zhang            | 46.26                     | —                                 |
| Bo He               | 46.89                     | —                                 |
| Zhi Ke              | 47.11                     | —                                 |
| Sang Zhi            | 48.08                     | —                                 |
| Che Qian Zi         | 48.15                     | —                                 |
| Bai Xian Pi         | 49.09                     | —                                 |
| Di Gu Pi            | 49.67                     | —                                 |
| Ce Bai Ye           | 50.48                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62731     | 62731               | 0.00                         | 25.34                           |
| 62732     | 62732               | 0.00                         | 24.31                           |

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 2.4-2022-02

Validated substance/substance group **Wu Jia Pi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002259-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Wu Jia Pi | G002H0402921 | 62758 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Dan Zhu Ye       | 15.31                     | —                                 |
| Yu Xing Cao      | 19.18                     | —                                 |
| Jing Jie         | 19.49                     | —                                 |
| Xian Mao         | 21.98                     | —                                 |
| Mang Xiao        | 23.15                     | —                                 |
| Sang Ye          | 24.55                     | —                                 |
| Sang Ji Shend    | 25.20                     | —                                 |
| Du Zhong         | 26.37                     | —                                 |
| Ding Xiang       | 28.43                     | —                                 |
| Yin Chen Hao     | 32.62                     | —                                 |
| Bu Gu Zhi        | 33.13                     | —                                 |
| (Sheng) Di Huang | 33.29                     | —                                 |
| Ge Gen           | 36.44                     | —                                 |
| Jin Qian Cao     | 36.48                     | —                                 |
| Sha Ren          | 43.77                     | —                                 |
| He Shou Wu       | 46.11                     | —                                 |
| Hua Shi          | 47.64                     | —                                 |
| Guang Huo Xiang  | 49.35                     | —                                 |
| Nü Zhen Zi       | 49.58                     | —                                 |
| Gu Sui Bu        | 50.48                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62757     | 62757                  | 0.00                            | 15.60                              |
| 62758     | 62758                  | 0.00                            | 15.31                              |

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 2.4-2022-02

Validated substance/substance group **Wu Mei**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60021-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Wu Mei                    | 1      | 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 |

## Validation samples

A total of 34 694 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 Mei*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Wu Mei    | G167H1026821 | 62478 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mang Xiao       | 24.35                     | —                                 |
| Guang Huo Xiang | 40.32                     | —                                 |
| Hua Shi         | 46.68                     | —                                 |
| Yu Xing Cao     | 49.64                     | —                                 |
| Wu Jia Pi       | 51.67                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62477     | 62477                  | 0.00                            | 24.39                              |
| 62478     | 62478                  | 0.00                            | 24.35                              |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Wu Wei Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60001-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Wu Wei Zi                 | 2      | 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 | G220HS048SN1 | 62705     | 40      | from supplier |
| PhytoComm | Wu Wei Zi | G220HS048SN1 | 62706     | 40      | from supplier |
| PhytoComm | Wu Wei Zi | G220HS048TK1 | 62783     | 40      | from supplier |
| PhytoComm | Wu Wei Zi | G220HS048TK1 | 62784     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Wei Zi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 | G220HS048SN1 | 62705 <sup>†</sup> | 20      |
| PhytoComm | Wu Wei Zi | G220HS048SN1 | 62706 <sup>†</sup> | 20      |
| PhytoComm | Wu Wei Zi | G220HS048TK1 | 62783 <sup>†</sup> | 20      |
| PhytoComm | Wu Wei Zi | G220HS048TK1 | 62784 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Shan Yao       | 26.68                     | —                                 |
| Jin Yin Hua    | 30.17                     | —                                 |
| Shen Qu        | 30.28                     | —                                 |
| Qing Hao       | 30.42                     | —                                 |
| Qing Pi        | 31.86                     | —                                 |
| Sang Ye        | 32.53                     | —                                 |
| Huang Bai      | 33.04                     | —                                 |
| Mang Xiao      | 33.36                     | —                                 |
| Jiao Gu Lan    | 36.07                     | —                                 |
| Hong Hua       | 39.44                     | —                                 |
| Yi Mu Cao      | 39.69                     | —                                 |
| Cang Er Zi     | 39.73                     | —                                 |
| Ku Shen        | 40.54                     | —                                 |
| Lian Qiao      | 41.03                     | —                                 |
| Du Zhong       | 41.43                     | —                                 |
| Mao Dong Qing  | 42.39                     | —                                 |
| Zhi Ke         | 43.86                     | —                                 |
| Jiang Huang    | 44.83                     | —                                 |
| Huang Lian     | 45.08                     | —                                 |
| Zi Hua Di Ding | 45.42                     | —                                 |
| Xie Bai        | 45.76                     | —                                 |
| Xi Xian Cao    | 45.93                     | —                                 |
| Hou Po         | 47.80                     | —                                 |
| Nü Zhen Zi     | 48.16                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62705     | 62705                  | 0.00                            | 27.58                              |
| 62706     | 62706                  | 0.00                            | 26.68                              |
| 62783     | 62783                  | 0.00                            | 30.28                              |
| 62784     | 62784                  | 0.00                            | 31.17                              |

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 2.4-2022-02

Validated substance/substance group **Wu Yao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60040-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Wu Yao                    | 1      | 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    | G140H1025921 | 62741     | 40      | from supplier |
| PhytoComm | Wu Yao    | G140H1025921 | 62742     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Yao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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    | G140H1025921 | 62741 <sup>†</sup> | 20      |
| PhytoComm | Wu Yao    | G140H1025921 | 62742 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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    | g140h1025221 | 1       |
| PhytoComm | Wu Yao    | G140H1025221 | 2       |
| Phytocomm | Wu Yao    | G140H1025521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 6              | 851           |

The substance/substance group *Wu 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| (Shi) Chang Pu      | 11.84                     | —                                 |
| Chen Pi             | 13.34                     | —                                 |
| He Huan Pi          | 15.45                     | —                                 |
| Jiang Huang         | 17.24                     | —                                 |
| Sha Ren             | 19.05                     | —                                 |
| Shan Yu Rou         | 20.03                     | —                                 |
| Gu Sui Bu           | 20.69                     | —                                 |
| Mu Dan Pi           | 21.16                     | —                                 |
| Chuan Lian Zi       | 22.16                     | —                                 |
| (Bai) Dou Kou       | 22.31                     | —                                 |
| Ju Hua              | 25.29                     | —                                 |
| Yin Chen Hao        | 25.40                     | —                                 |
| Mang Xiao           | 26.93                     | —                                 |
| Dang Gui            | 27.22                     | —                                 |
| Sang Ji Shend       | 28.06                     | —                                 |
| Hong Jing Tian      | 28.36                     | —                                 |
| He Shou Wu          | 29.12                     | —                                 |
| Xiang Fu            | 30.01                     | —                                 |
| Yi Mu Cao           | 30.05                     | —                                 |
| Shan Yao            | 30.60                     | —                                 |
| Xiao Hui Xiang      | 30.71                     | —                                 |
| Di Gu Pi            | 30.89                     | —                                 |
| Ba Ji Tian          | 31.14                     | —                                 |
| Sang Bai Pi         | 31.40                     | —                                 |
| Wu Zhu Yu           | 31.53                     | —                                 |
| E Zhu               | 32.93                     | —                                 |
| Yan Hu Suo          | 33.02                     | —                                 |
| Tu Si Zi            | 33.30                     | —                                 |
| Chuan Niu Xi        | 33.77                     | —                                 |
| Fang Feng           | 33.88                     | —                                 |
| Niu Bang Zi         | 36.61                     | —                                 |
| Xu Duan             | 36.93                     | —                                 |
| Huang Qi            | 37.38                     | —                                 |
| Bu Gu Zhi           | 38.70                     | —                                 |
| Bai Hua She She Cao | 38.90                     | —                                 |
| (Huai) Niu Xi       | 39.25                     | —                                 |
| Zi Su Zi            | 39.32                     | —                                 |
| Sang Zhi            | 39.40                     | —                                 |
| Ku Shen             | 40.13                     | —                                 |
| Zhi Gan Cao         | 40.34                     | —                                 |
| Zhi Ke              | 40.78                     | —                                 |
| Gan Jiang           | 40.84                     | —                                 |
| Ge Gen              | 41.07                     | —                                 |
| Huang Lian          | 41.21                     | —                                 |
| Tian Hua Fen        | 41.26                     | —                                 |
| Bai Zhi             | 41.71                     | —                                 |
| Xin Yi              | 41.74                     | —                                 |
| Du Huo              | 42.21                     | —                                 |
| Hu Zhang            | 42.69                     | —                                 |
| Lai Fu Zi           | 44.05                     | —                                 |
| Cang Er Zi          | 45.51                     | —                                 |
| Suan Zao Ren        | 45.91                     | —                                 |

*continued on the next page*



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| Substanz         | Distance in<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Wang Bu Liu Xing | 46.15                     | —                                 |
| Nü Zhen Zi       | 47.39                     | —                                 |
| Ze Lan           | 47.67                     | —                                 |
| Da Zao           | 48.58                     | —                                 |
| Jie Geng         | 49.73                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62741     | 62741                  | 0.00                            | 11.84                              |
| 62742     | 62742                  | 0.00                            | 11.84                              |

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 2.4-2022-02

Validated substance/substance group **Wu Zhu Yu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002260-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Wu Zhu Yu | G103H0766921 | 62782 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 1              | 1             | 1              | 854           |

The substance/substance group *Wu Zhu Yu* 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 99.9070 % (> 99.3221 %)  | n/a (n/a)                |

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

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

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

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

## 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| (Shi) Chang Pu      | 19.60                     | —                                 |
| Xiao Hui Xiang      | 20.03                     | —                                 |
| Yi Mu Cao           | 21.86                     | —                                 |
| Nü Zhen Zi          | 22.71                     | —                                 |
| Ju Hua              | 23.62                     | —                                 |
| Gu Sui Bu           | 24.11                     | —                                 |
| Sang Ji Shend       | 24.91                     | —                                 |
| Sang Bai Pi         | 25.85                     | —                                 |
| Sha Ren             | 26.76                     | —                                 |
| Shan Yu Rou         | 26.85                     | —                                 |
| Mang Xiao           | 26.88                     | —                                 |
| Ku Shen             | 27.74                     | —                                 |
| Fang Feng           | 28.98                     | —                                 |
| Yin Chen Hao        | 30.58                     | —                                 |
| Xu Duan             | 30.58                     | —                                 |
| Xiang Fu            | 30.96                     | —                                 |
| Chen Pi             | 30.99                     | —                                 |
| Hong Jing Tian      | 31.45                     | —                                 |
| Lian Qiao           | 32.59                     | —                                 |
| He Huan Pi          | 34.94                     | —                                 |
| Wu Yao              | 36.82                     | —                                 |
| Cang Er Zi          | 37.57                     | —                                 |
| Bai Hua She She Cao | 37.93                     | —                                 |
| Dang Gui            | 38.94                     | —                                 |
| Mu Dan Pi           | 39.36                     | —                                 |
| Jing Jie            | 40.00                     | —                                 |
| Di Gu Pi            | 40.56                     | —                                 |
| Sang Ye             | 42.61                     | —                                 |
| He Shou Wu          | 43.05                     | —                                 |
| Gou Teng            | 43.41                     | —                                 |
| Jiang Huang         | 43.89                     | —                                 |
| Shan Yao            | 46.28                     | —                                 |
| Bai Zhi             | 46.49                     | —                                 |
| (Bai) Dou Kou       | 46.55                     | —                                 |
| Ge Gen              | 46.72                     | —                                 |
| Niu Bang Zi         | 46.96                     | —                                 |
| Yan Hu Suo          | 47.07                     | —                                 |
| Xuan Fu Hua         | 47.31                     | —                                 |
| Pu Gong Ying        | 48.27                     | —                                 |
| Tu Si Zi            | 48.44                     | —                                 |
| Han Lian Cao        | 49.87                     | —                                 |
| Xin Yi              | 50.64                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62781     | 62781               | 0.00                         | 19.60                           |
| 62782     | 62782               | 0.00                         | 20.03                           |

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 2.4-2022-02

Validated substance/substance group **Xi Xian Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60103-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Xi Xian Cao               | 2      | 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 |
| PhytoComm | Xi Xian Cao | G229HS309SQ1 | 62791     | 40      | from supplier |
| PhytoComm | Xi Xian Cao | G229HS309SQ1 | 62792     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Xi Xian Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Xi Xian Cao | G229HS309SK1 | 62556 <sup>†</sup> | 20      |
| PhytoComm | Xi Xian Cao | G229HS309SQ1 | 62791 <sup>†</sup> | 20      |
| PhytoComm | Xi Xian Cao | G229HS309SQ1 | 62792 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G229H1431321 | 1       |
| PhytoComm | Xi Xian Cao | G229H1431521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 79            | 1              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 98.7500 % (> 95.0000 %)  |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Ze Lan              | 4.81                      | —                                 |
| Tu Fu Ling          | 7.65                      | —                                 |
| Yin Chen Hao        | 7.75                      | —                                 |
| Xin Yi              | 9.23                      | —                                 |
| Huang Lian          | 14.05                     | —                                 |
| Yu Xing Cao         | 14.35                     | —                                 |
| Pu Gong Ying        | 14.63                     | —                                 |
| Nü Zhen Zi          | 15.78                     | —                                 |
| Bai Hua She She Cao | 16.47                     | —                                 |
| Shan Yao            | 18.49                     | —                                 |
| Du Zhong            | 19.12                     | —                                 |
| Sang Ye             | 19.39                     | —                                 |
| Yu Jin              | 20.09                     | —                                 |
| Hu Zhang            | 21.23                     | —                                 |
| Jiang Huang         | 21.36                     | —                                 |
| Sha Ren             | 22.33                     | —                                 |
| Zhi Ke              | 22.84                     | —                                 |
| Qiang Huo           | 23.49                     | —                                 |
| Zhi Shi             | 23.81                     | —                                 |
| Bai Jiang Cao       | 24.27                     | —                                 |
| Fu Zi               | 24.41                     | —                                 |
| Han Lian Cao        | 25.65                     | —                                 |
| Jiao Gu Lan         | 25.78                     | —                                 |
| Dan Shen            | 27.83                     | —                                 |
| Mao Dong Qing       | 28.66                     | —                                 |
| Hou Po              | 28.68                     | —                                 |
| Bo He               | 29.13                     | —                                 |
| Mang Xiao           | 29.56                     | —                                 |
| Bai Xian Pi         | 30.39                     | —                                 |
| Ling Zhi            | 30.91                     | —                                 |
| Che Qian Zi         | 31.21                     | —                                 |
| Qing Pi             | 32.24                     | —                                 |
| Cang Er Zi          | 32.37                     | —                                 |
| Yin Yang Huo        | 32.45                     | —                                 |
| Chai Hu             | 32.63                     | —                                 |
| Xiang Fu            | 32.78                     | —                                 |
| Wang Bu Liu Xing    | 33.67                     | —                                 |
| Zi Hua Di Ding      | 33.76                     | —                                 |
| Ye Jiao Teng        | 33.84                     | —                                 |
| Huang Bai           | 34.55                     | —                                 |
| Dan Dou Chi         | 35.00                     | —                                 |
| Di Gu Pi            | 35.31                     | —                                 |
| He Huan Pi          | 35.52                     | —                                 |
| Hong Jing Tian      | 35.62                     | —                                 |
| Ce Bai Ye           | 35.97                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jin Yin Hua     | 37.52                     | —                                 |
| Yi Mu Cao       | 37.91                     | —                                 |
| E Zhu           | 39.32                     | —                                 |
| Zi Su Zi        | 39.87                     | —                                 |
| Fu Pen Zi       | 39.92                     | —                                 |
| Pi Pa Ye        | 39.98                     | —                                 |
| Xia Ku Cao      | 40.40                     | —                                 |
| Chuang Mu Xiang | 40.70                     | —                                 |
| Qing Hao        | 40.77                     | —                                 |
| Lian Zi         | 41.04                     | —                                 |
| Ma Huang        | 41.30                     | —                                 |
| Yan Hu Suo      | 42.09                     | —                                 |
| Jing Jie        | 43.62                     | —                                 |
| Lian Qiao       | 45.82                     | —                                 |
| Ren Dong Teng   | 45.86                     | —                                 |
| Suan Zao Ren    | 46.22                     | —                                 |
| Bai Shao Yao    | 46.51                     | —                                 |
| (Bai) Dou Kou   | 46.98                     | —                                 |
| Ji Xue Teng     | 47.04                     | —                                 |
| Niu Bang Zi     | 48.30                     | —                                 |
| Tian Hua Fen    | 48.99                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62555     | 62555                  | 0.00                            | 7.75                               |
| 62556     | 62556                  | 0.00                            | 7.67                               |
| 62791     | 62791                  | 0.00                            | 4.81                               |
| 62792     | 62792                  | 0.00                            | 5.73                               |

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 2.4-2022-02

Validated substance/substance group **Xia Ku Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60080-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Xia Ku Cao | G202HS232RM1 | 62284 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 | g202h1064121 | 1       |
| Phytocomm | Xia Ku Cao | G202H1064221 | 2       |
| PhytoComm | Xia Ku Cao | G202H1064221 | 2       |
| Phytocomm | Xia Ku Cao | G202H1064421 | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Xin Yi              | 16.29                     | —                                 |
| Zhi Shi             | 18.56                     | —                                 |
| Hu Zhang            | 20.45                     | —                                 |
| Bai Hua She She Cao | 22.13                     | —                                 |
| Han Lian Cao        | 23.49                     | —                                 |
| Mang Xiao           | 26.17                     | —                                 |
| Sang Ye             | 26.26                     | —                                 |
| Yi Mu Cao           | 27.19                     | —                                 |
| Xi Xian Cao         | 35.80                     | —                                 |
| Yu Xing Cao         | 38.18                     | —                                 |
| He Shou Wu          | 39.12                     | —                                 |
| Huang Lian          | 39.96                     | —                                 |
| He Huan Pi          | 40.30                     | —                                 |
| Gu Sui Bu           | 40.66                     | —                                 |
| Sha Ren             | 40.67                     | —                                 |
| Xuan Fu Hua         | 41.40                     | —                                 |
| Jiang Huang         | 42.06                     | —                                 |
| Gou Teng            | 42.49                     | —                                 |
| Sang Bai Pi         | 44.43                     | —                                 |
| Bu Gu Zhi           | 44.92                     | —                                 |
| Nü Zhen Zi          | 45.44                     | —                                 |
| Jing Jie            | 47.35                     | —                                 |
| Pu Gong Ying        | 47.42                     | —                                 |
| Ze Lan              | 48.71                     | —                                 |
| Shan Yao            | 48.98                     | —                                 |
| Wu Zhu Yu           | 49.21                     | —                                 |
| Sang Ji Shend       | 50.91                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62283     | 62283                  | 0.00                            | 16.29                              |
| 62284     | 62284                  | 0.00                            | 16.53                              |

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 2.4-2022-02

Validated substance/substance group **Xian Mao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60316-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Xian Mao; Curculiginis orchoidis rhizoma

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Xian Mao                  | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Xian Mao* 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 Mao*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Xian Mao  | G304H0549021 | 62985     | 40      | from supplier |
| PhytoComm | Xian Mao  | G304H0549021 | 62986     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Mao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 Mao*.
- 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 Mao  | G304H0549021 | 62985 <sup>†</sup> | 20      |
| PhytoComm | Xian Mao  | G304H0549021 | 62986 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Xian Mao*.
- 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 Mao  | G304H0549321 | 2       |
| Phytocomm | Xian Mao  | G304H0549521 | 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 *Xian Mao* 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 Mao* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 4              | 853           |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xian Mao* 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Wu Jia Pi        | 8.05                      | —                                 |
| Yu Xing Cao      | 9.98                      | —                                 |
| (Sheng) Di Huang | 15.45                     | —                                 |
| Dan Zhu Ye       | 16.70                     | —                                 |
| Mang Xiao        | 22.68                     | —                                 |
| Jing Jie         | 26.42                     | —                                 |
| Ding Xiang       | 28.97                     | —                                 |
| Sang Ji Shend    | 29.98                     | —                                 |
| Sang Ye          | 30.05                     | —                                 |
| Shu Di (Huang)   | 34.59                     | —                                 |
| Bu Gu Zhi        | 37.17                     | —                                 |
| Ge Gen           | 38.61                     | —                                 |
| Du Zhong         | 43.29                     | —                                 |
| Hua Shi          | 46.43                     | —                                 |
| Jin Qian Cao     | 49.19                     | —                                 |
| Yin Chen Hao     | 49.53                     | —                                 |
| Guang Huo Xiang  | 50.25                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xian Mao* 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62985     | 62985                  | 0.00                            | 8.05                               |
| 62986     | 62986                  | 0.00                            | 8.95                               |

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 2.4-2022-02

Validated substance/substance group **Xiang Fu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60185-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | G088H0930921 | 62777     | 40      | from supplier |
| PhytoComm | Xiang Fu  | G088H0930921 | 62778     | 40      | from supplier |
| PhytoComm | Xiang Fu  | G088H0930922 | 62937     | 40      | from supplier |
| PhytoComm | Xiang Fu  | G088H0930922 | 62938     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G088H0930921 | 62777 <sup>†</sup> | 20      |
| PhytoComm | Xiang Fu  | G088H0930921 | 62778 <sup>†</sup> | 20      |
| PhytoComm | Xiang Fu  | G088H0930922 | 62937 <sup>†</sup> | 20      |
| PhytoComm | Xiang Fu  | G088H0930922 | 62938 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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  | G088H0930321 | 1       |
| Phytocomm | Xiang Fu  | G088H0930521 | 5       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 1              | 0             | 8              | 848           |

The substance/substance group *Xiang Fu* 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 99.9483 % (> 99.3610 %)  | n/a (n/a)                |

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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Yi Mu Cao           | 14.35                     | —                                 |
| Zi Su Zi            | 16.94                     | —                                 |
| Wu Yao              | 18.81                     | —                                 |
| Niu Bang Zi         | 19.02                     | —                                 |
| Di Gu Pi            | 19.89                     | —                                 |
| Cang Er Zi          | 20.11                     | —                                 |
| Jiang Huang         | 21.16                     | —                                 |
| Shan Yao            | 21.34                     | —                                 |
| Yan Hu Suo          | 21.82                     | —                                 |
| Xiao Hui Xiang      | 21.87                     | —                                 |
| (Shi) Chang Pu      | 23.01                     | —                                 |
| Ku Shen             | 23.13                     | —                                 |
| Gu Sui Bu           | 23.45                     | —                                 |
| Sha Ren             | 23.90                     | —                                 |
| Zhi Gan Cao         | 24.19                     | —                                 |
| (Huai) Niu Xi       | 24.66                     | —                                 |
| Tian Hua Fen        | 24.72                     | —                                 |
| Xin Yi              | 24.82                     | —                                 |
| Ju Hua              | 24.85                     | —                                 |
| Bai Hua She She Cao | 25.04                     | —                                 |
| Chen Pi             | 25.64                     | —                                 |
| Pu Gong Ying        | 25.86                     | —                                 |
| Chuan Lian Zi       | 25.98                     | —                                 |
| Bai Zhi             | 25.99                     | —                                 |
| Lian Qiao           | 26.18                     | —                                 |
| Huang Qi            | 26.43                     | —                                 |
| (Bai) Dou Kou       | 26.66                     | —                                 |
| Chuan Niu Xi        | 26.71                     | —                                 |
| Dang Gui            | 26.96                     | —                                 |
| Chi Shao (Yao)      | 27.25                     | —                                 |
| Zhi Ke              | 27.49                     | —                                 |
| Shan Yu Rou         | 27.92                     | —                                 |
| Sang Ye             | 28.07                     | —                                 |
| Jie Geng            | 28.21                     | —                                 |
| Mang Xiao           | 28.24                     | —                                 |
| Xu Duan             | 28.35                     | —                                 |
| Ze Lan              | 29.28                     | —                                 |
| Yuan Zhi            | 29.81                     | —                                 |
| Bo He               | 30.98                     | —                                 |
| Sang Zhi            | 31.16                     | —                                 |
| Hu Zhang            | 31.49                     | —                                 |
| Wu Zhu Yu           | 31.91                     | —                                 |
| Xi Xian Cao         | 32.34                     | —                                 |

