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Questions & Answers on the EU framework for (traditional) herbal medicinal products, including those from a 'non-European' tradition

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1. Regulation of herbal medicinal products in the EU (Q&A 1-7)

Question 1

Where can I find the pharmaceutical legislation and dossier requirements for herbal medicinal products in the European Union?

Answer 1

The pharmaceutical legislation in the European Union (EU) can be found on the website of the European Commission:

http://ec.europa.eu/health/human-use/index_en.htm

The body of EU legislation in the pharmaceutical sector is compiled in Volume 1 and Volume 5 of the publication "The rules governing medicinal products in the European Union". The basic legislation is supported by a series of guidelines that are also published in the other volumes (2-4, 6-10) of the rules governing medicinal products in the EU.

The 10 volumes constitute what is referred to as Eudralex.

http://ec.europa.eu/health/documents/eudralex/index_en.htm

Volume 2 of the above-mentioned publications is called the **Notice to Applicants (NtA)**. It has been prepared by the European Commission, in consultation with the competent authorities of the Member States and the European Medicines Agency (EMA) and contains a list of regulatory guidelines related to procedural and regulatory requirements. The NtA is not legally binding and does not necessarily represent the final views of the European Commission. In case of doubt, therefore, reference should be made to the appropriate EU Directives and Regulations.

http://ec.europa.eu/health/documents/eudralex/vol-1/index_en.htm

A detailed explanation of the marketing authorisation procedures is found in [Chapter 1 of volume 2A](#) with a description of the different procedures, including those for traditional herbal medicinal products.

With a submission of a marketing authorisation application, the applicant has to indicate in the Administrative Module 1 of the dossier under which application type the dossier is submitted.

See Q&A 5 for application types.

Chapter 1 provides information about the approaches followed by for Norway, Iceland and Liechtenstein vis-à-vis decisions on approval of medicinal products taken by the EU (together with the 28 EU Member States, Norway, Iceland and Liechtenstein form the European Economic Area).

Question 2

What are herbal medicinal products, herbal substances and herbal preparations?

Answer 2

Definitions are found in Article 1 of Directive 2001/83/EC:

- **Herbal medicinal products:** any medicinal product, exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations,
- **Herbal substances:** all mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried form but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author).
- **Herbal preparations:** preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

Question 3

What is meant by “non-western medicine system”, in the framework of this Questions & Answers document?

Answer 3

In its “Report on the experience acquired as a result of the application of the provisions of Chapter 2a of Directive 2001/83/EC, as amended by Directive 2004/24/EC, on specific provisions applicable to traditional herbal medicinal products” [COM \(2008\)-584](#), the European Commission mentions a number of non-European medicine systems in which herbal medicinal products are traditionally used: Ayurvedic medicine, traditional Chinese medicine (TCM) as well as Kampo, Korean, Mongolian, Thai, Tibetan, Unani and Vietnamese traditional medicines.

Ayurvedic medicine and traditional Chinese medicine are cited in the European Commission Report as examples of non-western traditional medicine systems. These medicine systems have existed for centuries in other parts of the world and have their own specific products, some of which could qualify as traditional herbal medicinal products in the EU.

EU legislation has established specific requirements for traditional herbal medicinal products, under the Directive 2001/83/EC for medicinal products for human use. This legislation, laying down the procedures for placing products on the market, is based on a product-specific approach and does not regulate the practice of traditional medicine.

Question 4

What are traditional herbal medicinal products?

Answer 4

Traditional herbal medicinal products are herbal medicinal products for human use that fulfil the conditions laid down in Article 16a(1) of Directive 2001/83/EC, which are:

1. They have indications exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment;
2. They are exclusively for administration in accordance with a specified strength and posology;
3. They are an oral, external and/or inhalation preparation;
4. The period of traditional use as laid down in Article 16c(1)(c) has elapsed. This means that the herbal medicinal product has been in medicinal use throughout a period of at least 30 years preceding the date of the application, including at least 15 years within the EU;
5. The data on the traditional use of the herbal medicinal product are sufficient; in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-standing use and experience.

Article 16a(2) adds that the presence in the herbal medicinal product of vitamins or minerals for the safety of which there is well-documented evidence shall not prevent the product for being eligible for registration based on traditional use, provided that the action of the vitamins or minerals is ancillary to that of the herbal active ingredients regarding the specified claimed indication(s).

Question 5

Which legal basis/types of application are possible for herbal medicinal products?

Answer 5

The different application types are described in the section 5 'Application types' of the [Chapter 1 of Volume 2A](#) in the NtA.

