Guide
for the elaboration of monographs on homoeopathic preparations

> Stocks for homoeopathic preparations may be of mineral, chemical, botanical, zoological or human origin

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of monographs

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GUIDE FOR THE ELABORATION OF MONOGRAPHS ON HOMOEOPATHIC PREPARATIONS

GENERAL

Stocks for homoeopathic preparations may be of mineral, chemical, botanical, zoological or human origin.

A monograph on a stock for homoeopathic preparations is drafted with the same overall structure as other monographs of the European Pharmacopoeia (Ph. Eur.) and both the latest versions of the Technical Guide for the Elaboration of Monographs (referred to as the Technical Guide) and of the Ph. Eur. Style Guide apply to monographs on these homoeopathic preparations. This Guide develops the specific points which are appropriate to monographs for homoeopathic preparations and which are not presented in the 2 general Guides above.

The title of a monograph on a stock for homoeopathic preparations consists of the most widely accepted name of the stock used traditionally in homoeopathy followed by the expression “for homoeopathic preparations”. Where there is no traditional name, the title is derived from the scientific name. The Latin title is derived from the scientific name of the substance (herbal, chemical or biological substance). The English, French and Latin titles may be different. The only exception is for monograph titles for chemical substances that are based on recommended International Nonproprietary Names (INN). In this case, the INN is used for the titles as described in the Style Guide under ‘Monograph titles’.

All tests and assay methods described in a monograph must be validated according to the procedures stated in the Technical Guide. The complete data for validation according to the ICH guidelines are supplied to the Secretariat and examined by the rapporteur.

The general monographs *Homoeopathic preparations (1038), Methods of preparation of homoeopathic stocks and potentisation (2371)* and *Mother tinctures for homoeopathic preparations (2029)*, as appropriate, apply to all preparations for homoeopathic use, and their provisions must be taken into account when elaborating specific monographs.

Monographs on stocks of chemical origin (including minerals) are drafted according to the same rules as the other monographs, and both the Style Guide and the Technical Guide for the Elaboration of Monographs apply.

For stocks of biological origin, there are two parts to the monograph: the first describes the raw material and the second describes the mother tincture.

For monographs on herbal stocks, the Style Guide and the Technical Guide for the Elaboration of Monographs also apply. Descriptions of the raw material and of the mother tincture prepared from this drug are included in the same monograph.

The aspects specific to monographs on herbal drugs for homoeopathic preparations are described below.

The general monograph *Herbal drugs for homoeopathic preparations (2045)* applies to all herbal drugs for homoeopathic use and its provisions must be taken into account when elaborating specific monographs.

ELABORATION OF MONOGRAPHS ON HERBAL DRUGS FOR HOMOEOPATHIC PREPARATIONS

NOMENCLATURE

ENGLISH TITLE

The English name is given in capitals.

The title consists of the most widely accepted name used traditionally in homoeopathy, followed by the expression “for homoeopathic preparations”.

Examples: Belladonna for homoeopathic preparations

Cocculus for homoeopathic preparations

Ignatia for homoeopathic preparations

Where there is no traditional name, the English title is derived from the scientific name.

Example: Crataegus (fructus) for homoeopathic preparations

If different parts of the same plant are used traditionally in homoeopathy, the plant part used as starting material is named in Latin in the title.

Example: Arnica (radix) for homoeopathic preparations

The plant part used may be included in the title. In such cases, it is given in Latin in parentheses after the scientific name of the plant.

Example: Crataegus (fructus) for homoeopathic preparations / Crataegus (fructus et folium cum flore) for homoeopathic preparations

The state of the plant may be indicated in the title, in particular when the same part may be used in the fresh or dried state and when there is a specific monograph on each state. In such cases the state is mentioned after the scientific name of the plant.

Example: Gelsemium sempervirens for homoeopathic preparations, fresh

Gelsemium sempervirens for homoeopathic preparations, dried

LATIN TITLE

The Latin title consists of the scientific name of the plant (genus, species according to the *Kew index*) followed by "ad praeparationes homoeopathicas".

Examples: Atropa belladonna ad praeparationes homoeopathicas

Anamirta cocculus ad praeparationes homoeopathicas

Strychnos ignatii ad praeparationes homoeopathicas

Where necessary, the plant part is mentioned in the Latin title. In such cases, it consists of the species name (genitive) followed by the name of the organ used (nominative and singular) followed by "ad praeparationes homoeopathicas".