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| <b>Substanz</b>  | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|------------------|-----------------------------------|-------------------------------------------|
| Jin Yin Hua      | 32.97                             | —                                         |
| Gan Cao          | 33.08                             | —                                         |
| Gan Jiang        | 33.17                             | —                                         |
| He Huan Pi       | 33.38                             | —                                         |
| Huang Lian       | 33.46                             | —                                         |
| Tu Fu Ling       | 34.39                             | —                                         |
| Chuan Mu Tong    | 34.66                             | —                                         |
| Mao Dong Qing    | 34.92                             | —                                         |
| Zi Hua Di Ding   | 35.33                             | —                                         |
| E Zhu            | 35.96                             | —                                         |
| Du Zhong         | 36.80                             | —                                         |
| Bai Zhu          | 36.94                             | —                                         |
| Nü Zhen Zi       | 37.37                             | —                                         |
| Qiang Huo        | 38.01                             | —                                         |
| Dong Gua Zi      | 38.42                             | —                                         |
| Mu Dan Pi        | 38.50                             | —                                         |
| Mu Gua           | 38.64                             | —                                         |
| Hou Po           | 39.41                             | —                                         |
| Mi Huan Jun      | 39.67                             | —                                         |
| Fang Feng        | 39.68                             | —                                         |
| Han Lian Cao     | 40.62                             | —                                         |
| Qing Pi          | 40.65                             | —                                         |
| Bing Lang        | 40.71                             | —                                         |
| Fu Zi            | 40.77                             | —                                         |
| Ce Bai Ye        | 40.84                             | —                                         |
| Zhi Shi          | 41.65                             | —                                         |
| Lian Zi          | 41.65                             | —                                         |
| Wang Bu Liu Xing | 42.05                             | —                                         |
| Huang Bai        | 42.10                             | —                                         |
| Dan Shen         | 42.16                             | —                                         |
| Du Huo           | 42.35                             | —                                         |
| Yin Chen Hao     | 42.40                             | —                                         |
| Jiao Gu Lan      | 42.51                             | —                                         |
| Yu Xing Cao      | 42.58                             | —                                         |
| Bai Jiang Cao    | 42.59                             | —                                         |
| Yu Jin           | 43.03                             | —                                         |
| Suan Zao Ren     | 43.08                             | —                                         |
| Jing Jie         | 43.12                             | —                                         |
| Chuang Mu Xiang  | 43.16                             | —                                         |
| Cang Zhu         | 43.22                             | —                                         |
| Sha Shen (Bei)   | 43.34                             | —                                         |
| Chai Hu          | 43.79                             | —                                         |
| Dan Dou Chi      | 43.92                             | —                                         |
| Che Qian Zi      | 44.91                             | —                                         |
| Sang Ji Shend    | 44.92                             | —                                         |
| Bai Xian Pi      | 45.12                             | —                                         |
| He Shou Wu       | 45.27                             | —                                         |
| Bai He           | 45.50                             | —                                         |
| Hong Jing Tian   | 45.94                             | —                                         |
| Qing Hao         | 46.29                             | —                                         |
| Qin Jiao         | 46.43                             | —                                         |
| Ye Jiao Teng     | 46.54                             | —                                         |
| Shen Qu          | 46.81                             | —                                         |
| Xia Ku Cao       | 47.39                             | —                                         |
| Ba Ji Tian       | 47.75                             | —                                         |
| Lai Fu Zi        | 47.88                             | —                                         |
| Ji Li            | 47.93                             | —                                         |
| Ge Gen           | 48.22                             | —                                         |
| Zhe Bei Mu       | 49.26                             | —                                         |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Ren Dong Teng   | 49.47                             | —                                         |
| Sang Bai Pi     | 49.73                             | —                                         |

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:

| <b>Sample ID</b> | <b>Reference<br/>sample ID</b> | <b>Distance to<br/>reference sample</b> | <b>Distance to<br/>next foreign sample</b> |
|------------------|--------------------------------|-----------------------------------------|--------------------------------------------|
| 62777            | 62777                          | 0.00                                    | 17.13                                      |
| 62778            | 62778                          | 0.00                                    | 16.94                                      |
| 62937            | 62937                          | 0.00                                    | 14.37                                      |
| 62938            | 62938                          | 0.00                                    | 14.35                                      |

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 2.4-2022-02

Validated substance/substance group **Xiao Hui Xiang**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60209-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Xiao Hui Xiang; Foeniculi vulgaris fructus

### Special notes

When selecting the *Xiao Hui Xiang* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Xiao Hui Xiang            | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Xiao Hui 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 *Xiao Hui Xiang*:

| Supplier  | Substance      | Batch        | Sample ID | Spectra | Certificate   |
|-----------|----------------|--------------|-----------|---------|---------------|
| PhytoComm | Xiao Hui Xiang | G104H0339021 | 63003     | 40      | from supplier |
| PhytoComm | Xiao Hui Xiang | G104H0339021 | 63004     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Xiao Hui Xiang*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Xiao Hui 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 | Xiao Hui Xiang | G104H0339021 | 63003 <sup>†</sup> | 20      |
| PhytoComm | Xiao Hui Xiang | G104H0339021 | 63004 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 *Xiao Hui Xiang*.
- 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 | Xiao Hui Xiang | g104h0339321 | 1       |
| Phytocomm | Xiao Hui Xiang | G104H0339522 | 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 *Xiao Hui 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 *Xiao Hui 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 4              | 853           |

The substance/substance group *Xiao Hui 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xiao Hui 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Ku Shen             | 18.33                     | —                                 |
| Yi Mu Cao           | 18.41                     | —                                 |
| Xu Duan             | 21.85                     | —                                 |
| Xiang Fu            | 23.41                     | —                                 |
| Wu Zhu Yu           | 24.91                     | —                                 |
| Nü Zhen Zi          | 25.70                     | —                                 |
| Cang Er Zi          | 26.89                     | —                                 |
| Sha Ren             | 27.30                     | —                                 |
| (Shi) Chang Pu      | 28.34                     | —                                 |
| Lian Qiao           | 28.42                     | —                                 |
| Niu Bang Zi         | 29.01                     | —                                 |
| Mang Xiao           | 29.44                     | —                                 |
| Shan Yu Rou         | 30.18                     | —                                 |
| Yan Hu Suo          | 30.24                     | —                                 |
| (Bai) Dou Kou       | 31.92                     | —                                 |
| Jiang Huang         | 32.86                     | —                                 |
| Ju Hua              | 34.31                     | —                                 |
| Gu Sui Bu           | 35.17                     | —                                 |
| Chen Pi             | 36.07                     | —                                 |
| Shan Yao            | 36.65                     | —                                 |
| Sang Ji Shend       | 38.16                     | —                                 |
| Ze Lan              | 38.67                     | —                                 |
| Fang Feng           | 38.77                     | —                                 |
| He Huan Pi          | 38.80                     | —                                 |
| Zi Su Zi            | 39.09                     | —                                 |
| Wu Yao              | 39.65                     | —                                 |
| Bai Hua She She Cao | 40.50                     | —                                 |
| Yin Chen Hao        | 40.82                     | —                                 |
| Shen Qu             | 41.04                     | —                                 |
| Suan Zao Ren        | 41.30                     | —                                 |
| Di Gu Pi            | 42.49                     | —                                 |
| Sang Ye             | 42.92                     | —                                 |
| (Huai) Niu Xi       | 43.50                     | —                                 |
| Pu Gong Ying        | 43.59                     | —                                 |
| Sang Bai Pi         | 43.69                     | —                                 |
| Hong Jing Tian      | 44.42                     | —                                 |
| Han Lian Cao        | 45.62                     | —                                 |
| Dang Gui            | 45.66                     | —                                 |
| Wang Bu Liu Xing    | 47.06                     | —                                 |
| Bai Zhi             | 47.16                     | —                                 |
| Jing Jie            | 47.31                     | —                                 |
| Chuan Niu Xi        | 48.53                     | —                                 |
| Qiang Huo           | 48.71                     | —                                 |
| Gan Cao             | 49.68                     | —                                 |
| Bu Gu Zhi           | 50.21                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xiao Hui 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 63003     | 63003               | 0.00                         | 18.45                           |
| 63004     | 63004               | 0.00                         | 18.33                           |

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 2.4-2022-02

Validated substance/substance group **Xie Bai**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60362-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Xie Bai; Allii bulbos

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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   | G504HS334TK1 | 62819     | 40      | from supplier |
| PhytoComm | Xie Bai   | G504HS334TK1 | 62820     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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   | G504HS334TK1 | 62819 <sup>†</sup> | 20      |
| PhytoComm | Xie Bai   | G504HS334TK1 | 62820 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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   | G504H1830321 | 1       |
| Phytocomm | Xie Bai   | G504H1830421 | 1       |
| Phytocomm | Xie Bai   | G504H1830422 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Shan Yao        | 15.02                     | —                                 |
| Suan Zao Ren    | 16.17                     | —                                 |
| Lian Qiao       | 17.97                     | —                                 |
| San Qi          | 18.23                     | —                                 |
| Bai Shao Yao    | 18.31                     | —                                 |
| Mu Gua          | 18.78                     | —                                 |
| Cang Zhu        | 18.82                     | —                                 |
| Jiao Gu Lan     | 18.85                     | —                                 |
| Pi Pa Ye        | 18.98                     | —                                 |
| Lian Zi         | 19.02                     | —                                 |
| Bai Zi Ren      | 19.19                     | —                                 |
| Jie Geng        | 19.29                     | —                                 |
| Ku Shen         | 19.92                     | —                                 |
| Ji Li           | 20.47                     | —                                 |
| Gou Qi Zi       | 21.03                     | —                                 |
| Zhe Bei Mu      | 21.74                     | —                                 |
| Tian Hua Fen    | 21.87                     | —                                 |
| Zhi Mu          | 22.19                     | —                                 |
| Mao Dong Qing   | 22.62                     | —                                 |
| Chuang Mu Xiang | 23.09                     | —                                 |
| Ren Shen        | 23.33                     | —                                 |
| Ling Zhi        | 23.52                     | —                                 |
| Shen Qu         | 23.84                     | —                                 |
| Jin Yin Hua     | 24.47                     | —                                 |
| Dan Dou Chi     | 24.94                     | —                                 |
| Di Gu Pi        | 25.34                     | —                                 |
| Dan Shen        | 25.63                     | —                                 |
| Ze Xie          | 25.65                     | —                                 |
| Zhi Ke          | 25.88                     | —                                 |
| Dang Gui        | 27.05                     | —                                 |
| Hong Jing Tian  | 27.38                     | —                                 |
| Guang Huo Xiang | 27.51                     | —                                 |
| Chai Hu         | 27.68                     | —                                 |
| Long Yan Rou    | 27.91                     | —                                 |
| Mu Zei          | 28.31                     | —                                 |
| Zhu Ru          | 28.68                     | —                                 |
| Yuan Zhi        | 28.90                     | —                                 |
| Sheng Jiang     | 29.15                     | —                                 |
| Huo Ma Ren      | 29.32                     | —                                 |
| Hou Po          | 29.37                     | —                                 |
| He Huan Pi      | 29.44                     | —                                 |
| Lai Fu Zi       | 29.54                     | —                                 |
| Ren Dong Teng   | 29.65                     | —                                 |
| Ban Lan Gen     | 29.67                     | —                                 |
| Fu Ling         | 30.62                     | —                                 |
| Gu Sui Bu       | 31.19                     | —                                 |
| Gua Lou         | 31.31                     | —                                 |
| Lu Gen          | 32.04                     | —                                 |
| Ci Wu Jia       | 32.55                     | —                                 |
| Tu Fu Ling      | 33.29                     | —                                 |
| Mang Xiao       | 33.39                     | —                                 |
| She Gan         | 33.51                     | —                                 |

*continued on the next page*



continued from previous page

| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ye Jiao Teng    | 33.81                     | —                                 |
| Gan Cao         | 33.97                     | —                                 |
| Fu Zi           | 34.49                     | —                                 |
| Bai Xian Pi     | 34.69                     | —                                 |
| Gui Zhi         | 35.02                     | —                                 |
| Cang Er Zi      | 35.27                     | —                                 |
| Gou Teng        | 35.73                     | —                                 |
| Hong Hua        | 35.89                     | —                                 |
| Fu Pen Zi       | 36.73                     | —                                 |
| Zi Hua Di Ding  | 36.89                     | —                                 |
| Rou Gui         | 37.31                     | —                                 |
| Tao Ren         | 37.41                     | —                                 |
| Zhi Gan Cao     | 37.50                     | —                                 |
| Yan Hu Suo      | 38.38                     | —                                 |
| Ji Xue Teng     | 38.95                     | —                                 |
| Qing Pi         | 39.62                     | —                                 |
| Fo Shou         | 40.31                     | —                                 |
| Fu Xiao Mai     | 40.77                     | —                                 |
| Yin Yang Huo    | 40.93                     | —                                 |
| Ma Huang        | 41.36                     | —                                 |
| Qiang Huo       | 41.39                     | —                                 |
| Bo He           | 41.43                     | —                                 |
| Huang Qin       | 41.52                     | —                                 |
| Che Qian Zi     | 41.81                     | —                                 |
| Sang Zhi        | 42.56                     | —                                 |
| Ce Bai Ye       | 42.69                     | —                                 |
| Chi Shao (Yao)  | 43.02                     | —                                 |
| Yi Yi Ren       | 43.10                     | —                                 |
| Yu Jin          | 43.31                     | —                                 |
| Ma Huang Gen    | 45.85                     | —                                 |
| Zhu Ling        | 46.21                     | —                                 |
| Huang Bai       | 46.46                     | —                                 |
| Sha Ren         | 46.57                     | —                                 |
| Du Zhong        | 46.96                     | —                                 |
| Chuan Lian Zi   | 48.65                     | —                                 |
| (Fen) Bi Xie    | 48.84                     | —                                 |
| Huang Lian      | 49.77                     | —                                 |
| Ban Xia (Jiang) | 49.94                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62819     | 62819                  | 0.00                            | 15.02                              |
| 62820     | 62820                  | 0.00                            | 15.66                              |

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 2.4-2022-02

Validated substance/substance group **Xin Yi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60231-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Xin Yi                    | 3      | 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 |
| PhytoComm | Xin Yi    | G153HS139TK1 | 62885     | 40      | from supplier |
| PhytoComm | Xin Yi    | G153HS139TK1 | 62886     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Xin Yi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Xin Yi    | G153HS139SH1 | 62604 <sup>†</sup> | 20      |
| PhytoComm | Xin Yi    | G153HS139SP1 | 62725 <sup>†</sup> | 20      |
| PhytoComm | Xin Yi    | G153HS139SP1 | 62726 <sup>†</sup> | 20      |
| PhytoComm | Xin Yi    | G153HS139TK1 | 62885 <sup>†</sup> | 20      |
| PhytoComm | Xin Yi    | G153HS139TK1 | 62886 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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    | G153H0758321 | 1       |
| Phytocomm | Xin Yi    | G153H0758521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 119           | 1              | 11 277        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 99.1667 % (> 96.6667 %)  |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *Ma-halanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

| Substance           | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Bai Hua She She Cao | 5.35                      | —                                 |
| Zhi Shi             | 6.34                      | —                                 |
| Xi Xian Cao         | 6.49                      | —                                 |
| Pu Gong Ying        | 7.41                      | —                                 |
| Xia Ku Cao          | 9.73                      | —                                 |
| Ze Lan              | 10.33                     | —                                 |
| Han Lian Cao        | 10.61                     | —                                 |
| Tu Fu Ling          | 11.10                     | —                                 |
| Yu Xing Cao         | 12.06                     | —                                 |
| Yin Chen Hao        | 13.27                     | —                                 |
| Nü Zhen Zi          | 14.06                     | —                                 |
| Sang Ye             | 14.88                     | —                                 |
| Hu Zhang            | 15.08                     | —                                 |
| Shan Yao            | 17.51                     | —                                 |
| Huang Lian          | 18.61                     | —                                 |
| Jiang Huang         | 19.40                     | —                                 |
| Yi Mu Cao           | 20.89                     | —                                 |
| Du Zhong            | 24.81                     | —                                 |
| Sha Ren             | 26.25                     | —                                 |
| Yu Jin              | 26.41                     | —                                 |
| Mang Xiao           | 26.89                     | —                                 |
| Qiang Huo           | 26.99                     | —                                 |
| Fu Zi               | 28.61                     | —                                 |
| He Huan Pi          | 29.30                     | —                                 |
| Xiang Fu            | 30.95                     | —                                 |
| Bai Jiang Cao       | 31.77                     | —                                 |
| Dan Shen            | 31.88                     | —                                 |
| Zhi Ke              | 32.44                     | —                                 |
| Hou Po              | 33.52                     | —                                 |
| Gu Sui Bu           | 33.62                     | —                                 |
| Gou Teng            | 33.66                     | —                                 |
| Cang Er Zi          | 34.28                     | —                                 |
| Bo He               | 35.10                     | —                                 |
| Mao Dong Qing       | 36.67                     | —                                 |
| Che Qian Zi         | 36.73                     | —                                 |
| Qing Pi             | 36.85                     | —                                 |
| Wang Bu Liu Xing    | 37.02                     | —                                 |
| Jiao Gu Lan         | 37.65                     | —                                 |
| Hong Jing Tian      | 38.38                     | —                                 |
| Yin Yang Huo        | 38.89                     | —                                 |
| Zi Hua Di Ding      | 39.01                     | —                                 |
| Dan Dou Chi         | 39.14                     | —                                 |
| Bai Xian Pi         | 39.14                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Chai Hu         | 39.85                     | —                                 |
| Huang Bai       | 39.98                     | —                                 |
| Ling Zhi        | 40.71                     | —                                 |
| Di Gu Pi        | 41.21                     | —                                 |
| Ye Jiao Teng    | 41.26                     | —                                 |
| Zi Su Zi        | 41.81                     | —                                 |
| Jing Jie        | 42.50                     | —                                 |
| Ce Bai Ye       | 43.02                     | —                                 |
| Yan Hu Suo      | 43.32                     | —                                 |
| E Zhu           | 43.34                     | —                                 |
| Jin Yin Hua     | 43.59                     | —                                 |
| Fu Pen Zi       | 45.80                     | —                                 |
| Qing Hao        | 46.31                     | —                                 |
| Niu Bang Zi     | 47.31                     | —                                 |
| Chuang Mu Xiang | 47.56                     | —                                 |
| Bu Gu Zhi       | 47.74                     | —                                 |
| Ju Hua          | 48.29                     | —                                 |
| Wu Zhu Yu       | 48.40                     | —                                 |
| Ma Huang        | 48.62                     | —                                 |
| Sang Bai Pi     | 48.77                     | —                                 |
| Pi Pa Ye        | 49.00                     | —                                 |
| Chen Pi         | 49.91                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62603     | 62603                  | 0.00                            | 6.50                               |
| 62604     | 62604                  | 0.00                            | 6.49                               |
| 62725     | 62725                  | 0.00                            | 14.21                              |
| 62726     | 62726                  | 0.00                            | 14.83                              |
| 62885     | 62885                  | 0.00                            | 5.90                               |
| 62886     | 62886                  | 0.00                            | 5.35                               |

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 2.4-2022-02

Validated substance/substance group **Xu Duan**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60245-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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   | G092H2106922 | 62911     | 40      | from supplier |
| PhytoComm | Xu Duan   | G092H2106922 | 62912     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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   | G092H2106922 | 62911 <sup>†</sup> | 20      |
| PhytoComm | Xu Duan   | G092H2106922 | 62912 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Ku Shen             | 12.86                     | —                                 |
| Yi Mu Cao           | 16.37                     | —                                 |
| Xiang Fu            | 17.84                     | —                                 |
| Xiao Hui Xiang      | 23.70                     | —                                 |
| Chen Pi             | 24.44                     | —                                 |
| Cang Er Zi          | 25.16                     | —                                 |
| (Huai) Niu Xi       | 25.17                     | —                                 |
| Shan Yu Rou         | 25.99                     | —                                 |
| Chuan Niu Xi        | 27.13                     | —                                 |
| Lian Qiao           | 27.39                     | —                                 |
| Yan Hu Suo          | 28.45                     | —                                 |
| (Shi) Chang Pu      | 28.56                     | —                                 |
| Mang Xiao           | 29.03                     | —                                 |
| Wu Zhu Yu           | 29.36                     | —                                 |
| Niu Bang Zi         | 31.11                     | —                                 |
| Wu Yao              | 31.31                     | —                                 |
| Huang Qi            | 31.82                     | —                                 |
| Fang Feng           | 32.59                     | —                                 |
| Shan Yao            | 32.93                     | —                                 |
| Chuan Lian Zi       | 34.10                     | —                                 |
| Di Gu Pi            | 34.17                     | —                                 |
| Gan Cao             | 34.36                     | —                                 |
| Zi Su Zi            | 34.36                     | —                                 |
| Gu Sui Bu           | 34.56                     | —                                 |
| Bai Zhi             | 35.36                     | —                                 |
| Ju Hua              | 36.89                     | —                                 |
| Tian Hua Fen        | 37.04                     | —                                 |
| Pu Gong Ying        | 37.45                     | —                                 |
| Sha Ren             | 37.69                     | —                                 |
| Dang Gui            | 38.34                     | —                                 |
| Yuan Zhi            | 38.38                     | —                                 |
| Jie Geng            | 38.52                     | —                                 |
| Chi Shao (Yao)      | 38.56                     | —                                 |
| (Bai) Dou Kou       | 38.98                     | —                                 |
| Jiang Huang         | 39.10                     | —                                 |
| Zhi Ke              | 39.71                     | —                                 |
| Zhi Gan Cao         | 40.03                     | —                                 |
| Shen Qu             | 40.18                     | —                                 |
| He Huan Pi          | 40.90                     | —                                 |
| Sang Zhi            | 41.31                     | —                                 |
| Jin Yin Hua         | 42.69                     | —                                 |
| Sang Ye             | 43.11                     | —                                 |
| Xin Yi              | 43.27                     | —                                 |
| Nü Zhen Zi          | 43.65                     | —                                 |
| Ze Lan              | 43.86                     | —                                 |
| Bai Hua She She Cao | 44.09                     | —                                 |
| Dong Gua Zi         | 44.92                     | —                                 |
| Ba Ji Tian          | 46.50                     | —                                 |
| Sang Ji Shend       | 46.65                     | —                                 |
| Bai Zhu             | 47.87                     | —                                 |
| Hong Jing Tian      | 48.03                     | —                                 |
| Sang Bai Pi         | 48.59                     | —                                 |