Guidance on legal basis for applications can be found on the EMA website:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000021.jsp&mid=WC0b01ac0580022711

Examples of legal basis relevant for herbal medicinal products are:

Article 8(3) – Full/Stand alone application: For full applications according to Article 8(3) of Directive 2001/83/EC, the results of pharmaceutical tests, non-clinical tests and clinical trials need to be submitted. This type of application (legal basis) has to be followed for example for a herbal medicinal product based on a new herbal substance/herbal preparation. The application may consist of a combination of reports of limited non-clinical and/or clinical studies carried out by the applicant and

of bibliographical references (So-called 'full-mixed' application - see also section on 'mixed' marketing authorisation application in [Part II.7 of Annex I to the Directive](#)).

Article 10a – Well-established use application: According to Article 10a of Directive 2001/83/EC, it is possible to replace the results of non-clinical and clinical trials by detailed references to published scientific literature (information available in the public domain) if it can be demonstrated that the active substances of a medicinal products have been in well-established medicinal use (WEU) within the EU, for at least **10 years**, with recognised efficacy and an acceptable level of safety.

Specific guidance on WEU can be found in [Part II.1 of the Annex 1 to Directive 2001/83/EC](#).

NB: These two types of applications require a "complete dossier" on the basis of which quality, safety and efficacy will be assessed. Such applications do not include the requirement to demonstrate at least 30 years of medicinal use including at least 15 years in the EU as a mean to substitute for clinical evidence from tests and trials in humans.

Article 16a – Traditional use registration for a herbal medicinal product:

In order to overcome difficulties that were encountered by the Member States in applying pharmaceutical legislation to traditional herbal medicinal products in a uniform manner, a simplified registration procedure was introduced in 2004.

The simplified procedure allows the registration of herbal medicinal products without requiring particulars and documents on tests and trials on safety and efficacy, provided that there is sufficient evidence of the medicinal use of the product throughout a period of at least 30 years, including at least 15 years in the EU. The efficacy of the herbal medicinal product is considered plausible on the basis of long-standing use and experience. Non-clinical tests are not necessary, where the herbal medicinal product on the basis of the information on the traditional use proves not to be harmful in specified conditions of use. However, even a long tradition (within or outside the EU) does not exclude the possibility that there may be concerns with regard to the product's safety, and therefore the competent authorities are entitled to ask for all data necessary for assessing the safety.

No derogation is made with regard to the necessary physico-chemical, biological and/or micro-biological tests requested in the quality part of the application dossier, because the quality aspect of the herbal medicinal product is independent of its traditional use. Products should comply with quality standards found in relevant European Pharmacopoeia monographs and/or those in the pharmacopoeia of a Member State. See also Q&A 18.

A number of scientific guidelines have been established on quality requirements. They can be found here:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000365.jsp&mid=WC0b01ac0580029569

Question 6

Is it possible to combine the requirements from different types of application in one application?

Answer 6

No, this is not possible. With a submission of an application dossier, the applicant has to indicate in the Administrative Module 1 of the dossier under which legal basis the dossier is submitted. The choice of the legal basis is made by the applicant but only one of the legal bases can be chosen.

In case a full dossier is assessed on the proof of quality, safety and efficacy, the traditional use is not the main proof for the scientific assessment, although the applicant may choose to include information on traditional use(s) as supportive data.

	Full application Art. 8(3)	Well-established use Art. 10a	Traditional use Art. 16(a)
Product complies with all quality requirements	YES	YES	YES
Safety	Non-clinical safety data	Bibliographic data on acceptable level of safety <u>in EU</u>	Bibliographic expert report; safety data
Efficacy	Clinical trials	Bibliographic data on recognised efficacy <u>in EU</u>	Efficacy (or pharmacological effects) must be plausible on basis of long-standing use and experience.
Period of use taken into account	Not applicable	At least 10 years of proven medicinal use <u>in EU</u>	Evidence of medicinal use for at least 30 years of which at least 15 years <u>in EU</u>
Traditional use taken into account	Not required but possibly, as supportive data	Not required but possibly, as supportive data	YES
Indications for this application type	No restriction	No restriction	Indications are restricted. See Q&A 8
Evaluation of submissions	EMA, or national authority	EMA, or national authority	National authority

Question 7

For which indications of herbal medicinal products is an evaluation under the centralised procedure mandatory?

Answer 7

The centralised procedure is mandatory for certain medicinal products, it is optional for others.

It is mandatory for medicinal products containing a new active substance (which was not authorised in the EU on the date of entry into force of Regulation (EC) No 726/2004 i.e. 20 November 2005) for the treatment of one of the following diseases:

- Acquired immune deficiency syndrome (AIDS, HIV infections)
- cancer
- neurodegenerative disorder (including dementia and Alzheimer's disease)
- diabetes
- auto-immune diseases and other immune dysfunctions
- viral diseases.

Herbal medicinal products containing a new active substance for these indications must be assessed according to the centralised procedure, based on a full application. These indications are excluded for any application as 'traditional herbal medicinal product' as per their definition: 'traditional herbal medicinal products' are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment.

Herbal medicinal products having received an orphan status in a given indication will be assessed via the centralised procedure.