Example: Arnicae montanae radix ad praeparationes homoeopathicas

Similarly, where necessary, the state of the herbal drug is mentioned in the Latin title. In such cases, it consists of the species name (nominative) followed by the state of freshness of the herbal drug (nominative and singular) followed by "ad preparationes homoeopathicas".

Example: Gelsemium sempervirens recens ad praeparationes homoeopathicas

RAW MATERIAL OR HERBAL DRUG

Two cases:

a) The raw material is the subject of a Ph. Eur. monograph.

There is only a cross-reference to the existing monograph.

Example: the herbal drug complies with the requirements of the monograph *Goldenseal rhizome (1831)*

b) The raw material is not the subject of a Ph. Eur. monograph.

Herbal drugs used in the dried state must be distinguished from herbal drugs used in the fresh state. Certain tests are not performed on fresh herbal drugs due to the shortness of time between harvesting and the preparation of the mother tincture. The testing of dried herbal drugs is less affected by the time factor.

A. DRIED HERBAL DRUGS

In the absence of available examples in monographs on homoeopathic preparations, examples are taken from the Ph. Eur. section on Herbal drugs.

DEFINITION

Some or all of the following are usually included in the definition:

— The state of the dried herbal drug: whole, fragmented, broken, peeled and dried.

— The complete scientific name of the plant (genus, species, subspecies, variety, author) as obtained from the *Kew Index* and its supplements (*International Plant Names Index, IPNI*).

— The part or parts of the plant, written in the singular.

— Where appropriate, the stage in the growth cycle when harvesting takes place, or other necessary information.

— Where appropriate, the minimum content of one or more quantified constituents is stated. Dried herbal drugs very often contain a mixture of related substances. In such cases, the total content of quantified constituents may be determined and expressed as one of the constituents, usually the major constituent.

The statements “(dried drug)” or “(anhydrous drug)” imply that the monograph prescribes respectively a test for loss on drying (*2.2.32*) or a determination of water by distillation (*2.2.13)*. In practice, if the herbal drug to be examined is a dried drug, it is dried again to constant mass when the loss on drying is performed.

The title is not repeated in the definition.

Example: *Goldenseal rhizome (1831)*

CHARACTERS

This section contains a brief description of the physical characters of the dried herbal drug. The information given is not to be regarded as mandatory requirements.

ORGANOLEPTIC CHARACTERS

No reference is made to odour unless it is highly characteristic and can be described with reference to known odours. Terms such as “aromatic” and “characteristic” are not used.

MACROSCOPIC AND MICROSCOPIC BOTANICAL CHARACTERS

The description of botanical characters is included in the Identification section. However, some botanical characters that are highly variable and considered not compulsory for the identification of the plant may be described under Characters.

IDENTIFICATION

This section provides all the tests performed to identify the dried herbal drug including its colour.

All of the identifications mentioned below are not necessarily included; some may be absent when they are not feasible or are not significant for the purpose of identification.

The monograph may have a First identification and a simpler Second identification that is suitable for use when the equipment required for the main (first) identification tests is not available, or the tests are not otherwise feasible, or for any other reason, such as where the pharmacist, in some Member States, may have an obligation to identify a herbal drug, for example in a community pharmacy. Some tests may be specified in both the First and Second identifications. Application of the First and Second identifications is defined in the General Notices (1.). The identification section is introduced by a statement of the 2 identifications:

Example:

First identification: A, B, C, E

Second identification: B, D

MACROSCOPIC BOTANICAL CHARACTERS

When applicable, referred to as Identification A.

The important macroscopic botanical characters of the dried herbal drug are specified to permit a clear identification. When 2 species/subspecies of the same plant are included in the definition, the individual differences between the 2 are indicated. Further information for rapid identification of the drug is provided if necessary. When the definition states that the herbal drug can be either whole or fragmented, both the whole drug and the fragmented drug are described.

Example: *Nux-vomica for homoeopathic preparations (2514)*

MICROSCOPIC EXAMINATION

When applicable, referred to as Identification B.

The *Microscopic examination of herbal drugs* (*2.8.23*), reduced to a powder, describes the dominant or the most specific characters, including, if necessary, examination of the *stomata and stomatal index* (*2.8.3*). The colour of the powder, and the reagents used for the microscopic examination are specified. The sieve number needs to be stated in case the fineness of the powder diverges from sieve number 355 (*2.1.4*) as described in the general method (*2.8.23*). It may be necessary to perform the microscopic examination using more than 1 reagent in order to identify the specific characters. A specific stain may be prescribed for particular characters. Negative statements should be avoided since they usually refer to adulteration rather than to identification.

Illustrations of the main microscopic features of powders may be included.