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| Substanz   | Distance in<br>main model | Distance in<br>second-stage model |
|------------|---------------------------|-----------------------------------|
| Bo He      | 48.65                     | —                                 |
| Huang Lian | 49.60                     | —                                 |
| Bing Lang  | 49.89                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62911     | 62911                  | 0.00                            | 12.94                              |
| 62912     | 62912                  | 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 2.4-2022-02

Validated substance/substance group **Xuan Fu Hua**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60223-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Xuan Fu Hua; Inulae flos

### Special notes

When selecting the *Xuan Fu Hua* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Xuan Fu Hua               | 1      | 0      | 1      |

### Second-stage model

For differentiation of the substance/substance group *Xuan Fu 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 *Xuan Fu Hua*:

| Supplier  | Substance   | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-------------|--------------|-----------|---------|---------------|
| PhytoComm | Xuan Fu Hua | G126H1168921 | 62901     | 40      | from supplier |
| PhytoComm | Xuan Fu Hua | G126H1168921 | 62902     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Xuan Fu Hua*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Xuan Fu 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 | Xuan Fu Hua | G126H1168921 | 62901 <sup>†</sup> | 20      |
| PhytoComm | Xuan Fu Hua | G126H1168921 | 62902 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 *Xuan Fu Hua*.
- 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 | Xuan Fu Hua | G126H1168521 | 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 *Xuan Fu 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 *Xuan Fu 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 0              | 0             | 1              | 856           |

The substance/substance group *Xuan Fu 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xuan Fu 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| He Shou Wu          | 8.49                      | —                                 |
| Yin Chen Hao        | 10.65                     | —                                 |
| Gu Sui Bu           | 15.85                     | —                                 |
| Sang Ji Shend       | 15.87                     | —                                 |
| Jing Jie            | 16.54                     | —                                 |
| Sang Bai Pi         | 18.94                     | —                                 |
| He Huan Pi          | 21.67                     | —                                 |
| Mang Xiao           | 24.19                     | —                                 |
| Jin Qian Cao        | 24.85                     | —                                 |
| Sha Ren             | 25.02                     | —                                 |
| Du Zhong            | 25.88                     | —                                 |
| Gou Teng            | 27.01                     | —                                 |
| Wu Zhu Yu           | 27.07                     | —                                 |
| Nü Zhen Zi          | 29.01                     | —                                 |
| Bu Gu Zhi           | 33.38                     | —                                 |
| Ge Gen              | 33.40                     | —                                 |
| Chen Pi             | 33.51                     | —                                 |
| Sang Ye             | 34.77                     | —                                 |
| Dan Zhu Ye          | 35.00                     | —                                 |
| Yi Mu Cao           | 36.69                     | —                                 |
| Hong Jing Tian      | 37.66                     | —                                 |
| Ding Xiang          | 38.67                     | —                                 |
| Bai Hua She She Cao | 38.71                     | —                                 |
| Hu Zhang            | 38.92                     | —                                 |
| Wu Jia Pi           | 40.49                     | —                                 |
| Xia Ku Cao          | 40.83                     | —                                 |
| Xiao Hui Xiang      | 42.61                     | —                                 |
| Tu Si Zi            | 43.18                     | —                                 |
| Jiang Huang         | 46.42                     | —                                 |
| Wu Yao              | 48.42                     | —                                 |
| Xin Yi              | 49.76                     | —                                 |
| Hua Shi             | 50.09                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xuan Fu 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62901     | 62901                  | 0.00                            | 9.11                               |
| 62902     | 62902                  | 0.00                            | 8.49                               |

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 2.4-2022-02

Validated substance/substance group **Xuan Shen**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60095-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Xuan Shen                 | 1      | 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 | G223HS092ST1 | 62787     | 40      | from supplier |
| PhytoComm | Xuan Shen | G223HS092ST1 | 62788     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Xuan Shen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G223HS092ST1 | 62787 <sup>†</sup> | 20      |
| PhytoComm | Xuan Shen | G223HS092ST1 | 62788 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G223H0537421 | 1       |
| Phytocomm | Xuan Shen | g22h0537322  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Mang Xiao       | 20.36                     | —                                 |
| Jin Qian Cao    | 26.69                     | —                                 |
| Wu Jia Pi       | 29.56                     | —                                 |
| Jing Jie        | 29.57                     | —                                 |
| Du Zhong        | 30.60                     | —                                 |
| Jiu Da Huang    | 34.73                     | —                                 |
| Sang Ye         | 35.85                     | —                                 |
| Guang Huo Xiang | 36.67                     | —                                 |
| Ding Xiang      | 37.81                     | —                                 |
| Yu Xing Cao     | 44.53                     | —                                 |
| Xia Ku Cao      | 44.96                     | —                                 |
| Sang Ji Shend   | 46.03                     | —                                 |
| Xuan Fu Hua     | 46.30                     | —                                 |
| Yi Mu Cao       | 46.48                     | —                                 |
| Hong Jing Tian  | 47.03                     | —                                 |
| Hua Shi         | 48.45                     | —                                 |
| Dan Zhu Ye      | 48.50                     | —                                 |
| Gou Teng        | 51.03                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62787     | 62787                  | 0.00                            | 20.36                              |
| 62788     | 62788                  | 0.00                            | 20.39                              |

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



# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Yan Hu Suo**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60439-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | G081HS161SG1 | 62677     | 40      | from supplier |
| PhytoComm | Yan Hu Suo | G081HS161SG1 | 62678     | 40      | from supplier |
| PhytoComm | Yan Hu Suo | G081H0805021 | 62999     | 40      | from supplier |
| PhytoComm | Yan Hu Suo | G081H0805021 | 63000     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G081HS161SG1 | 62677 <sup>†</sup> | 20      |
| PhytoComm | Yan Hu Suo | G081HS161SG1 | 62678 <sup>†</sup> | 20      |
| PhytoComm | Yan Hu Suo | G081H0805021 | 62999 <sup>†</sup> | 20      |
| PhytoComm | Yan Hu Suo | G081H0805021 | 63000 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G081H0805223 | 1       |
| Phytocomm | Yan Hu Suo | G081H0805521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 0              | 1             | 5              | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Hou Po          | 5.96                      | —                                 |
| Fu Pen Zi       | 6.47                      | —                                 |
| She Gan         | 8.11                      | —                                 |
| Gu Sui Bu       | 8.30                      | —                                 |
| Shan Yao        | 9.00                      | —                                 |
| Pi Pa Ye        | 9.74                      | —                                 |
| Fu Zi           | 9.83                      | —                                 |
| Ce Bai Ye       | 10.38                     | —                                 |
| Dan Dou Chi     | 11.56                     | —                                 |
| Chai Hu         | 11.69                     | —                                 |
| Gan Cao         | 11.89                     | —                                 |
| Yu Jin          | 11.89                     | —                                 |
| Ren Dong Teng   | 12.20                     | —                                 |
| Che Qian Zi     | 12.85                     | —                                 |
| Zhu Ling        | 13.22                     | —                                 |
| Tian Hua Fen    | 13.35                     | —                                 |
| Jin Yin Hua     | 13.81                     | —                                 |
| Bai Xian Pi     | 13.84                     | —                                 |
| Mu Zei          | 13.92                     | —                                 |
| Guang Huo Xiang | 14.38                     | —                                 |
| Dan Shen        | 14.95                     | —                                 |
| Yin Yang Huo    | 15.18                     | —                                 |
| Qiang Huo       | 15.37                     | —                                 |
| Gan Jiang       | 15.64                     | —                                 |
| Ma Huang        | 15.91                     | —                                 |
| Di Gu Pi        | 15.99                     | —                                 |
| Zi Su Zi        | 16.00                     | —                                 |
| Jiang Huang     | 16.41                     | —                                 |
| Qing Pi         | 16.67                     | —                                 |
| Shen Qu         | 17.02                     | —                                 |
| Mi Huan Jun     | 17.09                     | —                                 |
| Ye Jiao Teng    | 17.26                     | —                                 |
| Lu Gen          | 17.32                     | —                                 |
| Zi Hua Di Ding  | 17.80                     | —                                 |
| Bai Shao Yao    | 17.81                     | —                                 |
| Ji Li           | 17.97                     | —                                 |
| Tu Fu Ling      | 18.00                     | —                                 |
| Mao Dong Qing   | 18.24                     | —                                 |
| (Bai) Dou Kou   | 18.30                     | —                                 |
| Ling Zhi        | 18.30                     | —                                 |
| Lian Qiao       | 18.46                     | —                                 |
| Zhi Gan Cao     | 18.49                     | —                                 |
| He Huan Pi      | 18.54                     | —                                 |

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| <b>Substanz</b>     | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|---------------------|-----------------------------------|-------------------------------------------|
| Jing Jie            | 18.58                             | —                                         |
| Ban Lan Gen         | 18.97                             | —                                         |
| Ji Xue Teng         | 19.09                             | —                                         |
| Hong Jing Tian      | 19.16                             | —                                         |
| (Fen) Bi Xie        | 19.27                             | —                                         |
| Lian Zi             | 19.31                             | —                                         |
| Ze Xie              | 19.75                             | —                                         |
| Sha Shen (Bei)      | 19.91                             | —                                         |
| Jiao Gu Lan         | 19.96                             | —                                         |
| Fu Ling             | 20.22                             | —                                         |
| Xiao Hui Xiang      | 20.65                             | —                                         |
| Zhe Bei Mu          | 20.74                             | —                                         |
| Du Zhong            | 20.82                             | —                                         |
| Cang Er Zi          | 20.86                             | —                                         |
| Xiang Fu            | 21.11                             | —                                         |
| Suan Zao Ren        | 21.22                             | —                                         |
| Huang Lian          | 21.72                             | —                                         |
| Zhi Ke              | 21.79                             | —                                         |
| Niu Bang Zi         | 22.17                             | —                                         |
| Ren Shen            | 22.29                             | —                                         |
| Sang Zhi            | 22.50                             | —                                         |
| Sheng Jiang         | 22.76                             | —                                         |
| Tao Ren             | 22.80                             | —                                         |
| Bai Zi Ren          | 23.35                             | —                                         |
| Qing Hao            | 23.73                             | —                                         |
| Bai Zhi             | 23.76                             | —                                         |
| Dang Gui            | 24.60                             | —                                         |
| Chuan Lian Zi       | 24.60                             | —                                         |
| Sha Ren             | 24.85                             | —                                         |
| (Huai) Niu Xi       | 25.03                             | —                                         |
| Gui Zhi             | 25.21                             | —                                         |
| Huo Ma Ren          | 25.21                             | —                                         |
| Huang Bai           | 25.56                             | —                                         |
| Bo He               | 25.76                             | —                                         |
| Jie Geng            | 26.36                             | —                                         |
| E Zhu               | 26.61                             | —                                         |
| Gua Lou             | 26.66                             | —                                         |
| Gou Teng            | 26.80                             | —                                         |
| Pu Gong Ying        | 27.44                             | —                                         |
| Rou Gui             | 27.71                             | —                                         |
| Chuan Mu Tong       | 28.37                             | —                                         |
| Cang Zhu            | 28.88                             | —                                         |
| Chen Pi             | 29.14                             | —                                         |
| Yi Mu Cao           | 29.41                             | —                                         |
| Ku Shen             | 29.78                             | —                                         |
| Ma Huang Gen        | 29.91                             | —                                         |
| Mang Xiao           | 30.10                             | —                                         |
| Bai Hua She She Cao | 30.21                             | —                                         |
| Huang Qin           | 30.52                             | —                                         |
| Ban Xia (Jiang)     | 31.61                             | —                                         |
| Sang Ye             | 32.39                             | —                                         |
| Lai Fu Zi           | 32.80                             | —                                         |
| Ze Lan              | 33.04                             | —                                         |
| Bai He              | 33.17                             | —                                         |
| Bai Jiang Cao       | 33.41                             | —                                         |
| Wang Bu Liu Xing    | 33.44                             | —                                         |
| Huang Qi            | 33.47                             | —                                         |
| Yi Yi Ren           | 33.80                             | —                                         |
| San Qi              | 34.37                             | —                                         |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Chuan Niu Xi    | 34.63                     | —                                 |
| Chuang Mu Xiang | 35.34                     | —                                 |
| Zhu Ru          | 35.43                     | —                                 |
| Xin Yi          | 35.54                     | —                                 |
| Ci Wu Jia       | 36.48                     | —                                 |
| Hong Hua        | 36.59                     | —                                 |
| Gou Qi Zi       | 36.68                     | —                                 |
| Shan Yu Rou     | 36.74                     | —                                 |
| Xie Bai         | 37.21                     | —                                 |
| Wu Yao          | 37.60                     | —                                 |
| Fu Xiao Mai     | 39.00                     | —                                 |
| Chi Shao (Yao)  | 39.03                     | —                                 |
| (Shi) Chang Pu  | 39.15                     | —                                 |
| Xi Xian Cao     | 39.70                     | —                                 |
| Qin Jiao        | 40.48                     | —                                 |
| Du Huo          | 41.81                     | —                                 |
| Bai Zhu         | 42.19                     | —                                 |
| Fu Shen         | 43.12                     | —                                 |
| Zhi Mu          | 43.66                     | —                                 |
| Ju Hua          | 43.92                     | —                                 |
| Xu Duan         | 44.29                     | —                                 |
| Sang Ji Shend   | 45.14                     | —                                 |
| Ban Zhi Lian    | 45.59                     | —                                 |
| Hu Zhang        | 46.31                     | —                                 |
| Fo Shou         | 46.40                     | —                                 |
| Dong Gua Zi     | 47.14                     | —                                 |
| Mu Dan Pi       | 47.59                     | —                                 |
| Yu Xing Cao     | 47.75                     | —                                 |
| Long Yan Rou    | 47.80                     | —                                 |
| Wu Wei Zi       | 48.13                     | —                                 |
| Fang Feng       | 48.20                     | —                                 |
| Long Dan (Cao)  | 48.74                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62677     | 62677                  | 0.00                            | 6.27                               |
| 62678     | 62678                  | 0.00                            | 5.96                               |
| 62999     | 62999                  | 0.00                            | 13.76                              |
| 63000     | 63000                  | 0.00                            | 13.65                              |

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.





# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Ye Jiao Teng**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60068-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Ye Jiao Teng | G288HS163RM1 | 62422 <sup>†</sup> | 20      |
| PhytoComm | Ye Jiao Teng | G288HS163SK1 | 62625 <sup>†</sup> | 20      |
| PhytoComm | Ye Jiao Teng | G288HS163SK1 | 62626 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | g228h0085223 | 1       |
| Phytocomm | Ye Jiao Teng | G288H0885223 | 1       |
| Phytocomm | Ye Jiao Teng | G288H0885522 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 2              | 158           | 2              | 22 278        |
| <b>Type B</b> | 1              | 77            | 3              | 11 316        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9926 % (> 99.9762 %)  | 98.7500 % (> 96.8750 %) |
| <b>Type B</b> | 99.9926 % (> 99.9604 %)  | 96.2500 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ji Xue Teng     | 5.00                      | —                                 |
| Bai Xian Pi     | 6.07                      | —                                 |
| Lu Gen          | 6.58                      | —                                 |
| Tu Fu Ling      | 6.92                      | —                                 |
| Dan Dou Chi     | 7.42                      | —                                 |
| Rou Gui         | 8.99                      | —                                 |
| Yin Yang Huo    | 9.20                      | —                                 |
| He Huan Pi      | 10.07                     | —                                 |
| Ren Dong Teng   | 10.22                     | —                                 |
| (Fen) Bi Xie    | 11.04                     | —                                 |
| Fu Zi           | 12.08                     | —                                 |
| Fo Shou         | 12.31                     | —                                 |
| Dan Shen        | 12.59                     | —                                 |
| Ma Huang Gen    | 12.63                     | —                                 |
| Ling Zhi        | 12.96                     | —                                 |
| Chai Hu         | 13.09                     | —                                 |
| Guang Huo Xiang | 13.24                     | —                                 |
| She Gan         | 13.74                     | —                                 |
| Gou Teng        | 13.85                     | —                                 |
| Bai Shao Yao    | 14.14                     | —                                 |
| Suan Zao Ren    | 14.57                     | —                                 |
| Mu Zei          | 14.61                     | —                                 |
| Huo Ma Ren      | 14.69                     | —                                 |
| Mao Dong Qing   | 14.75                     | —                                 |
| Jing Jie        | 14.96                     | —                                 |
| Gui Zhi         | 15.13                     | —                                 |
| Zhu Ling        | 15.36                     | —                                 |
| Lian Zi         | 15.49                     | —                                 |
| Shen Qu         | 15.53                     | —                                 |
| Yu Jin          | 15.79                     | —                                 |
| Ma Huang        | 15.89                     | —                                 |
| Tao Ren         | 16.16                     | —                                 |
| Ce Bai Ye       | 16.54                     | —                                 |
| Gu Sui Bu       | 17.01                     | —                                 |
| Hou Po          | 17.37                     | —                                 |
| Yan Hu Suo      | 17.81                     | —                                 |
| Fu Ling         | 18.29                     | —                                 |
| Sha Ren         | 18.49                     | —                                 |
| Qiang Huo       | 18.82                     | —                                 |
| Jin Yin Hua     | 19.20                     | —                                 |
| Sheng Jiang     | 19.26                     | —                                 |
| Gan Cao         | 19.53                     | —                                 |
| Zi Hua Di Ding  | 19.58                     | —                                 |

*continued on the next page*

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Fu Pen Zi       | 20.07                     | —                                 |
| Che Qian Zi     | 20.31                     | —                                 |
| Ci Wu Jia       | 20.51                     | —                                 |
| Pi Pa Ye        | 21.06                     | —                                 |
| Zhe Bei Mu      | 21.48                     | —                                 |
| Shan Yao        | 21.72                     | —                                 |
| Yi Yi Ren       | 21.93                     | —                                 |
| Ban Xia (Jiang) | 22.20                     | —                                 |
| Zhi Ke          | 22.75                     | —                                 |
| Fu Shen         | 22.97                     | —                                 |
| Bo He           | 23.52                     | —                                 |
| Lian Qiao       | 23.68                     | —                                 |
| Ze Xie          | 23.84                     | —                                 |
| Hong Jing Tian  | 24.18                     | —                                 |
| Huang Bai       | 24.22                     | —                                 |
| Du Zhong        | 24.23                     | —                                 |
| Lai Fu Zi       | 24.39                     | —                                 |
| Huang Lian      | 24.60                     | —                                 |
| Di Gu Pi        | 24.61                     | —                                 |
| Ji Li           | 24.71                     | —                                 |
| Tian Hua Fen    | 25.39                     | —                                 |
| Cang Zhu        | 26.98                     | —                                 |
| Jiao Gu Lan     | 27.63                     | —                                 |
| Ban Lan Gen     | 28.78                     | —                                 |
| Bai Zi Ren      | 29.41                     | —                                 |
| Fu Xiao Mai     | 29.86                     | —                                 |
| Zhi Gan Cao     | 30.78                     | —                                 |
| Mang Xiao       | 30.97                     | —                                 |
| Dang Gui        | 31.81                     | —                                 |
| Huang Qin       | 31.84                     | —                                 |
| Qing Pi         | 32.24                     | —                                 |
| Chuang Mu Xiang | 32.26                     | —                                 |
| Jie Geng        | 32.99                     | —                                 |
| Zhu Ru          | 33.65                     | —                                 |
| Ban Zhi Lian    | 33.91                     | —                                 |
| Ren Shen        | 34.13                     | —                                 |
| Gua Lou         | 35.06                     | —                                 |
| Bai Jiang Cao   | 35.89                     | —                                 |
| Chi Shao (Yao)  | 36.10                     | —                                 |
| Long Yan Rou    | 36.91                     | —                                 |
| Zhi Mu          | 37.26                     | —                                 |
| Sang Zhi        | 37.27                     | —                                 |
| San Qi          | 39.17                     | —                                 |
| Qing Hao        | 39.95                     | —                                 |
| Hong Hua        | 40.27                     | —                                 |
| Gou Qi Zi       | 42.11                     | —                                 |
| Pu Gong Ying    | 42.72                     | —                                 |
| Mu Gua          | 43.66                     | —                                 |
| Ze Lan          | 47.91                     | —                                 |
| Bai Zhu         | 48.09                     | —                                 |
| Ku Shen         | 48.85                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62421     | 62421               | 0.00                         | 5.00                            |
| 62422     | 62422               | 0.00                         | 5.37                            |
| 62625     | 62625               | 0.00                         | 6.27                            |
| 62626     | 62626               | 0.00                         | 6.07                            |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Yi Mu Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60105-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Yi Mu Cao                 | 3      | 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 |
| PhytoComm | Yi Mu Cao | G134H1050922 | 62877     | 40      | from supplier |
| PhytoComm | Yi Mu Cao | G134H1050922 | 62878     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Mu Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Yi Mu Cao | G134H1050821 | 62410 <sup>†</sup> | 20      |
| PhytoComm | Yi Mu Cao | G134H1050822 | 62541 <sup>†</sup> | 20      |
| PhytoComm | Yi Mu Cao | G134H1050822 | 62542 <sup>†</sup> | 20      |
| PhytoComm | Yi Mu Cao | G134H1050922 | 62877 <sup>†</sup> | 20      |
| PhytoComm | Yi Mu Cao | G134H1050922 | 62878 <sup>†</sup> | 20      |



- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G134H1050321 | 1       |
| Phytocomm | Yi Mu Cao | G134H1050521 | 1       |
| PhytoComm | Yi Mu Cao | G134H1050521 | 3       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 22 200        |
| <b>Type B</b> | 0              | 120           | 0              | 11 277        |
| <b>Type C</b> | 3              | 1             | 6              | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9355 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 99.5736 % (> 98.9864 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Nü Zhen Zi          | 17.03                     | —                                 |
| Cang Er Zi          | 21.45                     | —                                 |
| Xiang Fu            | 21.76                     | —                                 |
| Sha Ren             | 22.20                     | —                                 |
| Jiang Huang         | 23.27                     | —                                 |
| Gu Sui Bu           | 24.37                     | —                                 |
| Xiao Hui Xiang      | 24.71                     | —                                 |
| He Huan Pi          | 26.62                     | —                                 |
| Hu Zhang            | 27.29                     | —                                 |
| Mang Xiao           | 27.59                     | —                                 |
| Ju Hua              | 27.61                     | —                                 |
| Sang Ye             | 27.96                     | —                                 |
| Gou Teng            | 28.87                     | —                                 |
| Zhi Shi             | 29.59                     | —                                 |
| Shan Yao            | 30.61                     | —                                 |
| Ze Lan              | 30.63                     | —                                 |
| Han Lian Cao        | 30.71                     | —                                 |
| Shan Yu Rou         | 31.46                     | —                                 |
| Ku Shen             | 31.67                     | —                                 |
| Bai Hua She She Cao | 31.82                     | —                                 |
| Xin Yi              | 31.87                     | —                                 |
| Xu Duan             | 31.96                     | —                                 |
| Chen Pi             | 32.39                     | —                                 |
| Shen Qu             | 32.55                     | —                                 |
| Xia Ku Cao          | 33.00                     | —                                 |
| Pu Gong Ying        | 33.13                     | —                                 |
| Xi Xian Cao         | 33.44                     | —                                 |
| Jing Jie            | 33.93                     | —                                 |
| Wu Zhu Yu           | 34.06                     | —                                 |
| Wu Yao              | 35.16                     | —                                 |
| (Bai) Dou Kou       | 35.80                     | —                                 |
| Sang Bai Pi         | 37.74                     | —                                 |
| Yu Xing Cao         | 39.77                     | —                                 |
| Niu Bang Zi         | 39.89                     | —                                 |
| Yin Chen Hao        | 40.38                     | —                                 |
| Du Zhong            | 40.66                     | —                                 |
| Gan Cao             | 41.34                     | —                                 |
| Bu Gu Zhi           | 42.81                     | —                                 |
| Huang Lian          | 42.87                     | —                                 |
| Lian Qiao           | 43.06                     | —                                 |
| Tu Fu Ling          | 45.25                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Chuan Niu Xi   | 45.62                     | —                                 |
| Suan Zao Ren   | 46.22                     | —                                 |
| Di Gu Pi       | 46.62                     | —                                 |
| Yan Hu Suo     | 46.68                     | —                                 |
| Hong Jing Tian | 47.36                     | —                                 |
| Sang Ji Shend  | 47.96                     | —                                 |
| Qiang Huo      | 47.99                     | —                                 |
| (Shi) Chang Pu | 48.26                     | —                                 |
| Fang Feng      | 48.84                     | —                                 |
| He Shou Wu     | 49.54                     | —                                 |
| Qing Pi        | 49.67                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62409     | 62409                  | 0.00                            | 21.45                              |
| 62410     | 62410                  | 0.00                            | 21.63                              |
| 62541     | 62541                  | 0.00                            | 17.03                              |
| 62542     | 62542                  | 0.00                            | 17.35                              |
| 62877     | 62877                  | 0.00                            | 21.76                              |
| 62878     | 62878                  | 0.00                            | 22.22                              |