Example: *Nux-vomica for homoeopathic preparations (2514)*

THIN-LAYER CHROMATOGRAPHY (TLC)

When applicable, referred to as Identification C.

Two types of presentation are possible.

TLC PRESCRIBED FOR THE IDENTIFICATION OF THE DRIED HERBAL DRUG

TLC is used under Identification, even if other chromatographic methods, such as gas chromatography (GC) and liquid chromatography (LC) are subsequently used in the monograph. In this context, the TLC is aimed at elucidating the chromatogram of the drug with respect to selected reference compounds that are described for inclusion as reagents (e.g. *rutin R*). Wherever possible, existing reagents described in general chapter *4.1.1. Reagents* of the Ph. Eur. are used as reference compounds. Where necessary, a description of a new reagent (name, molecular formula, relative molecular mass, CAS Registry Number, chemical nomenclature) is appended to the draft monograph for subsequent inclusion in general chapter *4.1.1.* Availability of reference compounds as commercial reagents must be verified during monograph elaboration. Where they are not readily available, a CRS or a HRS will have to be established and availability of a suitable quantity must be verified during monograph elaboration.

The commercial name of the TLC plate used during monograph development is included as a footnote to the monograph and after adoption by the Ph. Eur. Commission is transferred to the EDQM *Knowledge* database.

A minimum of 2 reference compounds must be used to validate the separation and spacing between the zones, otherwise a resolution test is necessary.

All the information concerning the preparation of the reference solution and the test solution and the chromatographic conditions is clearly stated. The methodology used, where possible, must be such that the application volume of the reference solution and the test solution is the same.

The general chapter on *thin-layer chromatography* (*2.2.27*) covers both classical TLC and high performance TLC (HPTLC). Where these 2 methods give equivalent results with the development solvent and visualisation method prescribed, both may be included in the working conditions [HPTLC conditions in brackets, after those of the classical TLC]. When the results of the TLC and those of the HPTLC are different, the choice between the 2 methods should be made during the elaboration of the monograph. Only the better of the 2 methods is described in the monograph.

Where appropriate, the width of the zones is indicated in the monograph.

The chromatograms are described in the form of a table, which shows the upper, middle and lower third of the plate.

Only the characteristic zone(s) in the chromatogram obtained with the test solution are described in the table in relation to the position of the zones due to the reference compounds in the chromatogram obtained with the reference solution. The names of the constituents detected in the chromatogram obtained with the reference solution are always given. The names of the constituents detected in the chromatogram obtained with the test solution are given only if these constituents are present in the reference solution and if the nature of the substance is well established.

Chromatograms are never described in terms of R_F values.

It is usually necessary to indicate when faint zones other than those described are also present in the chromatogram of the test solution.

Zones may be detected by examination in daylight, ultraviolet light, with or without using a reagent.

A copy in colour of a suitable chromatogram has to be provided to the Secretariat.

Example: *Nux-vomica for homoeopathic preparations (2514)*

TLC PRESCRIBED UNDER TESTS AND IDENTIFICATION

If a TLC test is used both for the control of adulterations and for identification, the method is described entirely under Tests with a cross-reference under Identification. The table is always included in the Identification section.

LIQUID OR GAS CHROMATOGRAPHY

Where liquid or gas chromatography is used in a test or assay, it may also be referred to under Identification.

Example:

For LC, refer to *Cocculus for homoeopathic preparations (2486)*

For GC, refer to *Juniper oil (1832)*

CHEMICAL REACTIONS FOR IDENTIFICATION

Chemical reactions are included only if the chromatographic methods do not give sufficient identification and if the reaction is particularly characteristic of a constituent or a group of constituents. They must allow rapid identification without the use of complex equipment and not be so sensitive as to give a false positive result.

TESTS

TYPICAL TESTS

FOREIGN MATTER (*2.8.2*)

The general monograph *Herbal drugs for homoeopathic preparations (2045)* imposes for dried plants a limit of not more than 2 per cent *m/m* for foreign matter, unless otherwise prescribed in an individual monograph or otherwise justified and authorised. The test is prescribed in the individual monograph only where a limit for foreign matter is other than 2 per cent. The type of foreign matter is indicated where appropriate. Where necessary, the monograph indicates how the foreign matter is identified.

Example:

Foreign matter (*2.8.2*): maximum 8 per cent of lignified branches with a diameter greater than 2.5 mm and maximum of 2 per cent of other foreign matter.

TEST FOR ADULTERATION

The manner in which this test is carried out depends on the knowledge available on possible adulterations. Chromatographic or other tests can be used to detect plant species that are not part of the definition. The name of the unwanted plant species (the complete scientific name of the adulterant (genus, species, subspecies, variety, author) is usually obtained from the *Kew Index (IPNI))* or their constituent(s) is used as the title of the test. This title is written in bold, the unwanted plant species are written in bold italics.

Where the method is either TLC or HPTLC, it is described entirely under Tests and wherever feasible it is also used to identify the dried herbal drug. In the chromatogram obtained with the test solution only the position and colour of the zone(s) of the

constituent(s) that must be absent are described by comparison with the chromatogram obtained with the reference solution. The zones present in the chromatogram obtained with the test solution are not described under Tests but under Identification in the form of a table.

Example: *Ignatia for homoeopathic preparations (2513)*

GAS CHROMATOGRAPHY (*2.2.28*) OR LIQUID CHROMATOGRAPHY (*2.2.29*)

The use of GC or LC is indicated under Tests to detect plant species that are not part of the definition (e.g. essential oils), to limit certain constituents (e.g. estragole in fennel) or to control the possible degradation or evaporation of any constituents that must be present in the dried herbal drug at a certain level.

A system suitability criterion should be included in the monograph. The commercial name of the column or columns found suitable during elaboration of the monograph are included in a footnote and transferred to the EDQM *Knowledge* database after publication of the monograph. A typical chromatogram is included in the draft monograph published in Pharmeuropa Online and transferred to the EDQM *Knowledge* database after publication of the monograph.

When the same GC or LC method is used both for assay and for a test, the method is described entirely under Tests with a cross-reference under Assay.

LOSS ON DRYING (*2.2.32*)

Herbal drugs are dried for preservation purposes: if they are insufficiently dried, growth of yeasts or moulds may occur. This test determines the maximum amount of water that may be present in the dried drug under the stated conditions. The limit should be specified on the basis of the results obtained on a reasonable number of varied samples of acceptable quality. Monographs usually specify drying for a defined period (usually 2 h) rather than drying to constant mass.

The monograph indicates the amount of herbal drug necessary for the determination and the degree of size reduction of the drug or the fineness of the powder using the sieve number (*2.1.4*).

Example:

Loss on drying (*2.2.32*): maximum 10.0 per cent, determined on 1.000 g of the powdered drug (710) (*2.9.12*) by drying in an oven at 105 °C for 2 h.

WATER (*2.2.13*)

For herbal drugs containing more than 10 mL/kg (1 per cent) of essential oil, the determination of water by distillation (*2.2.13*) is carried out instead of the test for loss on drying. The degree of size reduction of the drug or the fineness of the powder using a sieve number (*2.1.4*) is indicated if required.

Example:

Water (*2.2.13*): maximum 120 mL/kg, determined on 20.0 g of the crushed herbal drug.

TOTAL ASH (*2.4.16*)

This test is included unless otherwise justified. It is to be carried out on the powdered drug. It is not necessary to state the sieve number.

Example:

Total ash (*2.4.16*): maximum 14.0 per cent.

ASH INSOLUBLE IN HYDROCHLORIC ACID (*2.8.1*)

This test may be carried out depending on the nature of the particular herbal drug and is used to detect unacceptable quantities of certain minerals.

Example:

Ash insoluble in hydrochloric acid (*2.8.1*): maximum 2.0 per cent.

SWELLING INDEX (*2.8.4*)

This test is applicable to certain hydrocolloid-containing dried herbal drugs, for example *Iceland moss (1439)*.

Example:

Swelling index (*2.8.4*): minimum 4.5, determined on the powdered drug (355) (*2.9.12*).

BITTERNESS VALUE (*2.8.15*)

This test is applicable to dried herbal drugs containing bitter principles.

Example:

Bitterness value (*2.8.15*): minimum 4000.

EXTRACTABLE MATTER

This test is applicable to dried herbal drugs such as *Hop strobile (1222)*. It is considered useful to determine extractable matter only where no constituent suitable for an assay is known or when the material is used to produce a preparation with a dry residue. In general, extraction may be done with water or ethanol.

Example:

Matter extractable by ethanol (70 per cent *V/V*): minimum 25.0 per cent.

To 10.0 g of the powdered drug (355) (*2.9.12*) add 300 mL of *ethanol (70 per cent V/V) R* and heat for 10 min on a water-bath under a reflux condenser. Allow to cool, filter and discard the first 10 mL of the filtrate. Evaporate 30.0 mL of the filtrate to dryness on a water-bath and dry in an oven at 100-105 °C for 2 h. The residue weighs a minimum of 0.250 g.