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 2.4-2022-02

Validated substance/substance group **Yi Yi Ren**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60174-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 | 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 |
| PhytoComm | Yi Yi Ren | G078H1701022 | 63011     | 40      | from supplier |
| PhytoComm | Yi Yi Ren | G078H1701022 | 63012     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 200 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 | G078HS336RL1 | 62279 <sup>†</sup> | 20      |
| PhytoComm | Yi Yi Ren | G078HS336RL1 | 62280 <sup>†</sup> | 20      |
| PhytoComm | Yi Yi Ren | G078HS336SH1 | 62675 <sup>†</sup> | 20      |
| PhytoComm | Yi Yi Ren | G078HS336SH1 | 62676 <sup>†</sup> | 20      |
| PhytoComm | Yi Yi Ren | G078H1701022 | 63011 <sup>†</sup> | 20      |
| PhytoComm | Yi Yi Ren | G078H1701022 | 63012 <sup>†</sup> | 20      |

- 11 277 spectra from a total of 279 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 | G078H1701323 | 6       |
| Phytocomm | Yi Yi Ren | G078H1701522 | 3       |

- 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 11             | 233           | 7              | 22 189        |
| <b>Type B</b> | 17             | 115           | 5              | 11 260        |
| <b>Type C</b> | 0              | 4             | 7              | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9678 % (> 99.9514 %)  | 97.0833 % (> 95.8333 %) |
| <b>Type B</b> | 99.9058 % (> 99.8735 %)  | 95.8333 % (> 93.3333 %) |
| <b>Type C</b> | 100.0000 % (> 98.8249 %) | n/a (n/a)               |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Fu Xiao Mai     | 1.99                      | —                                 |
| Zhu Ru          | 3.68                      | —                                 |
| Sheng Jiang     | 5.50                      | —                                 |
| Rou Gui         | 6.19                      | —                                 |
| Fu Ling         | 7.62                      | —                                 |
| Gui Zhi         | 7.99                      | —                                 |
| Di Gu Pi        | 8.38                      | —                                 |
| Fu Shen         | 9.74                      | —                                 |
| Ci Wu Jia       | 9.75                      | —                                 |
| He Huan Pi      | 10.73                     | —                                 |
| Ma Huang Gen    | 11.92                     | —                                 |
| Ji Li           | 12.54                     | —                                 |
| Lian Zi         | 12.85                     | —                                 |
| Tao Ren         | 13.05                     | —                                 |
| Shen Qu         | 13.11                     | —                                 |
| Ban Xia (Jiang) | 13.12                     | —                                 |
| Bai Shao Yao    | 14.30                     | —                                 |
| Gou Teng        | 14.64                     | —                                 |
| Bai Zi Ren      | 14.68                     | —                                 |
| Ji Xue Teng     | 14.81                     | —                                 |
| Ling Zhi        | 15.34                     | —                                 |
| Mu Zei          | 16.14                     | —                                 |
| Lai Fu Zi       | 16.99                     | —                                 |
| Zhe Bei Mu      | 17.67                     | —                                 |
| Bai Xian Pi     | 18.70                     | —                                 |
| Huo Ma Ren      | 20.16                     | —                                 |
| Fo Shou         | 21.26                     | —                                 |
| Tian Hua Fen    | 21.35                     | —                                 |
| Ye Jiao Teng    | 21.43                     | —                                 |
| Shan Yao        | 22.59                     | —                                 |
| Gu Sui Bu       | 22.87                     | —                                 |
| Yu Jin          | 23.84                     | —                                 |
| Pi Pa Ye        | 25.11                     | —                                 |
| Tu Fu Ling      | 27.00                     | —                                 |
| Ren Dong Teng   | 27.21                     | —                                 |
| Lu Gen          | 27.31                     | —                                 |
| Zhu Ling        | 27.92                     | —                                 |
| Lian Qiao       | 29.26                     | —                                 |
| Ze Xie          | 30.29                     | —                                 |
| Suan Zao Ren    | 31.15                     | —                                 |
| Yan Hu Suo      | 33.60                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Mang Xiao      | 33.99                     | —                                 |
| (Fen) Bi Xie   | 34.54                     | —                                 |
| Ren Shen       | 34.70                     | —                                 |
| Ce Bai Ye      | 36.16                     | —                                 |
| Dan Dou Chi    | 36.66                     | —                                 |
| Fu Zi          | 36.94                     | —                                 |
| Jin Yin Hua    | 37.15                     | —                                 |
| Zhi Mu         | 37.41                     | —                                 |
| San Qi         | 37.56                     | —                                 |
| She Gan        | 37.63                     | —                                 |
| Jiao Gu Lan    | 37.76                     | —                                 |
| Cang Zhu       | 37.79                     | —                                 |
| Jie Geng       | 38.34                     | —                                 |
| Fu Pen Zi      | 38.46                     | —                                 |
| Mao Dong Qing  | 39.04                     | —                                 |
| Zhi Ke         | 39.13                     | —                                 |
| Chai Hu        | 39.33                     | —                                 |
| Dan Shen       | 39.93                     | —                                 |
| Yin Yang Huo   | 41.69                     | —                                 |
| Huang Qin      | 41.79                     | —                                 |
| Yuan Zhi       | 43.10                     | —                                 |
| Dang Gui       | 43.10                     | —                                 |
| Gua Lou        | 43.23                     | —                                 |
| Che Qian Zi    | 43.91                     | —                                 |
| Hou Po         | 44.19                     | —                                 |
| Mu Gua         | 47.59                     | —                                 |
| Hong Jing Tian | 48.76                     | —                                 |
| Ban Lan Gen    | 49.44                     | —                                 |
| Qiang Huo      | 50.05                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62279     | 62279                  | 0.00                            | 3.74                               |
| 62280     | 62280                  | 0.00                            | 4.57                               |
| 62675     | 62675                  | 0.00                            | 2.02                               |
| 62676     | 62676                  | 0.00                            | 1.99                               |
| 63011     | 63011                  | 0.00                            | 46.43                              |
| 63012     | 63012                  | 0.00                            | 46.43                              |

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 2.4-2022-02

Validated substance/substance group **Yin Chen Hao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60163-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Yin Chen Hao              | 2      | 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 | G034H1030921 | 62971     | 40      | from supplier |
| PhytoComm | Yin Chen Hao | G034H1030921 | 62972     | 40      | from supplier |
| PhytoComm | Yin Chen Hao | G034HS213TN1 | 63025     | 40      | from supplier |
| PhytoComm | Yin Chen Hao | G034HS213TN1 | 63026     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Yin Chen Hao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 | G034H1030921 | 62971 <sup>†</sup> | 20      |
| PhytoComm | Yin Chen Hao | G034H1030921 | 62972 <sup>†</sup> | 20      |
| PhytoComm | Yin Chen Hao | G034HS213TN1 | 63025 <sup>†</sup> | 20      |
| PhytoComm | Yin Chen Hao | G034HS213TN1 | 63026 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 1              | 80            | 0              | 11 316        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 99.9926 % (> 99.9604 %)  | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Sang Ye             | 6.05                      | —                                 |
| Zhi Shi             | 8.36                      | —                                 |
| Pu Gong Ying        | 8.58                      | —                                 |
| Ze Lan              | 9.81                      | —                                 |
| Xin Yi              | 11.66                     | —                                 |
| Xi Xian Cao         | 12.15                     | —                                 |
| Nü Zhen Zi          | 12.21                     | —                                 |
| Xuan Fu Hua         | 12.68                     | —                                 |
| Gu Sui Bu           | 12.74                     | —                                 |
| Sang Bai Pi         | 13.66                     | —                                 |
| Tu Fu Ling          | 13.67                     | —                                 |
| Sang Ji Shend       | 14.25                     | —                                 |
| Shan Yao            | 14.54                     | —                                 |
| Sha Ren             | 16.17                     | —                                 |
| He Shou Wu          | 16.40                     | —                                 |
| Huang Lian          | 16.88                     | —                                 |
| Bu Gu Zhi           | 17.27                     | —                                 |
| Bai Jiang Cao       | 19.25                     | —                                 |
| He Huan Pi          | 20.79                     | —                                 |
| Qiang Huo           | 21.93                     | —                                 |
| Du Zhong            | 22.24                     | —                                 |
| Dan Shen            | 22.48                     | —                                 |
| Fu Zi               | 23.14                     | —                                 |
| Jing Jie            | 23.53                     | —                                 |
| Han Lian Cao        | 23.71                     | —                                 |
| Hu Zhang            | 24.09                     | —                                 |
| Jiang Huang         | 24.19                     | —                                 |
| Wu Zhu Yu           | 24.64                     | —                                 |
| Mang Xiao           | 26.04                     | —                                 |
| Yu Jin              | 26.10                     | —                                 |
| Zhi Ke              | 26.38                     | —                                 |
| Bo He               | 26.86                     | —                                 |
| Yu Xing Cao         | 27.32                     | —                                 |
| Tu Si Zi            | 27.47                     | —                                 |
| Huang Bai           | 27.53                     | —                                 |
| Dan Zhu Ye          | 28.09                     | —                                 |
| Zi Hua Di Ding      | 28.14                     | —                                 |
| Mao Dong Qing       | 28.46                     | —                                 |
| Chai Hu             | 28.90                     | —                                 |
| Hong Jing Tian      | 29.07                     | —                                 |
| Qing Pi             | 29.22                     | —                                 |
| Hou Po              | 29.90                     | —                                 |
| Jin Qian Cao        | 30.63                     | —                                 |
| Chen Pi             | 30.67                     | —                                 |
| Bai Hua She She Cao | 31.30                     | —                                 |
| Jiao Gu Lan         | 31.31                     | —                                 |
| Che Qian Zi         | 32.39                     | —                                 |
| Dan Dou Chi         | 32.42                     | —                                 |

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| Substanz         | Distance in<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Qing Hao         | 32.77                     | —                                 |
| Yin Yang Huo     | 33.66                     | —                                 |
| Cang Er Zi       | 33.68                     | —                                 |
| Ge Gen           | 34.56                     | —                                 |
| Yi Mu Cao        | 34.62                     | —                                 |
| Fu Pen Zi        | 34.70                     | —                                 |
| Ye Jiao Teng     | 35.52                     | —                                 |
| Ce Bai Ye        | 37.00                     | —                                 |
| Chuang Mu Xiang  | 37.00                     | —                                 |
| Wang Bu Liu Xing | 37.25                     | —                                 |
| Ma Huang         | 37.64                     | —                                 |
| (Bai) Dou Kou    | 37.69                     | —                                 |
| Jin Yin Hua      | 37.70                     | —                                 |
| Di Gu Pi         | 37.87                     | —                                 |
| Zi Su Zi         | 38.39                     | —                                 |
| Wu Yao           | 38.63                     | —                                 |
| Bai Xian Pi      | 39.08                     | —                                 |
| Xiang Fu         | 40.52                     | —                                 |
| Yan Hu Suo       | 41.39                     | —                                 |
| Wu Jia Pi        | 41.57                     | —                                 |
| Xia Ku Cao       | 42.28                     | —                                 |
| Ling Zhi         | 42.87                     | —                                 |
| Niu Bang Zi      | 43.21                     | —                                 |
| Pi Pa Ye         | 43.26                     | —                                 |
| Suan Zao Ren     | 43.35                     | —                                 |
| Gou Teng         | 43.95                     | —                                 |
| Gan Cao          | 44.32                     | —                                 |
| E Zhu            | 44.68                     | —                                 |
| Mu Dan Pi        | 45.02                     | —                                 |
| (Shi) Chang Pu   | 45.20                     | —                                 |
| Lian Qiao        | 46.35                     | —                                 |
| Bai Shao Yao     | 46.64                     | —                                 |
| Lian Zi          | 47.53                     | —                                 |
| Ren Dong Teng    | 47.55                     | —                                 |
| Hong Hua         | 47.56                     | —                                 |
| Chi Shao (Yao)   | 48.07                     | —                                 |
| Zhe Bei Mu       | 49.07                     | —                                 |
| Hua Shi          | 49.46                     | —                                 |
| Tian Hua Fen     | 50.06                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62971     | 62971                  | 0.00                            | 12.68                              |
| 62972     | 62972                  | 0.00                            | 12.69                              |

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| <b>Sample ID</b> | <b>Reference<br/>sample ID</b> | <b>Distance to<br/>reference sample</b> | <b>Distance to<br/>next foreign sample</b> |
|------------------|--------------------------------|-----------------------------------------|--------------------------------------------|
| 63025            | 63025                          | 0.00                                    | 6.26                                       |
| 63026            | 63026                          | 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 2.4-2022-02

Validated substance/substance group **Yin Yang Huo**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60228-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Yin Yang Huo | G098HS241SH1 | 62684 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 4              | 80            | 0              | 22 356        |
| <b>Type B</b> | 1              | 39            | 1              | 11 356        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 99.9864 % (> 99.9701 %)  | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9950 % (> 99.9630 %)  | 97.5000 % (> 90.0000 %)  |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bai Xian Pi     | 4.07                      | —                                 |
| Jing Jie        | 4.51                      | —                                 |
| Mao Dong Qing   | 5.26                      | —                                 |
| Dan Dou Chi     | 6.33                      | —                                 |
| Hou Po          | 6.83                      | —                                 |
| Ling Zhi        | 6.88                      | —                                 |
| Yu Jin          | 8.03                      | —                                 |
| Ye Jiao Teng    | 8.51                      | —                                 |
| Chai Hu         | 8.71                      | —                                 |
| Che Qian Zi     | 8.99                      | —                                 |
| Fu Zi           | 9.11                      | —                                 |
| Qiang Huo       | 9.21                      | —                                 |
| Ce Bai Ye       | 9.99                      | —                                 |
| Zi Hua Di Ding  | 10.72                     | —                                 |
| Ren Dong Teng   | 11.86                     | —                                 |
| Sha Ren         | 11.87                     | —                                 |
| Shen Qu         | 12.01                     | —                                 |
| Yan Hu Suo      | 12.37                     | —                                 |
| Tu Fu Ling      | 12.46                     | —                                 |
| Zhu Ling        | 13.07                     | —                                 |
| Du Zhong        | 13.91                     | —                                 |
| Lian Zi         | 14.02                     | —                                 |
| Shan Yao        | 14.45                     | —                                 |
| Fu Pen Zi       | 14.61                     | —                                 |
| Guang Huo Xiang | 14.70                     | —                                 |
| Dan Shen        | 14.78                     | —                                 |
| Bo He           | 14.88                     | —                                 |
| Ji Xue Teng     | 16.30                     | —                                 |
| Pi Pa Ye        | 16.31                     | —                                 |
| Huang Bai       | 16.81                     | —                                 |
| Ma Huang        | 17.25                     | —                                 |
| Gu Sui Bu       | 18.00                     | —                                 |
| (Fen) Bi Xie    | 18.75                     | —                                 |
| Ji Li           | 19.00                     | —                                 |
| Rou Gui         | 19.65                     | —                                 |
| Qing Pi         | 19.76                     | —                                 |
| Jin Yin Hua     | 20.24                     | —                                 |
| Ma Huang Gen    | 20.25                     | —                                 |
| Qing Hao        | 20.26                     | —                                 |
| Tian Hua Fen    | 20.26                     | —                                 |
| He Huan Pi      | 20.85                     | —                                 |
| Gan Cao         | 20.90                     | —                                 |
| Hong Jing Tian  | 20.94                     | —                                 |
| Suan Zao Ren    | 21.35                     | —                                 |
| Lian Qiao       | 21.86                     | —                                 |
| Gou Teng        | 22.03                     | —                                 |
| Huang Lian      | 22.69                     | —                                 |
| Lu Gen          | 22.81                     | —                                 |
| Jiao Gu Lan     | 23.09                     | —                                 |
| Bai Shao Yao    | 23.31                     | —                                 |
| Zhi Ke          | 23.64                     | —                                 |
| She Gan         | 23.82                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Sheng Jiang     | 24.15                     | —                                 |
| Bai Jiang Cao   | 24.28                     | —                                 |
| Huo Ma Ren      | 25.41                     | —                                 |
| Ban Lan Gen     | 25.48                     | —                                 |
| Fu Ling         | 25.59                     | —                                 |
| Mu Zei          | 25.73                     | —                                 |
| Di Gu Pi        | 26.08                     | —                                 |
| Gui Zhi         | 26.31                     | —                                 |
| Yi Yi Ren       | 26.67                     | —                                 |
| Zhi Gan Cao     | 29.36                     | —                                 |
| Chuang Mu Xiang | 30.16                     | —                                 |
| Ren Shen        | 30.58                     | —                                 |
| Zhe Bei Mu      | 31.12                     | —                                 |
| Tao Ren         | 31.34                     | —                                 |
| Mang Xiao       | 32.22                     | —                                 |
| Pu Gong Ying    | 34.90                     | —                                 |
| Cang Zhu        | 34.94                     | —                                 |
| Bai Zi Ren      | 36.78                     | —                                 |
| Ban Zhi Lian    | 36.84                     | —                                 |
| Ban Xia (Jiang) | 37.35                     | —                                 |
| Ci Wu Jia       | 37.43                     | —                                 |
| Fu Shen         | 38.13                     | —                                 |
| Chi Shao (Yao)  | 38.27                     | —                                 |
| Fu Xiao Mai     | 38.38                     | —                                 |
| Fo Shou         | 38.43                     | —                                 |
| Sang Zhi        | 38.85                     | —                                 |
| Ze Lan          | 38.85                     | —                                 |
| Hong Hua        | 38.91                     | —                                 |
| Ze Xie          | 40.61                     | —                                 |
| Huang Qin       | 40.78                     | —                                 |
| Zhu Ru          | 41.15                     | —                                 |
| Jie Geng        | 41.46                     | —                                 |
| Dang Gui        | 44.15                     | —                                 |
| Gua Lou         | 44.37                     | —                                 |
| Xi Xian Cao     | 44.49                     | —                                 |
| Cang Er Zi      | 44.68                     | —                                 |
| Sang Ye         | 44.88                     | —                                 |
| Xie Bai         | 44.97                     | —                                 |
| E Zhu           | 46.64                     | —                                 |
| San Qi          | 46.80                     | —                                 |
| Jiang Huang     | 46.83                     | —                                 |
| Long Yan Rou    | 47.78                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62683     | 62683               | 0.00                         | 4.07                            |
| 62684     | 62684               | 0.00                         | 4.07                            |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Yu Jin**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60171-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Yu Jin                    | 1      | 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 |

## Validation samples

A total of 34 694 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 Jin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Yu Jin    | G084HS357RN1 | 62278 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 3              | 40            | 0              | 11 354        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9826 % (> 99.9506 %)  | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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 *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.

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

| Substance       | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ling Zhi        | 5.60                      | —                                 |
| Mao Dong Qing   | 6.12                      | —                                 |
| Hou Po          | 6.76                      | —                                 |
| Yin Yang Huo    | 7.30                      | —                                 |
| Qiang Huo       | 7.35                      | —                                 |
| Du Zhong        | 8.39                      | —                                 |
| Jing Jie        | 8.95                      | —                                 |
| Bai Xian Pi     | 9.00                      | —                                 |
| Dan Dou Chi     | 9.34                      | —                                 |
| Ce Bai Ye       | 9.95                      | —                                 |
| Che Qian Zi     | 10.04                     | —                                 |
| Qing Hao        | 11.60                     | —                                 |
| Ye Jiao Teng    | 12.74                     | —                                 |
| Ren Dong Teng   | 13.35                     | —                                 |
| Fu Zi           | 13.35                     | —                                 |
| Sha Ren         | 13.76                     | —                                 |
| Yan Hu Suo      | 13.89                     | —                                 |
| Zi Hua Di Ding  | 14.08                     | —                                 |
| Shen Qu         | 14.42                     | —                                 |
| Shan Yao        | 14.49                     | —                                 |
| Chai Hu         | 14.66                     | —                                 |
| Fu Pen Zi       | 14.83                     | —                                 |
| Qing Pi         | 15.52                     | —                                 |
| Dan Shen        | 15.60                     | —                                 |
| Zhu Ling        | 16.24                     | —                                 |
| Bo He           | 16.92                     | —                                 |
| Guang Huo Xiang | 17.02                     | —                                 |
| Pi Pa Ye        | 17.86                     | —                                 |
| Jiao Gu Lan     | 18.01                     | —                                 |
| Ji Li           | 18.48                     | —                                 |
| Lian Zi         | 19.03                     | —                                 |
| Hong Jing Tian  | 19.43                     | —                                 |
| Huang Bai       | 19.71                     | —                                 |
| Ji Xue Teng     | 20.04                     | —                                 |
| Lian Qiao       | 20.10                     | —                                 |
| He Huan Pi      | 21.13                     | —                                 |
| Gu Sui Bu       | 21.15                     | —                                 |
| Tian Hua Fen    | 22.09                     | —                                 |
| Ma Huang        | 22.36                     | —                                 |
| Huang Lian      | 22.66                     | —                                 |
| Jin Yin Hua     | 23.08                     | —                                 |
| Zhi Ke          | 23.20                     | —                                 |
| Bai Jiang Cao   | 23.25                     | —                                 |
| Suan Zao Ren    | 23.67                     | —                                 |
| She Gan         | 24.74                     | —                                 |
| Gou Teng        | 25.43                     | —                                 |
| (Fen) Bi Xie    | 25.94                     | —                                 |
| Bai Shao Yao    | 26.29                     | —                                 |
| Tu Fu Ling      | 26.34                     | —                                 |
| Zhe Bei Mu      | 27.02                     | —                                 |
| Di Gu Pi        | 27.02                     | —                                 |
| Gan Cao         | 27.57                     | —                                 |
| Mu Zei          | 27.66                     | —                                 |
| Sheng Jiang     | 27.79                     | —                                 |
| Lu Gen          | 27.94                     | —                                 |
| Ban Lan Gen     | 28.51                     | —                                 |
| Huo Ma Ren      | 29.56                     | —                                 |
| Ma Huang Gen    | 29.72                     | —                                 |
| Ren Shen        | 30.46                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Fu Ling         | 31.39                     | —                                 |
| Rou Gui         | 31.86                     | —                                 |
| Tao Ren         | 32.24                     | —                                 |
| Chuang Mu Xiang | 32.29                     | —                                 |
| Mang Xiao       | 33.13                     | —                                 |
| Yi Yi Ren       | 33.38                     | —                                 |
| Pu Gong Ying    | 33.63                     | —                                 |
| Xi Xian Cao     | 34.76                     | —                                 |
| Gui Zhi         | 34.96                     | —                                 |
| Zhi Gan Cao     | 35.09                     | —                                 |
| Ze Lan          | 36.00                     | —                                 |
| Sang Ye         | 38.08                     | —                                 |
| Cang Zhu        | 40.05                     | —                                 |
| Bai Zi Ren      | 40.35                     | —                                 |
| Cang Er Zi      | 41.16                     | —                                 |
| Ban Zhi Lian    | 41.21                     | —                                 |
| Ze Xie          | 41.71                     | —                                 |
| Jie Geng        | 42.00                     | —                                 |
| Ci Wu Jia       | 42.23                     | —                                 |
| Nü Zhen Zi      | 42.28                     | —                                 |
| Hong Hua        | 42.47                     | —                                 |
| Ban Xia (Jiang) | 42.87                     | —                                 |
| Sang Zhi        | 42.98                     | —                                 |
| Chi Shao (Yao)  | 43.26                     | —                                 |
| Jiang Huang     | 43.30                     | —                                 |
| Xie Bai         | 43.48                     | —                                 |
| Gua Lou         | 43.59                     | —                                 |
| Zhu Ru          | 43.95                     | —                                 |
| Huang Qin       | 44.04                     | —                                 |
| E Zhu           | 44.16                     | —                                 |
| San Qi          | 46.11                     | —                                 |
| Fu Xiao Mai     | 46.59                     | —                                 |
| Fu Shen         | 46.89                     | —                                 |
| Ku Shen         | 48.19                     | —                                 |
| Wu Wei Zi       | 48.61                     | —                                 |
| Dang Gui        | 49.20                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62277     | 62277                  | 0.00                            | 5.60                               |
| 62278     | 62278                  | 0.00                            | 5.93                               |

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 2.4-2022-02

Validated substance/substance group **Yu Xing Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60606-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Yu Xing Cao; Houttuyniae herba

### Special notes

When selecting the *Yu Xing Cao* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Yu Xing Cao               | 2      | 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 |
| PhytoComm | Yu Xing Cao | G124HS244TL1 | 62889     | 40      | from supplier |
| PhytoComm | Yu Xing Cao | G124HS244TL1 | 62890     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Xing Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 <sup>†</sup> | 20      |
| PhytoComm | Yu Xing Cao | G124H1149823 | 62584 <sup>†</sup> | 20      |
| PhytoComm | Yu Xing Cao | G124HS244TL1 | 62889 <sup>†</sup> | 20      |
| PhytoComm | Yu Xing Cao | G124HS244TL1 | 62890 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G124H1149222 | 1       |
| Phytocomm | Yu Xing Cao | G124H1149423 | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Han Lian Cao        | 8.85                      | —                                 |
| Xi Xian Cao         | 10.04                     | —                                 |
| Hu Zhang            | 12.33                     | —                                 |
| Bai Hua She She Cao | 12.50                     | —                                 |
| Xin Yi              | 12.79                     | —                                 |
| (Sheng) Di Huang    | 13.39                     | —                                 |
| Pu Gong Ying        | 14.58                     | —                                 |
| Wu Jia Pi           | 14.79                     | —                                 |
| Sang Ye             | 15.44                     | —                                 |
| Ze Lan              | 16.08                     | —                                 |
| Tu Fu Ling          | 17.22                     | —                                 |
| Xian Mao            | 17.37                     | —                                 |
| Huang Lian          | 17.71                     | —                                 |
| Jiang Huang         | 17.86                     | —                                 |
| Zhi Shi             | 19.35                     | —                                 |
| Xia Ku Cao          | 21.08                     | —                                 |
| Shan Yao            | 21.30                     | —                                 |
| Mang Xiao           | 22.34                     | —                                 |
| Nü Zhen Zi          | 23.31                     | —                                 |
| Shu Di (Huang)      | 24.07                     | —                                 |
| Xiang Fu            | 24.92                     | —                                 |
| Yin Chen Hao        | 26.15                     | —                                 |
| Sha Ren             | 27.32                     | —                                 |
| Jing Jie            | 29.80                     | —                                 |
| Yi Mu Cao           | 32.02                     | —                                 |
| He Huan Pi          | 32.69                     | —                                 |
| Du Zhong            | 35.67                     | —                                 |
| Qiang Huo           | 36.29                     | —                                 |
| Fu Zi               | 37.15                     | —                                 |
| Yu Jin              | 38.13                     | —                                 |
| Dan Shen            | 39.86                     | —                                 |
| Bai Jiang Cao       | 40.38                     | —                                 |
| Dan Zhu Ye          | 40.53                     | —                                 |
| Sang Ji Shend       | 40.97                     | —                                 |
| Bo He               | 41.27                     | —                                 |
| Ding Xiang          | 41.61                     | —                                 |
| Cang Er Zi          | 42.19                     | —                                 |
| Gu Sui Bu           | 42.24                     | —                                 |
| Che Qian Zi         | 43.25                     | —                                 |
| Guang Huo Xiang     | 43.37                     | —                                 |
| Huang Bai           | 44.05                     | —                                 |
| Zhi Ke              | 44.27                     | —                                 |
| Mao Dong Qing       | 44.30                     | —                                 |
| E Zhu               | 44.69                     | —                                 |
| Hua Shi             | 45.53                     | —                                 |

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| Substanz         | Distance in<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Hou Po           | 45.73                     | —                                 |
| Jiao Gu Lan      | 46.21                     | —                                 |
| Hong Jing Tian   | 46.76                     | —                                 |
| Dan Dou Chi      | 47.10                     | —                                 |
| Wang Bu Liu Xing | 47.43                     | —                                 |
| Gou Teng         | 48.26                     | —                                 |
| Yin Yang Huo     | 49.29                     | —                                 |
| Qing Pi          | 49.40                     | —                                 |
| (Bai) Dou Kou    | 49.99                     | —                                 |
| Ge Gen           | 51.03                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62583     | 62583                  | 0.00                            | 14.08                              |
| 62584     | 62584                  | 0.00                            | 13.39                              |
| 62889     | 62889                  | 0.00                            | 9.34                               |
| 62890     | 62890                  | 0.00                            | 8.85                               |

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 2.4-2022-02

Validated substance/substance group **Yuan Zhi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60100-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Yuan Zhi                  | 2      | 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  | G194H1406921 | 62743     | 40      | from supplier |
| PhytoComm | Yuan Zhi  | G194H1406921 | 62744     | 40      | from supplier |
| PhytoComm | Yuan Zhi  | G194HS306TG1 | 62845     | 40      | from supplier |
| PhytoComm | Yuan Zhi  | G194HS306TG1 | 62846     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Yuan Zhi*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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  | G194H1406921 | 62743 <sup>†</sup> | 20      |
| PhytoComm | Yuan Zhi  | G194H1406921 | 62744 <sup>†</sup> | 20      |
| PhytoComm | Yuan Zhi  | G194HS306TG1 | 62845 <sup>†</sup> | 20      |
| PhytoComm | Yuan Zhi  | G194HS306TG1 | 62846 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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  | G194H1406222 | 1       |
| Phytocomm | Yuan Zhi  | G194H1406522 | 2       |
| 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 0              | 2             | 4              | 851           |

The substance/substance group *Yuan 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Bai Shao Yao   | 8.03                      | —                                 |
| (Huai) Niu Xi  | 9.36                      | —                                 |
| Ren Shen       | 11.78                     | —                                 |
| Jie Geng       | 12.57                     | —                                 |
| Huang Qi       | 12.98                     | —                                 |
| Zhi Mu         | 13.26                     | —                                 |
| Pi Pa Ye       | 13.47                     | —                                 |
| Ye Jiao Teng   | 14.13                     | —                                 |
| Fo Shou        | 14.26                     | —                                 |
| Bai Zhu        | 15.69                     | —                                 |
| Shan Yao       | 16.49                     | —                                 |
| Lian Qiao      | 17.66                     | —                                 |
| Mu Gua         | 18.21                     | —                                 |
| Cang Zhu       | 18.27                     | —                                 |
| Di Gu Pi       | 18.47                     | —                                 |
| Gou Qi Zi      | 18.77                     | —                                 |
| Ji Li          | 19.46                     | —                                 |
| Sang Zhi       | 19.85                     | —                                 |
| Chi Shao (Yao) | 19.89                     | —                                 |
| San Qi         | 19.94                     | —                                 |
| Zhu Ru         | 20.66                     | —                                 |
| He Huan Pi     | 21.76                     | —                                 |
| Zhi Gan Cao    | 21.98                     | —                                 |
| Chuan Lian Zi  | 22.50                     | —                                 |
| Gua Lou        | 22.66                     | —                                 |
| Tian Hua Fen   | 22.85                     | —                                 |
| Zi Su Zi       | 23.03                     | —                                 |
| Niu Bang Zi    | 23.17                     | —                                 |
| Rou Gui        | 23.34                     | —                                 |
| Ku Shen        | 23.48                     | —                                 |
| Dang Gui       | 23.51                     | —                                 |
| Zhe Bei Mu     | 23.77                     | —                                 |
| Ci Wu Jia      | 23.78                     | —                                 |
| Ren Dong Teng  | 23.97                     | —                                 |
| Shen Qu        | 24.38                     | —                                 |
| Fu Xiao Mai    | 24.55                     | —                                 |
| Lian Zi        | 25.10                     | —                                 |
| Jiao Gu Lan    | 25.88                     | —                                 |
| Xiang Fu       | 25.93                     | —                                 |
| Fu Ling        | 27.18                     | —                                 |
| Sheng Jiang    | 27.40                     | —                                 |
| Zhi Ke         | 27.60                     | —                                 |
| Bai Zi Ren     | 27.66                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Gan Cao         | 27.73                             | —                                         |
| Jin Yin Hua     | 27.92                             | —                                         |
| Mu Zei          | 27.97                             | —                                         |
| Xie Bai         | 28.97                             | —                                         |
| Mang Xiao       | 29.34                             | —                                         |
| Tu Fu Ling      | 29.46                             | —                                         |
| Gui Zhi         | 29.60                             | —                                         |
| Ban Lan Gen     | 29.77                             | —                                         |
| Huo Ma Ren      | 30.23                             | —                                         |
| Ban Xia (Jiang) | 30.74                             | —                                         |
| Suan Zao Ren    | 31.41                             | —                                         |
| Lai Fu Zi       | 31.96                             | —                                         |
| Hou Po          | 32.32                             | —                                         |
| Ling Zhi        | 32.58                             | —                                         |
| Huang Qin       | 32.67                             | —                                         |
| Tao Ren         | 32.97                             | —                                         |
| Gou Teng        | 33.16                             | —                                         |
| Ji Xue Teng     | 33.39                             | —                                         |
| Long Yan Rou    | 33.53                             | —                                         |
| Fu Zi           | 33.69                             | —                                         |
| Chuang Mu Xiang | 34.63                             | —                                         |
| Long Dan (Cao)  | 34.66                             | —                                         |
| Chuan Mu Tong   | 34.79                             | —                                         |
| Mao Dong Qing   | 34.83                             | —                                         |
| Qin Jiao        | 34.88                             | —                                         |
| Cang Er Zi      | 35.00                             | —                                         |
| (Shi) Chang Pu  | 35.06                             | —                                         |
| Bing Lang       | 35.40                             | —                                         |
| Dan Dou Chi     | 35.93                             | —                                         |
| Lu Gen          | 36.18                             | —                                         |
| Gan Jiang       | 36.37                             | —                                         |
| Yi Yi Ren       | 36.67                             | —                                         |
| Fu Pen Zi       | 37.04                             | —                                         |
| Bai He          | 37.17                             | —                                         |
| Du Huo          | 37.84                             | —                                         |
| Che Qian Zi     | 37.87                             | —                                         |
| Dan Shen        | 37.87                             | —                                         |
| Chuan Niu Xi    | 38.32                             | —                                         |
| Bai Zhi         | 38.54                             | —                                         |
| E Zhu           | 39.60                             | —                                         |
| Pu Gong Ying    | 39.67                             | —                                         |
| Sha Shen (Bei)  | 39.96                             | —                                         |
| Yan Hu Suo      | 40.17                             | —                                         |
| Bai Xian Pi     | 40.43                             | —                                         |
| Ze Xie          | 41.30                             | —                                         |
| Dong Gua Zi     | 41.95                             | —                                         |
| Qiang Huo       | 42.26                             | —                                         |
| Yi Mu Cao       | 42.56                             | —                                         |
| Gu Sui Bu       | 42.67                             | —                                         |
| Ju Hua          | 43.16                             | —                                         |
| Yin Yang Huo    | 43.70                             | —                                         |
| Chai Hu         | 43.89                             | —                                         |
| Xiao Hui Xiang  | 44.18                             | —                                         |
| Hong Jing Tian  | 44.21                             | —                                         |
| Wu Yao          | 44.43                             | —                                         |
| Ma Huang        | 45.65                             | —                                         |
| Xu Duan         | 46.90                             | —                                         |
| Ba Ji Tian      | 47.20                             | —                                         |
| Yu Jin          | 47.88                             | —                                         |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| She Gan         | 47.99                     | —                                 |
| (Bai) Dou Kou   | 48.06                     | —                                 |
| Fu Shen         | 48.13                     | —                                 |
| Ma Huang Gen    | 48.16                     | —                                 |
| Fang Feng       | 48.68                     | —                                 |
| Bo He           | 48.79                     | —                                 |
| Zi Hua Di Ding  | 49.02                     | —                                 |
| Ce Bai Ye       | 49.16                     | —                                 |
| Jiang Huang     | 49.17                     | —                                 |
| Guang Huo Xiang | 49.43                     | —                                 |
| Sha Ren         | 50.27                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62743     | 62743                  | 0.00                            | 9.36                               |
| 62744     | 62744                  | 0.00                            | 9.56                               |
| 62845     | 62845                  | 0.00                            | 8.40                               |
| 62846     | 62846                  | 0.00                            | 8.03                               |

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 2.4-2022-02

Validated substance/substance group **Ze Lan**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60322-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Ze Lan; Lycopi lucidi herba

### Special notes

When selecting the *Ze Lan* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ze Lan                    | 1      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Ze 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 *Ze Lan*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Ze Lan    | G268HS321TK1 | 62813     | 40      | from supplier |
| PhytoComm | Ze Lan    | G268HS321TK1 | 62814     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Ze Lan*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ze 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 | Ze Lan    | G268HS321TK1 | 62813 <sup>†</sup> | 20      |
| PhytoComm | Ze Lan    | G268HS321TK1 | 62814 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 *Ze Lan*.
- 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 | Ze Lan    | g268h1606221 | 1       |
| Phytocomm | Ze Lan    | G268H1606221 | 1       |
| PhytoComm | Ze Lan    | G268H1606221 | 1       |
| Phytocomm | Ze Lan    | G268H1606421 | 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 *Ze 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 *Ze 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 2              | 40            | 0              | 11 355        |
| <b>Type C</b> | 0              | 0             | 4              | 853           |

The substance/substance group *Ze Lan* 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 99.9876 % (> 99.9555 %)  | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ze 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Xi Xian Cao         | 7.94                      | —                                 |
| Tu Fu Ling          | 8.94                      | —                                 |
| Pu Gong Ying        | 10.85                     | —                                 |
| Yin Chen Hao        | 11.77                     | —                                 |
| Huang Lian          | 13.04                     | —                                 |
| Xin Yi              | 14.77                     | —                                 |
| Sang Ye             | 18.21                     | —                                 |
| Sha Ren             | 18.23                     | —                                 |
| Bai Jiang Cao       | 18.33                     | —                                 |
| Zhi Ke              | 18.36                     | —                                 |
| Shan Yao            | 19.43                     | —                                 |
| Yu Jin              | 19.44                     | —                                 |
| Nü Zhen Zi          | 20.09                     | —                                 |
| Jiao Gu Lan         | 20.09                     | —                                 |
| Du Zhong            | 20.68                     | —                                 |
| Zhi Shi             | 21.08                     | —                                 |
| Bai Hua She She Cao | 22.02                     | —                                 |
| Dan Shen            | 22.46                     | —                                 |
| Fu Zi               | 22.65                     | —                                 |
| Yu Xing Cao         | 23.00                     | —                                 |
| Jiang Huang         | 24.14                     | —                                 |
| Hu Zhang            | 24.83                     | —                                 |
| Mao Dong Qing       | 25.62                     | —                                 |
| Bo He               | 25.92                     | —                                 |
| Qiang Huo           | 25.96                     | —                                 |
| Che Qian Zi         | 26.34                     | —                                 |
| Huang Bai           | 28.09                     | —                                 |
| Chai Hu             | 28.75                     | —                                 |
| Bai Xian Pi         | 29.46                     | —                                 |
| Mang Xiao           | 29.54                     | —                                 |
| Han Lian Cao        | 29.64                     | —                                 |
| Hou Po              | 30.53                     | —                                 |
| Ye Jiao Teng        | 30.77                     | —                                 |
| Yin Yang Huo        | 32.51                     | —                                 |
| Zi Hua Di Ding      | 33.06                     | —                                 |
| Ling Zhi            | 33.16                     | —                                 |
| Dan Dou Chi         | 33.44                     | —                                 |
| Cang Er Zi          | 35.17                     | —                                 |
| Qing Hao            | 35.28                     | —                                 |
| Di Gu Pi            | 35.45                     | —                                 |
| Hong Jing Tian      | 35.82                     | —                                 |
| Fu Pen Zi           | 35.98                     | —                                 |
| Pi Pa Ye            | 36.58                     | —                                 |
| Qing Pi             | 36.81                     | —                                 |
| Wang Bu Liu Xing    | 37.42                     | —                                 |
| Jin Yin Hua         | 38.01                     | —                                 |
| Ce Bai Ye           | 38.03                     | —                                 |
| Chuang Mu Xiang     | 38.63                     | —                                 |
| E Zhu               | 39.11                     | —                                 |
| He Huan Pi          | 39.23                     | —                                 |
| Yi Mu Cao           | 40.04                     | —                                 |
| Jing Jie            | 40.17                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Ma Huang       | 40.64                     | —                                 |
| Lian Zi        | 40.65                     | —                                 |
| Yan Hu Suo     | 42.14                     | —                                 |
| Xiang Fu       | 42.30                     | —                                 |
| Zi Su Zi       | 42.54                     | —                                 |
| Ji Xue Teng    | 43.02                     | —                                 |
| Bai Shao Yao   | 43.03                     | —                                 |
| Suan Zao Ren   | 43.08                     | —                                 |
| Ren Dong Teng  | 43.56                     | —                                 |
| Tian Hua Fen   | 45.94                     | —                                 |
| Sha Shen (Bei) | 46.20                     | —                                 |
| Niu Bang Zi    | 46.43                     | —                                 |
| (Bai) Dou Kou  | 47.56                     | —                                 |
| Lian Qiao      | 47.90                     | —                                 |
| Ren Shen       | 48.09                     | —                                 |
| Gu Sui Bu      | 48.15                     | —                                 |
| Chi Shao (Yao) | 49.20                     | —                                 |
| Xia Ku Cao     | 49.23                     | —                                 |
| Shen Qu        | 49.58                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ze 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62813     | 62813                  | 0.00                            | 8.94                               |
| 62814     | 62814                  | 0.00                            | 7.94                               |

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 2.4-2022-02

Validated substance/substance group **Ze Xie**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10004523-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Ze Xie; Alismatis rhizoma

### Special notes

When selecting the *Ze Xie* substance/substance group, the following information is displayed to the user:

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Ze Xie                    | 1      | 0      | 3      |

### Second-stage model

For differentiation of the substance/substance group *Ze Xie* 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 *Ze Xie*:

| Supplier  | Substance | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-----------|--------------|-----------|---------|---------------|
| PhytoComm | Ze Xie    | G011HS320TG1 | 62955     | 40      | from supplier |
| PhytoComm | Ze Xie    | G011HS320TG1 | 62956     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Ze Xie*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 1 different batches.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ze Xie*.
- 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 | Ze Xie    | G011HS320TG1 | 62955 <sup>†</sup> | 20      |
| PhytoComm | Ze Xie    | G011HS320TG1 | 62956 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 4 batches from the substance/substance group *Ze Xie*.
- 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 | Ze Xie    | g011h1605122 | 1       |
| PhytoComm | Ze Xie    | G011H1605122 | 1       |
| Phytocomm | Ze Xie    | G011H1605422 | 1       |
| Phytocomm | Ze Xie    | G011H1605521 | 5       |
| PhytoComm | Ze Xie    | G011H1605521 | 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 *Ze Xie* 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 *Ze Xie* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 79            | 1              | 22 360        |
| <b>Type B</b> | 0              | 36            | 4              | 11 357        |
| <b>Type C</b> | 0              | 0             | 9              | 848           |