HEAVY METALS (*2.4.27*)

A general method *Heavy metals in herbal drugs and fatty oils (2.4.27)* is included in the Ph. Eur. It is applicable to herbal drugs for homoeopathic preparations.

A test for a specific heavy metal may be needed where a particular herbal drug is known to accumulate that metal. This is indicated in the general monograph *Herbal drugs for homoeopathic preparations (2045)*. Furthermore, limits for heavy metals (cadmium, lead and mercury) may be given in the specific monograph if these are different from those stated in this general monograph.

OTHER TESTS

In certain cases, additional microscopic examinations and/or additional chemical reactions are carried out. This is done particularly to detect adulteration by drugs that have related morphological appearance but which come from totally different species to demonstrate for example that a given drug is free of toxic substances, such as alkaloids and cardiotonic steroids.

Specific tests may also be applied when necessary to an individual monograph such as:

— The test for aflatoxins (*2.8.18*) is considered depending on the nature, geographical origin and production of the plant. It is also usually performed when the water content / loss on drying of the starting dried herbal drug is greater than 12 per cent.

— The test for ochratoxin A *(2.8.22)* is carried out where necessary.

— In certain special circumstances, the risk of radioactive contamination should be considered (e.g. mushrooms).

ASSAY

Where necessary, an assay is included.

Standards used for quantification are established as CRS or as HRS; availability of a sufficient quantity of a batch of suitable quality must be verified during monograph elaboration.

The complete data for validation according to the ICH guidelines are supplied to the Secretariat and examined by the rapporteur. The constituent chosen must be suitable for a determination of the quality of the drug or relevant to its toxicity.

Wherever possible, liquid or gas chromatography are the methods of choice to determine the content of specific constituents rather than a global determination by spectrophotometry.

LIQUID CHROMATOGRAPHY (*2.2.29*) AND GAS CHROMATOGRAPHY (*2.2.28*)

For the technical and editorial content of these analytical methods, see the Technical Guide and the Style Guide. The general methods on *Chromatographic separation techniques* (*2.2.46*), *Liquid chromatography* (*2.2.29*) and *Gas chromatography* (*2.2.28*) must also be consulted.

A system suitability criterion should be included in the monograph. The commercial name of the column(s) found suitable during elaboration of the monograph are included in a footnote and transferred to the EDQM *Knowledge* database after publication of the monograph in the Ph. Eur. A representative chromatogram is included in the draft monograph published in Pharmeuropa Online and transferred to the EDQM *Knowledge* database after publication of the monograph.

The expression used to calculate the result of the assay is given.

Example: *Goldenseal rhizome (1831)*

ULTRAVIOLET AND VISIBLE ABSORPTION SPECTROPHOTOMETRY (*2.2.25*)

Spectrophotometry allows a global determination of constituents that are very often a group of related substances. It may be used for the quantification of constituents when these are a mixture of related substances.

Example: an assay for alkaloids is given in the monograph on *Cinchona bark (0174)*.

VOLUMETRIC TITRATION

Examples: volumetric titration is used for the assay of alkaloids in the monographs on *Ipecacuanha root* (*0094*) and for the determination of total iodine in the monograph on *Kelp* (*1426*).

DETERMINATION OF TANNINS IN HERBAL DRUGS (*2.8.14*)

This assay is described as a general method.

Examples: *Hamamelis leaf (0909)* or *Rhatany root (0289)*

DETERMINATION OF ESSENTIAL OILS IN HERBAL DRUGS (*2.8.12*)

When a minimum content of essential oil is required in the Definition, the assay is carried out on the drug, reduced in size if necessary, as prescribed in the monograph.

Example: *Eucalyptus leaf (1320)*

STORAGE

The storage conditions described in the general monograph on *Herbal drugs for homoeopathic preparations (2045)* are applicable unless otherwise specified.

Where applicable, specific additional conditions are given in the individual monograph.

Example: do not store in powdered form.

B. FRESH HERBAL DRUGS

DEFINITION

Some or all of the following are usually included in the definition:

— The state of the fresh herbal drug: whole, fragmented, peeled etc.,

— The complete scientific name of the plant (genus, species, subspecies, variety, author) as obtained from the *Kew Index* and its supplements (*IPNI*),

— The part or parts of the plant used (written in the singular); several plant parts may be mentioned if necessary,

— Where appropriate, the stage in the growth cycle when harvesting takes place, or other necessary information.

The title is not repeated in the Definition.

Examples:

Whole, fresh mushroom (fruiting body) *Amanita phalloides* (Vaill. ex Fr.) Link.