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

|               | Specificity              | Recognition rate        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 98.7500 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 90.0000 % (> 82.5000 %) |
| <b>Type C</b> | 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 exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ze Xie* 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Pi Pa Ye        | 5.96                      | —                                 |
| Ren Dong Teng   | 7.73                      | —                                 |
| Tian Hua Fen    | 7.88                      | —                                 |
| Bai Shao Yao    | 8.61                      | —                                 |
| Mu Zei          | 8.73                      | —                                 |
| Shen Qu         | 8.79                      | —                                 |
| Fu Zi           | 8.82                      | —                                 |
| Shan Yao        | 9.00                      | —                                 |
| Lian Qiao       | 9.14                      | —                                 |
| Zhe Bei Mu      | 9.76                      | —                                 |
| Ban Lan Gen     | 10.44                     | —                                 |
| Jin Yin Hua     | 10.98                     | —                                 |
| Gua Lou         | 11.71                     | —                                 |
| Ling Zhi        | 11.94                     | —                                 |
| Huo Ma Ren      | 12.16                     | —                                 |
| He Huan Pi      | 12.28                     | —                                 |
| Gu Sui Bu       | 12.33                     | —                                 |
| Lai Fu Zi       | 12.53                     | —                                 |
| Fu Pen Zi       | 12.64                     | —                                 |
| Ji Li           | 12.67                     | —                                 |
| Ye Jiao Teng    | 12.68                     | —                                 |
| Lian Zi         | 13.46                     | —                                 |
| Dan Dou Chi     | 13.80                     | —                                 |
| Lu Gen          | 13.90                     | —                                 |
| Bai Zi Ren      | 13.99                     | —                                 |
| Hou Po          | 14.30                     | —                                 |
| Suan Zao Ren    | 14.56                     | —                                 |
| Tao Ren         | 14.67                     | —                                 |
| Gui Zhi         | 15.36                     | —                                 |
| Ji Xue Teng     | 15.40                     | —                                 |
| Cang Zhu        | 15.65                     | —                                 |
| Jiao Gu Lan     | 15.66                     | —                                 |
| Sheng Jiang     | 15.79                     | —                                 |
| Ci Wu Jia       | 16.19                     | —                                 |
| Di Gu Pi        | 16.24                     | —                                 |
| Dang Gui        | 16.40                     | —                                 |
| Dan Shen        | 16.69                     | —                                 |
| Jie Geng        | 16.70                     | —                                 |
| Gou Teng        | 16.81                     | —                                 |
| Fu Ling         | 16.82                     | —                                 |
| Guang Huo Xiang | 16.87                     | —                                 |
| San Qi          | 17.95                     | —                                 |
| Hong Jing Tian  | 18.36                     | —                                 |
| Yan Hu Suo      | 18.65                     | —                                 |
| She Gan         | 19.01                     | —                                 |
| Che Qian Zi     | 19.26                     | —                                 |
| Ce Bai Ye       | 19.29                     | —                                 |
| Ma Huang        | 19.69                     | —                                 |
| Yin Yang Huo    | 19.89                     | —                                 |
| Zhi Ke          | 20.00                     | —                                 |
| Zhu Ru          | 20.00                     | —                                 |
| Chai Hu         | 20.25                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bai Xian Pi     | 20.31                     | —                                 |
| Tu Fu Ling      | 20.50                     | —                                 |
| Rou Gui         | 20.71                     | —                                 |
| Ren Shen        | 20.78                     | —                                 |
| Ku Shen         | 21.46                     | —                                 |
| Mao Dong Qing   | 21.64                     | —                                 |
| (Fen) Bi Xie    | 21.69                     | —                                 |
| Fo Shou         | 21.70                     | —                                 |
| Yu Jin          | 21.93                     | —                                 |
| Ban Xia (Jiang) | 22.06                     | —                                 |
| Zhu Ling        | 22.52                     | —                                 |
| Gan Cao         | 22.84                     | —                                 |
| Zhi Mu          | 23.02                     | —                                 |
| Qiang Huo       | 23.97                     | —                                 |
| Gou Qi Zi       | 24.75                     | —                                 |
| Zhi Gan Cao     | 25.46                     | —                                 |
| Fu Xiao Mai     | 26.19                     | —                                 |
| Yi Yi Ren       | 26.21                     | —                                 |
| Huang Qin       | 26.75                     | —                                 |
| Ma Huang Gen    | 26.77                     | —                                 |
| Chuang Mu Xiang | 27.45                     | —                                 |
| Mu Gua          | 27.60                     | —                                 |
| Xie Bai         | 27.64                     | —                                 |
| Long Yan Rou    | 28.42                     | —                                 |
| Qing Pi         | 29.83                     | —                                 |
| Zi Hua Di Ding  | 30.73                     | —                                 |
| Mang Xiao       | 32.37                     | —                                 |
| Jing Jie        | 32.46                     | —                                 |
| Huang Lian      | 33.11                     | —                                 |
| Yuan Zhi        | 33.80                     | —                                 |
| Bo He           | 34.02                     | —                                 |
| Sang Zhi        | 34.36                     | —                                 |
| Chi Shao (Yao)  | 35.77                     | —                                 |
| Sha Ren         | 36.42                     | —                                 |
| Huang Bai       | 37.45                     | —                                 |
| Fu Shen         | 37.52                     | —                                 |
| Du Zhong        | 38.29                     | —                                 |
| Hong Hua        | 41.93                     | —                                 |
| Cang Er Zi      | 42.84                     | —                                 |
| Bai Jiang Cao   | 49.43                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ze Xie* 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62955     | 62955               | 0.00                         | 5.96                            |
| 62956     | 62956               | 0.00                         | 6.44                            |

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 2.4-2022-02

Validated substance/substance group **Zhe Bei Mu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50388-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Zhe Bei Mu                | 2      | 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 |
| PhytoComm | Zhe Bei Mu | G108HS138TT1 | 63027     | 40      | from supplier |
| PhytoComm | Zhe Bei Mu | G108HS138TT1 | 63028     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Zhe Bei Mu*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Zhe Bei Mu | G108HS138SG1 | 62688 <sup>†</sup> | 20      |
| PhytoComm | Zhe Bei Mu | G108HS138TT1 | 63027 <sup>†</sup> | 20      |
| PhytoComm | Zhe Bei Mu | G108HS138TT1 | 63028 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | G108H0712321 | 1       |
| Phytocomm | Zhe Bei Mu | G108H0712422 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 1              | 77            | 3              | 11 316        |
| <b>Type C</b> | 0              | 0             | 2              | 855           |

The substance/substance group *Zhe Bei Mu* 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 99.9950 % (> 99.9629 %)  | 96.2500 % (> 92.5000 %)  |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 *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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Lian Qiao       | 5.46                      | —                                 |
| Fu Zi           | 6.11                      | —                                 |
| Tian Hua Fen    | 6.55                      | —                                 |
| Ling Zhi        | 6.68                      | —                                 |
| Pi Pa Ye        | 6.95                      | —                                 |
| Ji Li           | 7.00                      | —                                 |
| Bai Shao Yao    | 7.10                      | —                                 |
| Shan Yao        | 7.46                      | —                                 |
| Bai Zi Ren      | 8.05                      | —                                 |
| He Huan Pi      | 10.05                     | —                                 |
| Jin Yin Hua     | 10.16                     | —                                 |
| Ze Xie          | 10.33                     | —                                 |
| Di Gu Pi        | 11.05                     | —                                 |
| Hou Po          | 11.14                     | —                                 |
| Lai Fu Zi       | 11.77                     | —                                 |
| Ren Dong Teng   | 11.96                     | —                                 |
| Ban Xia (Jiang) | 12.05                     | —                                 |
| Ye Jiao Teng    | 12.44                     | —                                 |
| Gu Sui Bu       | 12.73                     | —                                 |
| Sheng Jiang     | 12.82                     | —                                 |
| Mu Zei          | 13.00                     | —                                 |
| Shen Qu         | 13.03                     | —                                 |
| Huo Ma Ren      | 13.03                     | —                                 |
| Yan Hu Suo      | 14.01                     | —                                 |
| Zhu Ru          | 14.18                     | —                                 |
| Tao Ren         | 14.39                     | —                                 |
| Lian Zi         | 14.64                     | —                                 |
| Gui Zhi         | 15.31                     | —                                 |
| Jiao Gu Lan     | 15.41                     | —                                 |
| Ku Shen         | 15.46                     | —                                 |
| Yi Yi Ren       | 15.73                     | —                                 |
| Ji Xue Teng     | 15.73                     | —                                 |
| Che Qian Zi     | 16.38                     | —                                 |
| Fu Pen Zi       | 16.45                     | —                                 |
| Ci Wu Jia       | 16.48                     | —                                 |
| Fu Xiao Mai     | 16.60                     | —                                 |
| Tu Fu Ling      | 16.98                     | —                                 |
| Ren Shen        | 17.17                     | —                                 |
| Fu Ling         | 17.38                     | —                                 |
| Chai Hu         | 17.39                     | —                                 |
| Rou Gui         | 17.43                     | —                                 |
| San Qi          | 17.48                     | —                                 |
| Yu Jin          | 17.69                     | —                                 |
| Gua Lou         | 18.90                     | —                                 |
| Suan Zao Ren    | 19.18                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Zhu Ling        | 19.49                             | —                                         |
| Ban Lan Gen     | 19.49                             | —                                         |
| Ce Bai Ye       | 19.93                             | —                                         |
| Dan Shen        | 20.12                             | —                                         |
| Lu Gen          | 20.27                             | —                                         |
| Mao Dong Qing   | 20.34                             | —                                         |
| Gou Teng        | 20.46                             | —                                         |
| Dan Dou Chi     | 21.46                             | —                                         |
| Dang Gui        | 22.34                             | —                                         |
| She Gan         | 22.78                             | —                                         |
| Fo Shou         | 22.85                             | —                                         |
| Bai Xian Pi     | 22.95                             | —                                         |
| Qing Pi         | 23.04                             | —                                         |
| Guang Huo Xiang | 23.10                             | —                                         |
| Zhi Ke          | 23.35                             | —                                         |
| Qiang Huo       | 24.29                             | —                                         |
| Yin Yang Huo    | 24.63                             | —                                         |
| Huang Qin       | 24.76                             | —                                         |
| Gan Cao         | 24.79                             | —                                         |
| Zhi Gan Cao     | 25.11                             | —                                         |
| Xie Bai         | 25.74                             | —                                         |
| Cang Zhu        | 25.77                             | —                                         |
| Ma Huang        | 26.46                             | —                                         |
| Jie Geng        | 26.52                             | —                                         |
| Zhi Mu          | 26.66                             | —                                         |
| Gou Qi Zi       | 27.00                             | —                                         |
| (Fen) Bi Xie    | 28.76                             | —                                         |
| Du Zhong        | 28.86                             | —                                         |
| Hong Jing Tian  | 29.07                             | —                                         |
| Zi Hua Di Ding  | 29.22                             | —                                         |
| Huang Lian      | 30.76                             | —                                         |
| Ma Huang Gen    | 31.80                             | —                                         |
| Fu Shen         | 32.49                             | —                                         |
| Mang Xiao       | 33.33                             | —                                         |
| Mu Gua          | 34.23                             | —                                         |
| Yuan Zhi        | 35.79                             | —                                         |
| Bo He           | 36.83                             | —                                         |
| Sha Ren         | 37.27                             | —                                         |
| Chuang Mu Xiang | 37.44                             | —                                         |
| Jing Jie        | 37.56                             | —                                         |
| Chi Shao (Yao)  | 37.97                             | —                                         |
| Sang Zhi        | 38.29                             | —                                         |
| Cang Er Zi      | 39.10                             | —                                         |
| Sang Ye         | 39.30                             | —                                         |
| Huang Bai       | 40.36                             | —                                         |
| Long Yan Rou    | 40.94                             | —                                         |
| Hong Hua        | 43.18                             | —                                         |
| Qing Hao        | 43.18                             | —                                         |
| Bai Jiang Cao   | 48.01                             | —                                         |

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                         | 6.55                            |
| 62688     | 62688               | 0.00                         | 7.10                            |
| 63027     | 63027               | 0.00                         | 5.96                            |
| 63028     | 63028               | 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 2.4-2022-02

Validated substance/substance group **Zhi Gan Cao**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60016-2022-06-27  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Zhi Gan Cao; Glycyrrhizae radix et rhizoma praeparata cum melle

### Special notes

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

*no information*

### Applicable documents

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Zhi Gan Cao               | 2      | 0      | 2      |

### Second-stage model

For differentiation of the substance/substance group *Zhi 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 *Zhi Gan Cao*:

| Supplier  | Substance   | Batch        | Sample ID | Spectra | Certificate   |
|-----------|-------------|--------------|-----------|---------|---------------|
| PhytoComm | Zhi Gan Cao | G118HS089SV2 | 62869     | 40      | from supplier |
| PhytoComm | Zhi Gan Cao | G118HS089SV2 | 62870     | 40      | from supplier |
| PhytoComm | Zhi Gan Cao | G118H0881923 | 62899     | 40      | from supplier |
| PhytoComm | Zhi Gan Cao | G118H0881923 | 62900     | 40      | from supplier |

## Validation samples

A total of 34 694 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 Gan Cao*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 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 | Zhi Gan Cao | G118HS089SV2 | 62869 <sup>†</sup> | 20      |
| PhytoComm | Zhi Gan Cao | G118HS089SV2 | 62870 <sup>†</sup> | 20      |
| PhytoComm | Zhi Gan Cao | G118H0881923 | 62899 <sup>†</sup> | 20      |
| PhytoComm | Zhi Gan Cao | G118H0881923 | 62900 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 *Zhi Gan 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 | Zhi Gan Cao | g118h0881322 | 1       |
| PhytoComm | Zhi Gan Cao | G118H0881322 | 1       |
| Phytocomm | Zhi Gan Cao | G118H0881522 | 4       |

- 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 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 *Zhi 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 160           | 0              | 22 279        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 4              | 3             | 3              | 847           |

The substance/substance group *Zhi Gan 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 99.9963 % (> 99.9799 %)  | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 99.7708 % (> 99.1837 %)  | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Huang Qi        | 6.56                      | —                                 |
| Jin Yin Hua     | 7.12                      | —                                 |
| Hong Jing Tian  | 7.51                      | —                                 |
| Zi Hua Di Ding  | 9.57                      | —                                 |
| Gan Cao         | 10.58                     | —                                 |
| Jiao Gu Lan     | 11.31                     | —                                 |
| Bai Zhu         | 11.34                     | —                                 |
| Ban Lan Gen     | 11.92                     | —                                 |
| Zhi Ke          | 11.92                     | —                                 |
| Dan Shen        | 12.53                     | —                                 |
| Dan Dou Chi     | 13.30                     | —                                 |
| Hong Hua        | 13.93                     | —                                 |
| Hou Po          | 14.31                     | —                                 |
| Mu Gua          | 14.39                     | —                                 |
| Jie Geng        | 14.74                     | —                                 |
| Guang Huo Xiang | 15.55                     | —                                 |
| Ma Huang        | 15.79                     | —                                 |
| Fu Pen Zi       | 16.04                     | —                                 |
| Fu Zi           | 16.23                     | —                                 |
| Qing Pi         | 16.85                     | —                                 |
| Chuang Mu Xiang | 16.85                     | —                                 |
| Chi Shao (Yao)  | 16.87                     | —                                 |
| Long Dan (Cao)  | 16.96                     | —                                 |
| Shan Yao        | 17.15                     | —                                 |
| Qiang Huo       | 17.51                     | —                                 |
| (Huai) Niu Xi   | 17.66                     | —                                 |
| Pi Pa Ye        | 17.71                     | —                                 |
| Qin Jiao        | 17.78                     | —                                 |
| Gu Sui Bu       | 18.02                     | —                                 |
| Chai Hu         | 18.19                     | —                                 |
| Ren Dong Teng   | 18.20                     | —                                 |
| Bo He           | 18.35                     | —                                 |
| Suan Zao Ren    | 18.42                     | —                                 |
| Tian Hua Fen    | 18.42                     | —                                 |
| Cang Zhu        | 18.79                     | —                                 |
| Yan Hu Suo      | 19.03                     | —                                 |
| Chuan Lian Zi   | 19.23                     | —                                 |
| Yin Yang Huo    | 19.24                     | —                                 |
| Huang Bai       | 19.28                     | —                                 |
| She Gan         | 19.30                     | —                                 |
| Sang Zhi        | 19.35                     | —                                 |
| Yuan Zhi        | 19.69                     | —                                 |
| Ren Shen        | 19.86                     | —                                 |
| Ye Jiao Teng    | 19.86                     | —                                 |
| Mu Zei          | 20.18                     | —                                 |

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| <b>Substanz</b> | <b>Distance in<br/>main model</b> | <b>Distance in<br/>second-stage model</b> |
|-----------------|-----------------------------------|-------------------------------------------|
| Di Gu Pi        | 20.75                             | —                                         |
| Bai Shao Yao    | 20.93                             | —                                         |
| Lian Qiao       | 21.33                             | —                                         |
| Sha Ren         | 21.77                             | —                                         |
| Ku Shen         | 22.13                             | —                                         |
| Ze Xie          | 22.31                             | —                                         |
| Lu Gen          | 22.34                             | —                                         |
| Mao Dong Qing   | 23.36                             | —                                         |
| Ji Li           | 24.26                             | —                                         |
| Zhe Bei Mu      | 24.40                             | —                                         |
| Huang Lian      | 24.69                             | —                                         |
| Jing Jie        | 24.98                             | —                                         |
| Ce Bai Ye       | 24.99                             | —                                         |
| Lian Zi         | 25.03                             | —                                         |
| Du Zhong        | 25.46                             | —                                         |
| He Huan Pi      | 26.03                             | —                                         |
| Bai Xian Pi     | 26.16                             | —                                         |
| Qing Hao        | 26.37                             | —                                         |
| Dang Gui        | 26.39                             | —                                         |
| Xie Bai         | 26.46                             | —                                         |
| Huang Qin       | 26.80                             | —                                         |
| Sang Ye         | 27.36                             | —                                         |
| Bai He          | 27.38                             | —                                         |
| Gou Qi Zi       | 27.77                             | —                                         |
| Che Qian Zi     | 28.06                             | —                                         |
| Yu Jin          | 28.37                             | —                                         |
| Shen Qu         | 28.42                             | —                                         |
| Ji Xue Teng     | 28.48                             | —                                         |
| Gua Lou         | 28.63                             | —                                         |
| Mang Xiao       | 28.78                             | —                                         |
| Zi Su Zi        | 29.62                             | —                                         |
| Bing Lang       | 29.68                             | —                                         |
| Tao Ren         | 30.25                             | —                                         |
| Long Yan Rou    | 30.39                             | —                                         |
| Chuan Mu Tong   | 30.42                             | —                                         |
| Cang Er Zi      | 30.90                             | —                                         |
| San Qi          | 31.01                             | —                                         |
| Bai Jiang Cao   | 31.14                             | —                                         |
| Ling Zhi        | 31.15                             | —                                         |
| Zhu Ling        | 31.50                             | —                                         |
| Gou Teng        | 31.64                             | —                                         |
| (Fen) Bi Xie    | 31.89                             | —                                         |
| Sheng Jiang     | 31.99                             | —                                         |
| Tu Fu Ling      | 32.19                             | —                                         |
| Chuan Niu Xi    | 32.30                             | —                                         |
| Gui Zhi         | 32.89                             | —                                         |
| Rou Gui         | 33.34                             | —                                         |
| Bai Zi Ren      | 33.39                             | —                                         |
| Bai Zhi         | 33.55                             | —                                         |
| Lai Fu Zi       | 33.60                             | —                                         |
| Sha Shen (Bei)  | 34.01                             | —                                         |
| Fu Ling         | 35.66                             | —                                         |
| Huo Ma Ren      | 36.06                             | —                                         |
| Gan Jiang       | 36.24                             | —                                         |
| (Shi) Chang Pu  | 37.03                             | —                                         |
| Zhi Mu          | 37.05                             | —                                         |
| E Zhu           | 38.80                             | —                                         |
| Ci Wu Jia       | 38.99                             | —                                         |
| Pu Gong Ying    | 40.23                             | —                                         |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ze Lan          | 40.73                     | —                                 |
| Ban Zhi Lian    | 41.30                     | —                                 |
| Niu Bang Zi     | 43.05                     | —                                 |
| Ban Xia (Jiang) | 43.18                     | —                                 |
| Mi Huan Jun     | 43.86                     | —                                 |
| Zhu Ru          | 43.91                     | —                                 |
| Ma Huang Gen    | 43.98                     | —                                 |
| Wu Wei Zi       | 45.33                     | —                                 |
| Chen Pi         | 47.01                     | —                                 |
| Ju Hua          | 47.88                     | —                                 |
| Fang Feng       | 48.32                     | —                                 |
| Yi Yi Ren       | 48.74                     | —                                 |
| Xiang Fu        | 49.09                     | —                                 |
| Xi Xian Cao     | 49.76                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zhi 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62869     | 62869                  | 0.00                            | 7.12                               |
| 62870     | 62870                  | 0.00                            | 7.70                               |
| 62899     | 62899                  | 0.00                            | 6.90                               |
| 62900     | 62900                  | 0.00                            | 6.56                               |

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 2.4-2022-02

Validated substance/substance group **Zhi Ke**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60158-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |
| PhytoComm | Zhi Ke    | G043HS169RR1 | 62440 <sup>†</sup> | 20      |
| PhytoComm | Zhi Ke    | G043HS169SL1 | 62703 <sup>†</sup> | 20      |
| PhytoComm | Zhi Ke    | G043HS169SL1 | 62704 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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    | G043H0921221 | 1       |
| Phytocomm | Zhi Ke    | G043H0921422 | 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 80            | 0              | 11 317        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 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.)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Jin Yin Hua     | 9.72                      | —                                 |
| Gan Cao         | 12.30                     | —                                 |
| Zhi Gan Cao     | 12.71                     | —                                 |
| Lian Qiao       | 13.05                     | —                                 |
| Jiao Gu Lan     | 13.50                     | —                                 |
| Hou Po          | 13.72                     | —                                 |
| Ma Huang        | 14.22                     | —                                 |
| Zi Hua Di Ding  | 14.93                     | —                                 |
| Ku Shen         | 16.00                     | —                                 |
| Dan Dou Chi     | 17.09                     | —                                 |
| Ban Lan Gen     | 17.95                     | —                                 |
| Cang Zhu        | 18.21                     | —                                 |
| Zhe Bei Mu      | 18.36                     | —                                 |
| Yan Hu Suo      | 18.43                     | —                                 |
| Fu Zi           | 18.49                     | —                                 |
| Fu Pen Zi       | 18.62                     | —                                 |
| San Qi          | 18.73                     | —                                 |
| Pi Pa Ye        | 18.73                     | —                                 |
| Hong Jing Tian  | 18.78                     | —                                 |
| Guang Huo Xiang | 19.12                     | —                                 |
| Dan Shen        | 19.33                     | —                                 |
| Yin Yang Huo    | 19.69                     | —                                 |
| Shan Yao        | 19.93                     | —                                 |
| Ye Jiao Teng    | 19.96                     | —                                 |
| Tian Hua Fen    | 20.30                     | —                                 |
| Suan Zao Ren    | 20.99                     | —                                 |
| Qing Pi         | 21.64                     | —                                 |
| Chai Hu         | 22.55                     | —                                 |
| Qiang Huo       | 22.80                     | —                                 |
| Chuang Mu Xiang | 23.58                     | —                                 |
| Gou Qi Zi       | 23.74                     | —                                 |
| Lu Gen          | 23.75                     | —                                 |
| Ren Dong Teng   | 24.14                     | —                                 |
| Lai Fu Zi       | 24.23                     | —                                 |
| Hong Hua        | 24.40                     | —                                 |
| Bai Shao Yao    | 24.87                     | —                                 |
| He Huan Pi      | 25.21                     | —                                 |
| Huang Lian      | 25.25                     | —                                 |
| Gua Lou         | 25.26                     | —                                 |
| Mu Zei          | 25.52                     | —                                 |
| She Gan         | 25.65                     | —                                 |
| Huang Qin       | 25.73                     | —                                 |
| Ling Zhi        | 26.28                     | —                                 |
| Bo He           | 26.32                     | —                                 |
| Ze Xie          | 26.39                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dang Gui        | 26.48                     | —                                 |
| Huang Bai       | 26.74                     | —                                 |
| Bai Zi Ren      | 27.05                     | —                                 |
| Xie Bai         | 27.34                     | —                                 |
| Sha Ren         | 27.58                     | —                                 |
| Ren Shen        | 27.93                     | —                                 |
| Di Gu Pi        | 28.25                     | —                                 |
| Gu Sui Bu       | 28.65                     | —                                 |
| Jing Jie        | 29.34                     | —                                 |
| Jie Geng        | 30.04                     | —                                 |
| Lian Zi         | 30.10                     | —                                 |
| Ji Li           | 30.13                     | —                                 |
| Sang Ye         | 30.32                     | —                                 |
| Tao Ren         | 30.47                     | —                                 |
| Mang Xiao       | 30.96                     | —                                 |
| Qing Hao        | 31.74                     | —                                 |
| Che Qian Zi     | 31.80                     | —                                 |
| Du Zhong        | 32.25                     | —                                 |
| Mao Dong Qing   | 32.27                     | —                                 |
| Bai Xian Pi     | 32.56                     | —                                 |
| Ce Bai Ye       | 32.60                     | —                                 |
| Mu Gua          | 33.10                     | —                                 |
| Ji Xue Teng     | 33.39                     | —                                 |
| Zhi Mu          | 34.35                     | —                                 |
| Chi Shao (Yao)  | 34.79                     | —                                 |
| Rou Gui         | 35.04                     | —                                 |
| Bai Jiang Cao   | 35.17                     | —                                 |
| Cang Er Zi      | 35.90                     | —                                 |
| Sheng Jiang     | 37.16                     | —                                 |
| Gui Zhi         | 37.33                     | —                                 |
| Huo Ma Ren      | 37.57                     | —                                 |
| Yu Jin          | 38.31                     | —                                 |
| Zhu Ru          | 40.25                     | —                                 |
| Yuan Zhi        | 40.33                     | —                                 |
| Zhu Ling        | 40.34                     | —                                 |
| Ci Wu Jia       | 40.52                     | —                                 |
| Gou Teng        | 40.60                     | —                                 |
| (Fen) Bi Xie    | 41.05                     | —                                 |
| Shen Qu         | 41.76                     | —                                 |
| Fu Ling         | 41.82                     | —                                 |
| Yi Yi Ren       | 43.19                     | —                                 |
| Tu Fu Ling      | 44.41                     | —                                 |
| Ze Lan          | 45.52                     | —                                 |
| Wu Wei Zi       | 46.03                     | —                                 |
| Long Yan Rou    | 47.32                     | —                                 |
| Fu Xiao Mai     | 48.49                     | —                                 |
| Ban Xia (Jiang) | 48.64                     | —                                 |
| Pu Gong Ying    | 48.88                     | —                                 |
| Ban Zhi Lian    | 49.27                     | —                                 |
| Sang Zhi        | 50.09                     | —                                 |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 62439     | 62439               | 0.00                         | 10.70                           |
| 62440     | 62440               | 0.00                         | 9.72                            |
| 62703     | 62703               | 0.00                         | 13.05                           |
| 62704     | 62704               | 0.00                         | 13.18                           |

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 2.4-2022-02

Validated substance/substance group **Zhi Mu**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60196-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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    | G019HS153SW1 | 62959     | 40      | from supplier |
| PhytoComm | Zhi Mu    | G019HS153SW1 | 62960     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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    | G019HS153SW1 | 62959 <sup>†</sup> | 20      |
| PhytoComm | Zhi Mu    | G019HS153SW1 | 62960 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).



**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bai Shao Yao    | 7.26                      | —                                 |
| Jie Geng        | 9.56                      | —                                 |
| Pi Pa Ye        | 10.40                     | —                                 |
| Yuan Zhi        | 10.68                     | —                                 |
| Shan Yao        | 10.89                     | —                                 |
| San Qi          | 13.01                     | —                                 |
| Fo Shou         | 13.45                     | —                                 |
| Ren Shen        | 14.03                     | —                                 |
| Ku Shen         | 14.24                     | —                                 |
| Zhu Ru          | 14.34                     | —                                 |
| Gua Lou         | 14.42                     | —                                 |
| Ye Jiao Teng    | 14.75                     | —                                 |
| Ji Li           | 14.92                     | —                                 |
| Shen Qu         | 15.50                     | —                                 |
| Di Gu Pi        | 15.53                     | —                                 |
| Mu Gua          | 15.60                     | —                                 |
| Fu Xiao Mai     | 16.46                     | —                                 |
| Cang Zhu        | 17.13                     | —                                 |
| Lian Zi         | 17.26                     | —                                 |
| He Huan Pi      | 18.63                     | —                                 |
| Sheng Jiang     | 19.45                     | —                                 |
| Tian Hua Fen    | 19.57                     | —                                 |
| Bai Zi Ren      | 19.67                     | —                                 |
| Rou Gui         | 19.78                     | —                                 |
| Lian Qiao       | 20.01                     | —                                 |
| Ci Wu Jia       | 20.49                     | —                                 |
| Lai Fu Zi       | 20.61                     | —                                 |
| Fu Ling         | 21.25                     | —                                 |
| Ren Dong Teng   | 21.49                     | —                                 |
| Zhe Bei Mu      | 21.53                     | —                                 |
| Ling Zhi        | 21.59                     | —                                 |
| Dang Gui        | 21.63                     | —                                 |
| Mu Zei          | 21.81                     | —                                 |
| Gui Zhi         | 21.85                     | —                                 |
| Tu Fu Ling      | 22.20                     | —                                 |
| Gou Qi Zi       | 22.25                     | —                                 |
| Huo Ma Ren      | 22.88                     | —                                 |
| Xie Bai         | 24.39                     | —                                 |
| Jiao Gu Lan     | 25.32                     | —                                 |
| Yi Yi Ren       | 25.51                     | —                                 |
| Ban Lan Gen     | 26.11                     | —                                 |
| Tao Ren         | 26.19                     | —                                 |
| Suan Zao Ren    | 26.43                     | —                                 |
| Jin Yin Hua     | 26.62                     | —                                 |
| Mao Dong Qing   | 27.69                     | —                                 |
| Gou Teng        | 29.04                     | —                                 |
| Hou Po          | 29.39                     | —                                 |
| Fu Zi           | 29.41                     | —                                 |
| Ban Xia (Jiang) | 29.52                     | —                                 |
| Bai Xian Pi     | 29.63                     | —                                 |
| Lu Gen          | 30.58                     | —                                 |
| Ze Xie          | 30.78                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zhi Ke          | 30.90                     | —                                 |
| Dan Dou Chi     | 30.91                     | —                                 |
| Ji Xue Teng     | 31.46                     | —                                 |
| Fu Pen Zi       | 31.46                     | —                                 |
| Long Yan Rou    | 31.78                     | —                                 |
| Chuang Mu Xiang | 32.01                     | —                                 |
| Dan Shen        | 32.87                     | —                                 |
| Che Qian Zi     | 33.29                     | —                                 |
| Gu Sui Bu       | 33.41                     | —                                 |
| Mang Xiao       | 33.76                     | —                                 |
| Huang Qin       | 34.32                     | —                                 |
| Gan Cao         | 34.94                     | —                                 |
| Yu Jin          | 37.53                     | —                                 |
| Ma Huang Gen    | 37.87                     | —                                 |
| Yan Hu Suo      | 38.58                     | —                                 |
| Hong Jing Tian  | 39.03                     | —                                 |
| Chai Hu         | 39.39                     | —                                 |
| Ce Bai Ye       | 40.40                     | —                                 |
| Yin Yang Huo    | 40.85                     | —                                 |
| (Fen) Bi Xie    | 41.46                     | —                                 |
| Guang Huo Xiang | 42.72                     | —                                 |
| Ma Huang        | 43.07                     | —                                 |
| Zhu Ling        | 43.44                     | —                                 |
| Fu Shen         | 43.55                     | —                                 |
| Sang Zhi        | 43.87                     | —                                 |
| Qiang Huo       | 44.58                     | —                                 |
| Chi Shao (Yao)  | 45.93                     | —                                 |
| She Gan         | 47.06                     | —                                 |
| Qing Pi         | 48.47                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62959     | 62959                  | 0.00                            | 7.36                               |
| 62960     | 62960                  | 0.00                            | 7.26                               |

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



# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Zhi Shi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60145-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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   | G044HS168ST1 | 62979     | 40      | from supplier |
| PhytoComm | Zhi Shi   | G044HS168ST1 | 62980     | 40      | from supplier |
| PhytoComm | Zhi Shi   | G044HS168TK1 | 62981     | 40      | from supplier |
| PhytoComm | Zhi Shi   | G044HS168TK1 | 62982     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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   | G044HS168ST1 | 62979 <sup>†</sup> | 20      |
| PhytoComm | Zhi Shi   | G044HS168ST1 | 62980 <sup>†</sup> | 20      |
| PhytoComm | Zhi Shi   | G044HS168TK1 | 62981 <sup>†</sup> | 20      |
| PhytoComm | Zhi Shi   | G044HS168TK1 | 62982 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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   | g044h0922221 | 1       |
| Phytocomm | Zhi Shi   | G044H0922221 | 2       |
| PhytoComm | Zhi Shi   | G044H0922221 | 3       |
| phytocomm | Zhi Shi   | g044h0922321 | 1       |
| Phytocomm | Zhi Shi   | G044H0922321 | 2       |
| PhytoComm | Zhi Shi   | G044H0922321 | 2       |
| Phytocomm | Zhi Shi   | G044H0922521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 22 280        |
| <b>Type B</b> | 0              | 79            | 1              | 11 317        |
| <b>Type C</b> | 0              | 0             | 14             | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9673 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9356 %) | 98.7500 % (> 95.0000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8246 %) | n/a (n/a)                |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Yin Chen Hao        | 4.46                      | —                                 |
| Sang Ye             | 6.01                      | —                                 |
| Bai Hua She She Cao | 8.88                      | —                                 |
| Hu Zhang            | 9.05                      | —                                 |
| Xin Yi              | 9.64                      | —                                 |
| Ze Lan              | 12.76                     | —                                 |
| Pu Gong Ying        | 13.55                     | —                                 |
| Yu Xing Cao         | 15.55                     | —                                 |
| Xia Ku Cao          | 15.64                     | —                                 |
| Shan Yao            | 15.80                     | —                                 |
| Han Lian Cao        | 16.33                     | —                                 |
| Huang Lian          | 16.36                     | —                                 |
| Nü Zhen Zi          | 16.38                     | —                                 |
| Sha Ren             | 17.15                     | —                                 |
| Bai Jiang Cao       | 17.80                     | —                                 |
| Tu Fu Ling          | 21.65                     | —                                 |
| Xi Xian Cao         | 21.86                     | —                                 |
| Qiang Huo           | 23.32                     | —                                 |
| Huang Bai           | 24.58                     | —                                 |
| Mang Xiao           | 26.17                     | —                                 |
| Fu Zi               | 27.15                     | —                                 |
| Jiang Huang         | 27.58                     | —                                 |
| Zi Hua Di Ding      | 28.00                     | —                                 |
| Yi Mu Cao           | 28.00                     | —                                 |
| Du Zhong            | 28.06                     | —                                 |
| Qing Pi             | 28.42                     | —                                 |
| Bo He               | 29.19                     | —                                 |
| Hong Jing Tian      | 29.58                     | —                                 |
| Mao Dong Qing       | 29.95                     | —                                 |
| Dan Shen            | 30.16                     | —                                 |
| Qing Hao            | 30.52                     | —                                 |
| Jing Jie            | 31.08                     | —                                 |
| Ma Huang            | 31.66                     | —                                 |
| Zhi Ke              | 31.97                     | —                                 |
| Gu Sui Bu           | 32.44                     | —                                 |
| Chai Hu             | 32.80                     | —                                 |
| He Huan Pi          | 32.90                     | —                                 |
| Dan Dou Chi         | 33.48                     | —                                 |
| Hou Po              | 33.58                     | —                                 |
| Gou Teng            | 34.81                     | —                                 |
| Fu Pen Zi           | 35.47                     | —                                 |

*continued on the next page*



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| Substanz         | Distance in<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Yin Yang Huo     | 36.90                     | —                                 |
| Jiao Gu Lan      | 37.03                     | —                                 |
| Cang Er Zi       | 37.35                     | —                                 |
| Xiang Fu         | 37.42                     | —                                 |
| Gan Cao          | 38.86                     | —                                 |
| Ye Jiao Teng     | 39.71                     | —                                 |
| Che Qian Zi      | 40.02                     | —                                 |
| Hong Hua         | 40.17                     | —                                 |
| Ce Bai Ye        | 40.29                     | —                                 |
| Chuang Mu Xiang  | 40.60                     | —                                 |
| Yu Jin           | 40.69                     | —                                 |
| Zi Su Zi         | 41.34                     | —                                 |
| Wang Bu Liu Xing | 41.96                     | —                                 |
| Jin Yin Hua      | 42.45                     | —                                 |
| Niu Bang Zi      | 42.70                     | —                                 |
| Wu Zhu Yu        | 44.29                     | —                                 |
| Ju Hua           | 44.32                     | —                                 |
| Yan Hu Suo       | 45.53                     | —                                 |
| Wu Wei Zi        | 45.86                     | —                                 |
| Suan Zao Ren     | 46.58                     | —                                 |
| Zhe Bei Mu       | 47.68                     | —                                 |
| Di Gu Pi         | 48.03                     | —                                 |
| Lian Qiao        | 48.39                     | —                                 |
| Xiao Hui Xiang   | 49.43                     | —                                 |
| Zhi Gan Cao      | 50.10                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62979     | 62979                  | 0.00                            | 8.88                               |
| 62980     | 62980                  | 0.00                            | 9.05                               |
| 62981     | 62981                  | 0.00                            | 5.56                               |
| 62982     | 62982                  | 0.00                            | 4.46                               |

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 2.4-2022-02

Validated substance/substance group **Zhu Ling**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 10002254-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | G199HS318TK1 | 62847     | 40      | from supplier |
| PhytoComm | Zhu Ling  | G199HS318TK1 | 62848     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G199HS318TK1 | 62847 <sup>†</sup> | 20      |
| PhytoComm | Zhu Ling  | G199HS318TK1 | 62848 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|-----------|-----------|--------------|---------|
| Mediherb  | Zhu Ling  |              | 1       |
| PhytoComm | Zhu Ling  | G199H1509022 | 1       |
| Phytocomm | Zhu Ling  | G199H1509421 | 2       |
| PhytoComm | Zhu Ling  | G199H1509521 | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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.

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

### 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ling Zhi        | 6.85                      | —                                 |
| Ren Dong Teng   | 7.21                      | —                                 |
| Bai Xian Pi     | 7.25                      | —                                 |
| Dan Dou Chi     | 8.48                      | —                                 |
| Rou Gui         | 10.70                     | —                                 |
| Gou Teng        | 10.97                     | —                                 |
| She Gan         | 11.21                     | —                                 |
| Huo Ma Ren      | 11.35                     | —                                 |
| (Fen) Bi Xie    | 11.51                     | —                                 |
| Ye Jiao Teng    | 11.59                     | —                                 |
| Bai Shao Yao    | 12.00                     | —                                 |
| Lian Zi         | 12.17                     | —                                 |
| He Huan Pi      | 12.21                     | —                                 |
| Ce Bai Ye       | 12.68                     | —                                 |
| Lu Gen          | 13.07                     | —                                 |
| Yi Yi Ren       | 13.12                     | —                                 |
| Ma Huang Gen    | 13.52                     | —                                 |
| Gui Zhi         | 13.79                     | —                                 |
| Fu Ling         | 13.85                     | —                                 |
| Sheng Jiang     | 14.31                     | —                                 |
| Yu Jin          | 14.46                     | —                                 |
| Mao Dong Qing   | 14.57                     | —                                 |
| Guang Huo Xiang | 14.64                     | —                                 |
| Yin Yang Huo    | 14.70                     | —                                 |
| Shen Qu         | 15.54                     | —                                 |
| Ji Xue Teng     | 15.67                     | —                                 |
| Tu Fu Ling      | 15.72                     | —                                 |
| Mu Zei          | 16.11                     | —                                 |
| Ji Li           | 16.54                     | —                                 |
| Fu Xiao Mai     | 16.73                     | —                                 |
| Chai Hu         | 16.87                     | —                                 |
| Yan Hu Suo      | 17.16                     | —                                 |
| Gu Sui Bu       | 17.67                     | —                                 |
| Dan Shen        | 18.46                     | —                                 |
| Che Qian Zi     | 18.97                     | —                                 |
| Tian Hua Fen    | 19.30                     | —                                 |
| Tao Ren         | 19.51                     | —                                 |
| Lian Qiao       | 19.77                     | —                                 |
| Fu Zi           | 19.85                     | —                                 |
| Fo Shou         | 20.08                     | —                                 |
| Hou Po          | 20.53                     | —                                 |
| Zhe Bei Mu      | 20.65                     | —                                 |
| Pi Pa Ye        | 20.86                     | —                                 |
| Shan Yao        | 21.00                     | —                                 |
| Ci Wu Jia       | 21.19                     | —                                 |
| Jing Jie        | 21.77                     | —                                 |
| Qiang Huo       | 22.51                     | —                                 |
| Ban Xia (Jiang) | 22.59                     | —                                 |
| Suan Zao Ren    | 23.55                     | —                                 |
| Fu Pen Zi       | 23.97                     | —                                 |
| Di Gu Pi        | 24.26                     | —                                 |
| Zi Hua Di Ding  | 24.77                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Ma Huang        | 24.97                     | —                                 |
| Jiao Gu Lan     | 25.06                     | —                                 |
| Gan Cao         | 25.12                     | —                                 |
| Sha Ren         | 25.26                     | —                                 |
| Bai Zi Ren      | 25.55                     | —                                 |
| Jin Yin Hua     | 26.23                     | —                                 |
| Fu Shen         | 26.60                     | —                                 |
| Zhu Ru          | 27.05                     | —                                 |
| Hong Jing Tian  | 28.61                     | —                                 |
| Du Zhong        | 28.91                     | —                                 |
| Ban Lan Gen     | 29.69                     | —                                 |
| Lai Fu Zi       | 30.77                     | —                                 |
| Zhi Ke          | 32.02                     | —                                 |
| Huang Lian      | 32.07                     | —                                 |
| Mang Xiao       | 33.08                     | —                                 |
| Ren Shen        | 33.52                     | —                                 |
| Ze Xie          | 33.52                     | —                                 |
| Bo He           | 33.71                     | —                                 |
| Qing Pi         | 34.25                     | —                                 |
| Cang Zhu        | 35.09                     | —                                 |
| Zhi Gan Cao     | 36.73                     | —                                 |
| Huang Bai       | 37.23                     | —                                 |
| Gua Lou         | 38.40                     | —                                 |
| Chuang Mu Xiang | 38.57                     | —                                 |
| Sang Zhi        | 39.83                     | —                                 |
| Jie Geng        | 40.79                     | —                                 |
| Dang Gui        | 41.11                     | —                                 |
| Huang Qin       | 41.53                     | —                                 |
| San Qi          | 41.84                     | —                                 |
| Chi Shao (Yao)  | 45.84                     | —                                 |
| Qing Hao        | 46.28                     | —                                 |
| Long Yan Rou    | 46.73                     | —                                 |
| Bai Jiang Cao   | 47.42                     | —                                 |
| Ban Zhi Lian    | 49.71                     | —                                 |
| Xie Bai         | 49.87                     | —                                 |
| Bai Zhu         | 49.89                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62847     | 62847                  | 0.00                            | 7.11                               |
| 62848     | 62848                  | 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 2.4-2022-02

Validated substance/substance group **Zhu Ru**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60241-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Zhu Ru                    | 2      | 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 |
| PhytoComm | Zhu Ru    | G047HS109SW1 | 62913     | 40      | from supplier |
| PhytoComm | Zhu Ru    | G047HS109SW1 | 62914     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Zhu Ru*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Zhu Ru    | G047HS109SK1 | 62658 <sup>†</sup> | 20      |
| PhytoComm | Zhu Ru    | G047HS109SW1 | 62913 <sup>†</sup> | 20      |
| PhytoComm | Zhu Ru    | G047HS109SW1 | 62914 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were

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

**Type C** Spectra of independent samples not included in the database structure. *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 | 1       |
| Phytocomm | Zhu Ru    | G047H0625321 | 2       |
| PhytoComm | Zhu Ru    | G047H0625321 | 1       |
| Phytocomm | Zhu Ru    | G047H0625422 | 3       |
| Phytocomm | Zhu Ru    | G047h625321  | 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 2              | 154           | 6              | 22 278        |
| <b>Type B</b> | 4              | 57            | 23             | 11 313        |
| <b>Type C</b> | 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        |
|---------------|--------------------------|-------------------------|
| <b>Type A</b> | 99.9950 % (> 99.9787 %)  | 96.2500 % (> 94.3750 %) |
| <b>Type B</b> | 99.9752 % (> 99.9430 %)  | 71.2500 % (> 67.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8251 %) | n/a (n/a)               |

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

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Yi Yi Ren       | 3.09                      | —                                 |
| Gui Zhi         | 3.89                      | —                                 |
| Fu Xiao Mai     | 4.19                      | —                                 |
| Sheng Jiang     | 4.87                      | —                                 |
| Di Gu Pi        | 4.89                      | —                                 |
| He Huan Pi      | 6.34                      | —                                 |
| Ban Xia (Jiang) | 6.80                      | —                                 |
| Ci Wu Jia       | 7.52                      | —                                 |
| Bai Shao Yao    | 7.79                      | —                                 |
| Rou Gui         | 7.98                      | —                                 |
| Fu Ling         | 8.09                      | —                                 |
| Ji Li           | 8.99                      | —                                 |
| Tao Ren         | 9.84                      | —                                 |
| Shen Qu         | 10.27                     | —                                 |
| Bai Zi Ren      | 11.13                     | —                                 |
| Lian Zi         | 11.18                     | —                                 |
| Gou Teng        | 13.38                     | —                                 |
| Lai Fu Zi       | 13.56                     | —                                 |
| Zhe Bei Mu      | 13.87                     | —                                 |
| Ling Zhi        | 14.11                     | —                                 |
| Mu Zei          | 14.39                     | —                                 |
| Tian Hua Fen    | 15.96                     | —                                 |
| Fo Shou         | 16.15                     | —                                 |
| Huo Ma Ren      | 16.73                     | —                                 |
| Ji Xue Teng     | 16.87                     | —                                 |
| Ye Jiao Teng    | 16.88                     | —                                 |
| Bai Xian Pi     | 16.94                     | —                                 |
| Gu Sui Bu       | 17.83                     | —                                 |
| Pi Pa Ye        | 18.93                     | —                                 |
| Ma Huang Gen    | 18.98                     | —                                 |
| Shan Yao        | 19.03                     | —                                 |
| Lu Gen          | 20.12                     | —                                 |
| Fu Shen         | 21.90                     | —                                 |
| Yu Jin          | 22.60                     | —                                 |
| Ren Dong Teng   | 22.71                     | —                                 |
| Lian Qiao       | 23.78                     | —                                 |
| Tu Fu Ling      | 23.91                     | —                                 |
| Ze Xie          | 24.00                     | —                                 |
| Zhu Ling        | 26.66                     | —                                 |
| (Fen) Bi Xie    | 26.82                     | —                                 |
| Jin Yin Hua     | 27.10                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Zhi Mu          | 27.17                     | —                                 |
| Suan Zao Ren    | 28.02                     | —                                 |
| Ren Shen        | 28.17                     | —                                 |
| Yan Hu Suo      | 28.27                     | —                                 |
| Jie Geng        | 28.74                     | —                                 |
| Gua Lou         | 29.88                     | —                                 |
| Fu Zi           | 30.87                     | —                                 |
| Ce Bai Ye       | 31.23                     | —                                 |
| San Qi          | 31.30                     | —                                 |
| Fu Pen Zi       | 31.45                     | —                                 |
| Cang Zhu        | 32.15                     | —                                 |
| Yuan Zhi        | 32.31                     | —                                 |
| Jiao Gu Lan     | 32.53                     | —                                 |
| Dang Gui        | 32.72                     | —                                 |
| Dan Shen        | 32.74                     | —                                 |
| Dan Dou Chi     | 33.68                     | —                                 |
| Huang Qin       | 33.80                     | —                                 |
| Mang Xiao       | 33.82                     | —                                 |
| Mao Dong Qing   | 34.36                     | —                                 |
| Yin Yang Huo    | 35.33                     | —                                 |
| Zhi Ke          | 35.58                     | —                                 |
| Ban Lan Gen     | 35.60                     | —                                 |
| She Gan         | 36.19                     | —                                 |
| Mu Gua          | 36.23                     | —                                 |
| Chai Hu         | 37.57                     | —                                 |
| Hou Po          | 37.65                     | —                                 |
| Che Qian Zi     | 37.99                     | —                                 |
| Ku Shen         | 39.53                     | —                                 |
| Gou Qi Zi       | 40.04                     | —                                 |
| Ma Huang        | 42.59                     | —                                 |
| Hong Jing Tian  | 43.82                     | —                                 |
| Qiang Huo       | 44.18                     | —                                 |
| Long Yan Rou    | 45.32                     | —                                 |
| Gan Cao         | 45.97                     | —                                 |
| Guang Huo Xiang | 46.25                     | —                                 |
| Sang Zhi        | 46.97                     | —                                 |
| Huang Lian      | 47.18                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62657     | 62657                  | 0.00                            | 3.25                               |
| 62658     | 62658                  | 0.00                            | 3.09                               |
| 62913     | 62913                  | 0.00                            | 3.89                               |
| 62914     | 62914                  | 0.00                            | 4.61                               |