Fresh bulb, with roots removed, of the garden onion, *Allium cepa* var. *cepa* L.

CHARACTERS

This section contains a brief description of the physical characters of the fresh herbal drug. The information given is not to be regarded as mandatory requirements.

ORGANOLEPTIC CHARACTERS

No reference is made to odour unless it is highly characteristic and can be described with reference to known odours. Terms such as “aromatic” and “characteristic” are not used.

Example:

The cut drug has a strong lachrymatory effect.

MACROSCOPIC AND MICROSCOPIC BOTANICAL CHARACTERS

The description of botanical characters is usually included in the Identification section. However, some botanical characters that are highly variable and considered not compulsory for the identification of the plant may be described under Characters.

IDENTIFICATION

This section includes tests performed to identify the fresh herbal drug including its colour.

All the identifications mentioned below are not necessarily included, some may be absent when they are not feasible or are not significant for the purpose of identification.

MACROSCOPIC BOTANICAL CHARACTERS

When applicable, referred to as identification A.

The important macroscopic botanical characters of the fresh herbal drug are specified to permit a clear identification. When 2 species/subspecies of the same plant are included in the definition, the individual differences between the 2 are indicated.

Example: *Hypericum for homoeopathic preparations (2028)*

Further useful information for rapid identification of the fresh herbal drug is described where necessary such as examination under a lens (x magnification) or examination in ultraviolet light.

Example:

Examine under a lens (×10). The upper surface is shiny, dry, appearing somewhat uneven, with no remains of the veil.

MICROSCOPIC BOTANICAL CHARACTERS

When applicable, referred to as identification B.

In some cases, when 2 similar species are used to produce 2 different preparations and/or when there may be confusion between 2 fresh herbal drugs, identification by microscopic examination of the fresh herbal drug may be needed. This is done by examining a significant tissue or organ, for example, the lower epidermis of a leaf or the spores of a fungus.

The dominant or the most specific characters of the epidermis, including, if necessary, the *stomata and stomatal index* (*2.8.3*) are described based on an examination of a sample. The reagents used for the microscopic examination are specified. It may be necessary to perform the microscopic examination using more than 1 reagent in order to identify the specific characters. A specific stain may be prescribed for particular characters. Negative statements should be avoided since they usually refer to adulteration rather than to identification.

Example:

Examine under a microscope using a solution containing 1.5 g of *iodine R*, 5 g of *potassium iodide R* and 100 g of *chloral hydrate R* in 100 mL of *distilled water R*. The spores are bluish-black (starch reaction), short elliptical to subspherical, 8-11 µm long and 7-9 µm in diameter.

TESTS

TYPICAL TESTS

FOREIGN MATTER (*2.8.2*)

For fresh plants, the content of foreign matter is as low as possible. A maximum limit is given on a case by case basis, followed by “unless otherwise justified and authorised”. An acceptable maximum content of foreign matter is usually 5 per cent *m/m*. Whenever possible, an indication of the type of foreign matter is given in the specific monograph. Where necessary, the monograph indicates how the foreign matter is identified.

Example:

Foreign matter (*2.8.2*): maximum 5 per cent.

Foreign matter (*2.8.2*): maximum 4 per cent of fruits and maximum 1 per cent of other foreign matter.

TEST FOR ADULTERATION

In certain cases, botanical examinations (macroscopic and/or microscopic) and/or additional chemical reactions are carried out. In particular, this is done to detect

adulteration by herbal drugs with similar characteristics but which originate from different species.

The name of the unwanted species - there may be more than 1 plant species or other species of the genus - (the complete scientific name of the adulterant (genus, species, subspecies, variety, author) as usually obtained from *Kew Index (IPNI)* or their constituent(s) is used as the title of the test. The title is written in bold, the unwanted plant species are written in bold italics.

Example: *Agaricus phalloides for homoeopathic preparations (2290)*

LOSS ON DRYING (*2.2.32*)

Such a test is performed when fresh plants are processed more than 24 h after harvesting. The temperature and drying period should be specified in the monograph. A minimum limit should be specified on the basis of the results obtained on a reasonable number of varied samples of acceptable quality. The monograph indicates the amount necessary to perform the test and how finely divided the fresh herbal drug is.

Example:

Loss on drying (*2.2.32*): minimum 75.0 per cent, determined on 5.0 g of the finely cut drug by drying in an oven at 105 °C for 2 h.

OTHER TESTS

Specific tests may also be performed if necessary as prescribed in the general monograph *Herbal drugs for homoeopathic preparations (2045)*.

MOTHER TINCTURE

Mother tinctures must comply with the requirements of the general monograph on *Mother tinctures for homoeopathic preparations (2029).* The provisions of the general monograph are not repeated in individual monographs but any specific information required for application of the general monograph is included.

When a method used for the mother tincture is the same as the one used for the herbal drug and when the herbal drug and the mother tincture are part of the same monograph, the method is not repeated but simply referred to.

DEFINITION

Reference is made to the monograph on the herbal drug to be used as a homoeopathic raw material from which the mother tincture is prepared. The preparation method is specified in the Production section and is not described in the Definition.

Assay limits are included where appropriate, for example a lower limit may be specified, or, for mother tinctures that are toxic, upper and lower assay limits should be given. The limits depend on the preparation method defined in the monograph *Methods of preparation of homoeopathic stocks and potentisation (2371)* or in the Production section of the relevant monograph; where necessary, the preparation method is mentioned in parentheses, after the specified value.

Examples: *Hydrastis canadensis for homoeopathic preparations (2500),* on *Hyoscyamus for homoeopathic preparations (2091)* and on *Nux-vomica for homoeopathic preparations (2514)*

Other example:

Content: minimum 0.80 per cent of picrotoxinin ($C_{15}H_{16}O_6$; M_r 292.3) (dried drug).

PRODUCTION

This section mentions the preparation method(s) defined in the monograph *Methods of preparation of homoeopathic stocks and potentisation (2371)*. Other methods described in an official national pharmacopoeia of a Member State may be considered in drafting the monograph. Such methods are then described in detail in the individual monograph. Specific aspects of the production methods (such as the degree of size reduction of the drug, the extraction solvent and the duration of maceration etc.) are taken into consideration, if necessary, and described in the individual monograph.

Example:

The mother tincture is prepared from the cut drug (2800) according to the following methods prescribed in the monograph *Methods of preparation of homoeopathic stocks and potentisation (2371)*:

— method 1.1.3,

— method 1.1.10, using ethanol (45 per cent *V/V*) and maceration for 3-5 weeks.

CHARACTERS

Physical description of the mother tincture.

Taste is not mentioned and odour is only mentioned if it is very characteristic and can be described with reference to known odours.

Example:

CHARACTERS

Appearance: brown liquid.

IDENTIFICATION

If 2 methods of preparation produce different products, the identification tests to be carried out in each case are specified at the beginning of the section.

Example: *Agaricus phalloides for homoeopathic preparations (2290)*

THIN-LAYER CHROMATOGRAPHY (TLC)

Where applicable, refer to as method A.

Where it exists, the preferred method is that used for the herbal drug. In this case, the method is usually described entirely under the herbal drug with a cross reference under the mother tincture.

Example: *Nux-vomica for homoeopathic preparations (2514)*

Two types of presentation are possible.

TLC PRESCRIBED FOR THE IDENTIFICATION OF THE MOTHER TINCTURE

TLC is used under Identification, even if other chromatographic methods, such as GC and LC are subsequently used in the monograph. In this context the TLC is aimed at elucidating the chromatogram of the mother tincture with respect to selected reference compounds that are described for inclusion as reagents (e.g. *rutin R*). Wherever possible, existing reagents described in general chapter *4.1.1. Reagents* of the Ph. Eur. are used as

reference compounds. Where necessary, a description of a new reagent (name, molecular formula, relative molecular mass, CAS Registry Number, chemical nomenclature) is appended to the draft monograph for subsequent inclusion in general chapter *4.1.1.* Availability of reference compounds as commercial reagents must be verified during monograph elaboration. Where they are not readily available, a CRS or a HRS will have to be established and availability of a suitable quantity must be verified during monograph elaboration.

The commercial name of the TLC plate used during monograph development is included as a footnote to the monograph and after adoption by the Commission is transferred to the EDQM *Knowledge* database.

A minimum of 2 reference compounds must be used to validate the separation and spacing between the zones, otherwise a resolution test is necessary.

All the information concerning the preparation of the reference solution and the test solution and the chromatographic conditions is clearly stated. The methodology used, where possible, must be such that the application volume of the reference solution and the test solution is the same.

The general chapter on thin-layer chromatography covers both classical TLC and high performance TLC (HPTLC). Where these 2 methods give equivalent results with the development solvent and visualisation method prescribed both may be included in the working conditions [HPTLC conditions in brackets, after those of the classical TLC]. When the results of the TLC and those of the HPTLC are different, the choice between the 2 methods should be made during the elaboration of the monograph. Only the better of the 2 methods is described in the monograph.

Where appropriate, the width of the zones is indicated in the monograph. The chromatograms are described in the form of a table, which shows the upper, middle and lower third of the plate.