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

# VALIDATION REPORT

## IdentModule 2.4-2022-02

Validated substance/substance group **Zi Hua Di Ding**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 50376-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Zi Hua Di Ding            | 2      | 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 |
| PhytoComm | Zi Hua Di Ding | G249HS269SW1 | 62803     | 40      | from supplier |
| PhytoComm | Zi Hua Di Ding | G249HS269SW1 | 62804     | 40      | from supplier |

## Validation samples

A total of 34 694 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 *Zi Hua Di Ding*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 22 280 spectra from a total of 280 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *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 <sup>†</sup> | 20      |
| PhytoComm | Zi Hua Di Ding | G249HS269SK1 | 62628 <sup>†</sup> | 20      |
| PhytoComm | Zi Hua Di Ding | G249HS269SW1 | 62803 <sup>†</sup> | 20      |
| PhytoComm | Zi Hua Di Ding | G249HS269SW1 | 62804 <sup>†</sup> | 20      |

- 11 317 spectra from a total of 280 batches from further 168 substances. These spectra were



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

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 1              | 160           | 0              | 22 279        |
| <b>Type B</b> | 1              | 78            | 2              | 11 316        |
| <b>Type C</b> | 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 99.9963 % (> 99.9799 %)  | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 99.9926 % (> 99.9604 %)  | 97.5000 % (> 93.7500 %)  |
| <b>Type C</b> | 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

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

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Dan Shen        | 4.85                      | —                                 |
| Fu Zi           | 4.86                      | —                                 |
| Qing Pi         | 7.05                      | —                                 |
| Jiao Gu Lan     | 7.48                      | —                                 |
| Qiang Huo       | 7.48                      | —                                 |
| Chai Hu         | 7.84                      | —                                 |
| Hong Jing Tian  | 8.12                      | —                                 |
| Fu Pen Zi       | 8.53                      | —                                 |
| Bo He           | 8.56                      | —                                 |
| Gan Cao         | 8.68                      | —                                 |
| Qing Hao        | 8.89                      | —                                 |
| Hou Po          | 9.56                      | —                                 |
| Jin Yin Hua     | 9.92                      | —                                 |
| Mao Dong Qing   | 10.38                     | —                                 |
| Jing Jie        | 10.49                     | —                                 |
| Huang Bai       | 10.95                     | —                                 |
| Dan Dou Chi     | 11.54                     | —                                 |
| Ce Bai Ye       | 11.66                     | —                                 |
| Du Zhong        | 12.35                     | —                                 |
| Yin Yang Huo    | 12.81                     | —                                 |
| Sha Ren         | 13.33                     | —                                 |
| Yu Jin          | 13.41                     | —                                 |
| Ban Lan Gen     | 13.90                     | —                                 |
| Zhi Ke          | 13.99                     | —                                 |
| Shan Yao        | 14.01                     | —                                 |
| Guang Huo Xiang | 14.28                     | —                                 |
| Zhi Gan Cao     | 14.31                     | —                                 |
| Ma Huang        | 14.64                     | —                                 |
| Ye Jiao Teng    | 14.84                     | —                                 |
| Pi Pa Ye        | 15.02                     | —                                 |
| Ling Zhi        | 15.52                     | —                                 |
| Tian Hua Fen    | 15.81                     | —                                 |
| Yan Hu Suo      | 16.48                     | —                                 |
| Ren Dong Teng   | 16.73                     | —                                 |
| She Gan         | 16.84                     | —                                 |
| Gu Sui Bu       | 17.04                     | —                                 |
| Ji Li           | 17.06                     | —                                 |
| Bai Xian Pi     | 17.10                     | —                                 |
| Bai Jiang Cao   | 17.46                     | —                                 |
| Hong Hua        | 17.56                     | —                                 |
| Huang Lian      | 17.60                     | —                                 |
| Shen Qu         | 19.01                     | —                                 |
| Bai Shao Yao    | 19.16                     | —                                 |
| Lian Zi         | 19.26                     | —                                 |
| Suan Zao Ren    | 19.50                     | —                                 |
| Zhe Bei Mu      | 19.58                     | —                                 |
| Ren Shen        | 19.86                     | —                                 |
| Che Qian Zi     | 19.87                     | —                                 |

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| Substanz        | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Di Gu Pi        | 20.68                     | —                                 |
| Sang Ye         | 20.69                     | —                                 |
| Lian Qiao       | 21.44                     | —                                 |
| Ji Xue Teng     | 22.03                     | —                                 |
| Mu Zei          | 22.44                     | —                                 |
| Lu Gen          | 22.61                     | —                                 |
| Chuang Mu Xiang | 23.52                     | —                                 |
| He Huan Pi      | 23.74                     | —                                 |
| Zhu Ling        | 23.75                     | —                                 |
| (Fen) Bi Xie    | 24.08                     | —                                 |
| Cang Zhu        | 24.30                     | —                                 |
| Tu Fu Ling      | 24.34                     | —                                 |
| Ze Xie          | 25.64                     | —                                 |
| Xie Bai         | 26.74                     | —                                 |
| Cang Er Zi      | 26.85                     | —                                 |
| Jie Geng        | 27.18                     | —                                 |
| Ku Shen         | 27.26                     | —                                 |
| Pu Gong Ying    | 27.49                     | —                                 |
| Gou Teng        | 28.35                     | —                                 |
| Sheng Jiang     | 29.79                     | —                                 |
| Chi Shao (Yao)  | 30.28                     | —                                 |
| Ze Lan          | 30.41                     | —                                 |
| Tao Ren         | 30.52                     | —                                 |
| Mang Xiao       | 30.94                     | —                                 |
| Fu Ling         | 31.21                     | —                                 |
| Xi Xian Cao     | 31.78                     | —                                 |
| Dang Gui        | 31.90                     | —                                 |
| Huang Qin       | 32.01                     | —                                 |
| Huo Ma Ren      | 32.11                     | —                                 |
| Gua Lou         | 32.71                     | —                                 |
| Bai Zi Ren      | 34.19                     | —                                 |
| San Qi          | 34.30                     | —                                 |
| Gui Zhi         | 34.80                     | —                                 |
| Rou Gui         | 35.31                     | —                                 |
| Ma Huang Gen    | 35.47                     | —                                 |
| Sang Zhi        | 35.69                     | —                                 |
| Long Yan Rou    | 37.11                     | —                                 |
| Nü Zhen Zi      | 39.11                     | —                                 |
| Gou Qi Zi       | 39.17                     | —                                 |
| Wu Wei Zi       | 39.51                     | —                                 |
| Ban Zhi Lian    | 39.71                     | —                                 |
| Ci Wu Jia       | 40.20                     | —                                 |
| Ban Xia (Jiang) | 41.07                     | —                                 |
| Zhu Ru          | 42.12                     | —                                 |
| Jiang Huang     | 42.28                     | —                                 |
| Yi Yi Ren       | 43.66                     | —                                 |
| E Zhu           | 43.87                     | —                                 |
| Niu Bang Zi     | 44.05                     | —                                 |
| Lai Fu Zi       | 44.39                     | —                                 |
| Zhi Shi         | 44.52                     | —                                 |
| Yi Mu Cao       | 44.58                     | —                                 |
| Zhi Mu          | 45.74                     | —                                 |
| Zi Su Zi        | 46.85                     | —                                 |
| Xin Yi          | 47.27                     | —                                 |
| Mu Gua          | 48.45                     | —                                 |
| Fu Xiao Mai     | 48.99                     | —                                 |

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

stance/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                         | 7.05                            |
| 62628     | 62628               | 0.00                         | 4.85                            |
| 62803     | 62803               | 0.00                         | 7.48                            |
| 62804     | 62804               | 0.00                         | 7.48                            |

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 2.4-2022-02

Validated substance/substance group **Zi Su Zi**  
Substance class TCM - Granulated herbal extracts (PhytoComm)  
Report date 27/06/2022  
Report number 60133-2022-06-27  
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

978-3-7692-7517-9 *European Pharmacopoeia 10th Edition, Basic Version 2020* [3]  
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]  
AA004 *Erstellung und Validierung eines IdentModul-Updates*

### Validation method

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

1. The chemometric model is 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/substance group | 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  | G183H1213922 | 62835     | 40      | from supplier |
| PhytoComm | Zi Su Zi  | G183H1213922 | 62836     | 40      | from supplier |

## Validation samples

A total of 34 694 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.
- 22 360 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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  | G183H1213922 | 62835 <sup>†</sup> | 20      |
| PhytoComm | Zi Su Zi  | G183H1213922 | 62836 <sup>†</sup> | 20      |

- 11 357 spectra from a total of 281 batches from further 168 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

**Type C** Spectra of independent samples not included in the database structure. *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 22 360        |
| <b>Type B</b> | 0              | 40            | 0              | 11 357        |
| <b>Type C</b> | 1              | 0             | 0              | 856           |

The substance/substance group *Zi Su 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9674 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9359 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 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 *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.

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

| Substance           | Distance in<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Gan Jiang           | 5.83                      | —                                 |
| Cang Er Zi          | 11.59                     | —                                 |
| Sha Shen (Bei)      | 13.98                     | —                                 |
| Chuan Lian Zi       | 15.65                     | —                                 |
| Niu Bang Zi         | 16.67                     | —                                 |
| Sang Zhi            | 17.80                     | —                                 |
| (Huai) Niu Xi       | 18.59                     | —                                 |
| Tian Hua Fen        | 18.69                     | —                                 |
| Di Gu Pi            | 18.92                     | —                                 |
| Yan Hu Suo          | 20.00                     | —                                 |
| E Zhu               | 20.06                     | —                                 |
| Jie Geng            | 21.76                     | —                                 |
| Jiang Huang         | 23.60                     | —                                 |
| Shan Yao            | 24.45                     | —                                 |
| Suan Zao Ren        | 24.80                     | —                                 |
| Mi Huan Jun         | 26.43                     | —                                 |
| (Bai) Dou Kou       | 26.58                     | —                                 |
| Dang Gui            | 26.59                     | —                                 |
| Lai Fu Zi           | 26.61                     | —                                 |
| Mang Xiao           | 27.21                     | —                                 |
| Xiao Hui Xiang      | 27.60                     | —                                 |
| Xiang Fu            | 27.82                     | —                                 |
| Chen Pi             | 28.10                     | —                                 |
| Sha Ren             | 28.28                     | —                                 |
| Lian Qiao           | 28.69                     | —                                 |
| Huang Qi            | 29.73                     | —                                 |
| Long Dan (Cao)      | 30.43                     | —                                 |
| Chuan Mu Tong       | 31.01                     | —                                 |
| Chuan Niu Xi        | 31.68                     | —                                 |
| Zhi Gan Cao         | 32.22                     | —                                 |
| Ku Shen             | 32.43                     | —                                 |
| (Shi) Chang Pu      | 33.16                     | —                                 |
| Bai Zhu             | 33.87                     | —                                 |
| Bai Zhi             | 35.24                     | —                                 |
| Pu Gong Ying        | 37.04                     | —                                 |
| Shan Yu Rou         | 37.12                     | —                                 |
| Bai He              | 37.92                     | —                                 |
| Qin Jiao            | 38.07                     | —                                 |
| Du Huo              | 38.46                     | —                                 |
| Bai Hua She She Cao | 38.79                     | —                                 |
| He Huan Pi          | 40.18                     | —                                 |
| Yi Mu Cao           | 40.77                     | —                                 |
| Dong Gua Zi         | 40.89                     | —                                 |
| Wu Yao              | 41.34                     | —                                 |
| Bai Xian Pi         | 42.27                     | —                                 |
| Huang Lian          | 42.30                     | —                                 |
| Qiang Huo           | 42.65                     | —                                 |
| Jin Yin Hua         | 43.15                     | —                                 |
| Fu Ling             | 43.49                     | —                                 |
| Lian Zi             | 43.86                     | —                                 |
| Tu Fu Ling          | 44.56                     | —                                 |
| Ce Bai Ye           | 44.98                     | —                                 |
| Zi Hua Di Ding      | 45.20                     | —                                 |
| Ji Li               | 45.54                     | —                                 |
| Ban Zhi Lian        | 45.64                     | —                                 |
| Da Zao              | 45.72                     | —                                 |
| Zhi Ke              | 45.93                     | —                                 |
| Wang Bu Liu Xing    | 46.80                     | —                                 |
| Yuan Zhi            | 46.90                     | —                                 |

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| Substanz       | Distance in<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Chi Shao (Yao) | 46.98                     | —                                 |
| Bo He          | 46.98                     | —                                 |
| Fang Feng      | 47.80                     | —                                 |
| Sang Ji Shend  | 48.00                     | —                                 |
| Ba Ji Tian     | 48.24                     | —                                 |
| Xin Yi         | 48.99                     | —                                 |
| Mu Dan Pi      | 49.42                     | —                                 |
| Ju Hua         | 49.99                     | —                                 |
| Du Zhong       | 50.18                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 62835     | 62835                  | 0.00                            | 5.83                               |
| 62836     | 62836                  | 0.00                            | 6.39                               |

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.



## *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 128 batches. From these, 179 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       |

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

| Supplier  | Substance    | Batch        | Spectra |
|-----------|--------------|--------------|---------|
| Phytocomm | Bai Bian Dou | g093h0510221 | 1       |
| Phytocomm | Bai Bian Dou | G093H0510221 | 1       |
| Phytocomm | Bai Bu       | G235H0608321 | 1       |
| PhytoComm | Bai Bu       | G235H0608221 | 1       |
| Phytocomm | Bai Guo      | G114H0509321 | 2       |
| Phytocomm | Bai Guo      | G114H0509521 | 1       |
| Phytocomm | Bai Mao Gen  | G125H0512221 | 2       |
| Phytocomm | Bai Tou Weng | G207H0511521 | 4       |
| PhytoComm | Bai Tou Weng | G207H0511221 | 3       |
| PhytoComm | Bie Jia      | G507H2401121 | 1       |
| PhytoComm | Bie Jia      | G507H2401321 | 1       |

| Supplier  | Substance    | Batch         | Spectra |
|-----------|--------------|---------------|---------|
| PhytoComm | Cao Guo      | E241050       | 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 Xiong  | g136h0305121  | 1       |
| Phytocomm | Chuan Xiong  | G136H0305421  | 2       |
| PhytoComm | Chuan Xiong  | G136H0305221  | 3       |

| Supplier  | Substance  | Batch        | Spectra |
|-----------|------------|--------------|---------|
| Phytocomm | Da Fu Pi   | G293H0321221 | 1       |
| Phytocomm | Da Qing Ye | G127H0318421 | 2       |
| EuRho     | Dang Shen  | g077h2001222 | 2       |

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| Supplier  | Substance    | Batch        | Spectra |
|-----------|--------------|--------------|---------|
| Phytocomm | Dang Shen    | G077H2001022 | 1       |
| Phytocomm | Dang Shen    | G077H2001521 | 4       |
| PhytoComm | Dang Shen    | G077H2001621 | 1       |
| 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       |

| Supplier  | Substance    | Batch        | Spectra |
|-----------|--------------|--------------|---------|
| PhytoComm | E Bu Shi Cao | G061H180122  | 1       |
| Phytocomm | E Jiao       | g036h0861121 | 1       |
| Phytocomm | E Jiao       | g036h0861221 | 1       |
| Phytocomm | E Jiao       | G036H0861421 | 2       |
| PhytoComm | E Jiao       | G036H0861221 | 4       |

| Supplier  | Substance | Batch        | Spectra |
|-----------|-----------|--------------|---------|
| Phytocomm | Fang Ji   | G236H0727321 | 1       |
| PhytoComm | Fang Ji   | G236H0727123 | 1       |

| Supplier  | Substance   | Batch        | Spectra |
|-----------|-------------|--------------|---------|
| PhytoComm | Geng Mi     | G329H1320121 | 1       |
| Phytocomm | Gua Lou Ren | g243h1095123 | 1       |
| PhytoComm | Gua Lou Ren | G243H1095421 | 1       |

| Supplier  | Substance  | Batch        | Spectra |
|-----------|------------|--------------|---------|
| PhytoComm | He Zi      | G291H1239221 | 2       |
| Phytocomm | Huai Hua   | G263H1423421 | 1       |
| Phytocomm | Huang Bo   | h1203022     | 1       |
| Phytocomm | Huang Bo   | g188h1203123 | 1       |
| PhytoComm | Huang Bo   | G188H1203321 | 4       |
| Phytocomm | Huang Jing | g196h1206121 | 1       |
| Phytocomm | Huang Jing | G196H1206121 | 1       |

| Supplier  | Substance  | Batch        | Spectra |
|-----------|------------|--------------|---------|
| Phytocomm | Ji Nei Jin | G259H2102321 | 1       |
| Phytocomm | Ji Nei Jin | g259h2102321 | 1       |
| Phytocomm | Jie Cao    | H2111921     | 1       |

| Supplier  | Substance     | Batch    | Spectra |
|-----------|---------------|----------|---------|
| PhytoComm | Kuan Dong Hua | H1219921 | 1       |

| Supplier  | Substance      | Batch        | Spectra |
|-----------|----------------|--------------|---------|
| Phytocomm | Long Gu        | g0251706122  | 1       |
| PhytoComm | Long Gu        | G025H1706122 | 1       |
| 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       |

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| Supplier  | Substance  | Batch        | Spectra |
|-----------|------------|--------------|---------|
| Phytocomm | Lu Lu Tong | G142H1336521 | 2       |
| PhytoComm | Lu Lu Tong | G142H1336122 | 1       |

| Supplier  | Substance    | Batch        | Spectra |
|-----------|--------------|--------------|---------|
| Phytocomm | Ma Bian Cao  | G248H1085221 | 1       |
| PhytoComm | Ma Chi Xian  | G255F110310  | 1       |
| Phytocomm | Mai Men Dong | g176h1118221 | 1       |
| Phytocomm | Mai Men Dong | G176H1118521 | 3       |
| Phytocomm | Mai Ya       | g123h1119022 | 1       |
| Phytocomm | Mai Ya       | G123H1119521 | 1       |
| PhytoComm | Mai Ya       | G123H1119821 | 1       |
| Phytocomm | Mo Yao       | G1690732222  | 1       |
| PhytoComm | Mo Yao       | G169H0732222 | 2       |

| Supplier  | Substance | Batch        | Spectra |
|-----------|-----------|--------------|---------|
| Phytocomm | Qian Hu   | G185H0926322 | 4       |
| Phytocomm | Qian Shi  | G102H0836422 | 1       |
| PhytoComm | Qian Shi  | G102H0836121 | 1       |
| Phytocomm | Quan Xie  | G222F110314  | 1       |

| Supplier  | Substance | Batch        | Spectra |
|-----------|-----------|--------------|---------|
| Phytocomm | Ru Xiang  | G174H0820231 | 1       |
| Phytocomm | Ru Xiang  | G174H0820421 | 3       |

| Supplier  | Substance      | Batch          | Spectra |
|-----------|----------------|----------------|---------|
| 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 | Sheng Ma       | g068h04317121  | 1       |
| Phytocomm | Sheng Ma       | G068H0437421   | 2       |
| PhytoComm | Suo Yang       | G260H1831121   | 1       |

| Supplier  | Substance     | Batch        | Spectra |
|-----------|---------------|--------------|---------|
| Phytocomm | Tai Zi Shen   | G204H0446221 | 1       |
| Phytocomm | Tai Zi Shen   | G204H0446521 | 1       |
| Phytocomm | Tian Men Dong | G037H0415221 | 1       |
| Phytocomm | Tian Men Dong | g037h0415221 | 1       |
| Phytocomm | Tian Men Dong | g03h0415521  | 1       |
| Phytocomm | Tian Men Dong | G037H0415321 | 1       |

| Supplier  | Substance     | Batch        | Spectra |
|-----------|---------------|--------------|---------|
| 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       |

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| Supplier  | Substance | Batch       | Spectra |
|-----------|-----------|-------------|---------|
| Phytocomm | Wu Gong   | G311H411321 | 1       |

| Supplier  | Substance    | Batch        | Spectra |
|-----------|--------------|--------------|---------|
| Phytocomm | Xi Yang Shen | G324H0647321 | 1       |
| Phytocomm | Xi Yang Shen | g324h0647321 | 1       |
| Phytocomm | Xi Yang Shen | G324HS4070L1 | 1       |
| phytocomm | Xian He Cao  | g008h0547321 | 1       |
| Phytocomm | Xian He Cao  | G008H0547121 | 1       |
| Phytocomm | Xian He Cao  | G008H0547321 | 1       |

| Supplier  | Substance  | Batch        | Spectra |
|-----------|------------|--------------|---------|
| Phytocomm | Yi Zhi Ren | G015H1051321 | 2       |
| Phytocomm | Yi Zhi Ren | G015H1051521 | 1       |
| Phytocomm | Yu Zhu     | G195H0517421 | 2       |
| PhytoComm | Yu Zhu     | G195H0517121 | 1       |

| Supplier  | Substance   | Batch        | Spectra |
|-----------|-------------|--------------|---------|
| Phytocomm | Zhen Zhu Mu | g155h0979221 | 1       |
| Phytocomm | Zhi Zi      | g110h1137121 | 1       |
| Phytocomm | Zhi Zi      | G110H1137521 | 4       |
| PhytoComm | Zhi Zi      | G110H1137121 | 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).

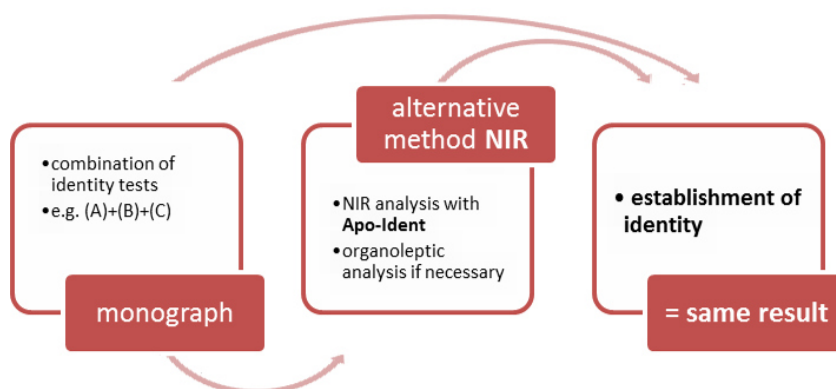


**Figure 2:** The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

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 2020*. 10. Ausgabe. Deutscher Apotheker Verlag (978-3-7692-7517-9)
- [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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Zizyphi jujubae fructus, *see* Da Zao, [221](#)  
Zizyphi spinosae semen, *see* Suan Zao Ren, [763](#)