Only the characteristic zone(s) in the chromatogram obtained with the test solution are described in the table in relation to the position of the zones due to the reference compounds in the chromatogram obtained with the reference solution. The names of the constituents detected in the chromatogram obtained with the reference solution are always given. The names of the constituents detected in the chromatogram obtained with the test solution are given only if these constituents are present in the reference solution and if the nature of the substance is well established.

Chromatograms are never described in terms of R_F values.

It is usually necessary to indicate that faint zones other than those described are also present in the chromatogram of the test solution.

Zones may be detected by examination in daylight, ultraviolet light, with or without using a reagent.

A copy in colour of a suitable chromatogram has to be provided to the Secretariat.

Example: *Hydrastis canadensis for homoeopathic preparations (2500)*

TLC PRESCRIBED UNDER TESTS AND IDENTIFICATION

If a TLC test is used both for the control of adulterations and for identification, the method is described entirely under Tests with a cross-reference under Identification.

LIQUID OR GAS CHROMATOGRAPHY

Where liquid or gas chromatography is used in a test or assay, it may also be referred to under Identification.

Example: *Agaricus phalloides for homoeopathic preparations (2290)*

CHEMICAL REACTIONS FOR IDENTIFICATION

Chemical reactions are included only if TLC/HPTLC does not give sufficient identification and if the reaction is particularly characteristic of a constituent or a group of constituents. They must allow rapid identification without the use of complex equipment and not be so sensitive as to give a false positive result.

TESTS

Standard tests are covered by the general monograph *Mother tinctures for homoeopathic preparations (2029)*. Specific tests are described in the monograph on the mother tincture. The limits in specific monographs take the production method into account.

RELATIVE DENSITY

The relative density is measured according to method *2.2.5*. The method of preparation of the mother tincture is mentioned.

Example:

Relative density (*2.2.5*): 0.900 to 0.920 when method 1.1.3 is used.

ETHANOL

The ethanol content is measured according to method *2.9.10*. It is expressed as a range of + or - 5 per cent around the value for the content specified for the method of preparation.

Example:

Ethanol *(2.9.10)*: 40 per cent V/V to 50 per cent V/V when method 1.1.10 is used.

METHANOL

Where justified, the limit may be given in the specific monograph if this is different from that stated in the general monograph *Mother tinctures for homoeopathic preparations (2029)*.

Example:

Methanol (*2.9.11*): maximum 0.10 per cent *V/V*.

DRY RESIDUE

The dry residue is measured according to method *2.8.16* and is expressed as a minimum value. If 2 methods of preparation produce 2 mother tinctures with different dry residues, the 2 minimum values are indicated, each followed by the number for the method of preparation in parentheses.

Example:

Dry residue (*2.8.16*): minimum 1.4 per cent.

ASSAY

An assay is described where necessary. The same method as used for the herbal drug should be used, wherever possible.

STORAGE

Storage conditions described in the general monograph on *Mother tinctures for homoeopathic preparations (2029)* are applicable and, unless otherwise specified, state: "store protected from light".

A maximum storage temperature may be specified.

Specific conditions additional to these are given in the specific monograph.

LABELLING

Most of the statements required for labelling are covered by the general monograph *Mother tinctures for homoeopathic preparations (2029).*

REAGENTS

For the technical content and the style see both the Technical Guide and the Style Guide.

Commercial availability of constituents and markers that are described as reagents must be verified during elaboration of the monograph. Where a reagent may be difficult to obtain, the names and addresses of suppliers are included in footnotes and transferred to the EDQM *Knowledge* database after publication of the monograph.

The description of the reagents includes their name, molecular formula, relative molecular mass, CAS Registry Number and chemical nomenclature. The EDQM adds a unique identifier (7-digit number in italics) when the reagent is included in the reagents list.

CHEMICAL REFERENCE SUBSTANCES AND HERBAL REFERENCE STANDARDS

Reference standards, which may be qualitatively and quantitatively used, are established as CRS or HRS.

Establishment of CRS or HRS is co-ordinated by the EDQM laboratory (DLab); the Group of Experts should advise on a supplier of a batch of suitable quality. A representative of DLab is usually present at meetings of the group when draft monographs are discussed.

Guide

for the elaboration of monographs on

homoeopathic preparations

The EDQM is a directorate of the Council of Europe, an international organisation founded in 1949 that covers almost the entire continent of Europe. The Council of Europe aims to develop common democratic and legal principles based on the European Convention on Human Rights and other reference texts on the protection of individuals.

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