Guidance on orphan medicinal products can be found on the EMA website at http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp&mid=WC0b01ac05800240ce

It is optional for other medicinal products containing new active substance and when, at its request, the applicant shows that it constitutes a significant therapeutic, scientific or technical innovation or that the granting of an authorisation at Union level is in the interest of patients.

Further guidance is available in the document 'Scientific Aspects and Working Definitions for the Mandatory Scope of the Centralised Procedure' (EMA/CHMP/121944/2007) and in the EMA pre-submission guidance which can be found at:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000021.jsp&mid=WC0b01ac0580022711

2. Specific provisions for traditional herbal medicinal products (Q&A 8-17)

Question 8

Which indications can be granted for traditional herbal medicinal products?

Answer 8

Guidance can be found in the section 3.4 'Procedure for traditional herbal medicinal products' in [Chapter 1 of the Volume 2A](#) in the NTA:

'Indications must be exclusively appropriate to traditional herbal medicinal products, which by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment. However, to prevent treatment of more serious pathologies with traditional herbal medicinal products, it is possible for the indications of traditional herbal medicinal products to refer to the use after exclusion of serious conditions by a medical doctor. In any case, the traditional herbal medicinal product still needs to be intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment. The traditional herbal medicinal product has to be a non-prescription medicinal product.'

The EMA has also published a [public statement](#) on this aspect in the context of the establishment of Community herbal monographs.

Further guidance on therapeutic indications can be found in the following HMPC guideline:

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003644.pdf

The HMPC has expressed the view that therapeutic indications that involve diseases, disorders or conditions such as cancer, psychiatric diseases, infectious diseases such as hepatitis or influenza, cardio-vascular diseases such as heart failure, metabolic diseases such as diabetes, are not acceptable for traditional herbal medicinal products. Indications relating to specific concepts of traditional medicines may be acceptable if they fulfil the criteria given for safe self-medication i.e. indications appropriate for traditional use. The nature and type of the tradition should be clearly expressed with the indication. A transposition of complex traditional terms into modern medicine's concepts & terminology should be avoided, unless it is guaranteed that both meanings are fully identical. Terms deriving from pharmacological actions should be avoided if the claim is based on a specific traditional concept that does not derive from a pharmacological model.

Question 9

What length of time of medicinal use has to be demonstrated for a traditional herbal medicinal product?

Answer 9

Applications for registration as a traditional herbal medicinal product should be accompanied by bibliographical or expert evidence to the effect that the herbal medicinal product in question, or a corresponding product, has been in medicinal use throughout a period of at least 30 years preceding the date of the application, including at least 15 years within the EU.

The HMPC has established guidance for interpreting what 'corresponding product' means:

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003644.pdf

'A corresponding product is defined as having:

- The same active ingredients, irrespective of the excipients used,
- The same or similar intended purpose,
- Equivalent strength and posology,
- And the same or similar route of administration.'

'As the legislation refers to the *same active ingredients*, the herbal substance/herbal preparation must be the same in terms of the declaration¹ of active substances. This will include the plant/part of the plant, the type of herbal preparation and, for extracts, the primary solvent. As the drug/extract ratio may be difficult to retrieve from the literature, comparison with a range of similar products on the market might be acceptable.'

If no comparable product is currently marketed, reference to scientific reference handbooks, official compendia for prescriptions or official pharmacopoeias of the Member States can be considered.

'Evidence of the traditional use of the single active substances of a fixed combination will not be sufficient to establish a traditional use of a combination product.

The requirement is also satisfied if the number or the quantity of ingredients has been reduced during the time period. It should be considered, however, whether such a reduction or elimination may have resulted in an increased dose of the remaining constituents thus making a more extensive assessment of safety necessary. The elimination of a number of active constituents or a significant reduction in posology may make it difficult to accept the plausibility of an indication'.

See also Q&A 10 and Q&A 11.

Question 10

What happens in cases of doubt regarding the adequacy of evidence of the long-standing use for a traditional herbal medicinal product?

Answer 10

When a Member State has doubts on the adequacy of evidence of the long-standing use for a traditional herbal medicinal product, it can refer the matter to the HMPC in accordance with Article 16c(1)c of Directive 2001/83/EC.

Guidance on this referral procedure is provided in [Chapter 3 of the Volume 2A](#) in the NtA:

'This referral may be started at the request of the Member State where an application for traditional use registration for a traditional herbal medicinal product has been submitted.

The HMPC is asked to draw up an opinion on the adequacy of the evidence of the long-standing use of the product, or of the corresponding product, where it has been in medicinal use throughout a period of at least 30 years preceding the date of the application, including at least 15 years in the EU.

¹ Please refer to the HMPC 'Guideline on declaration of HS/HP in HMP/THMP in the SmPC'

Namely, it assesses whether the data on long-standing use and experience of the traditional herbal medicinal product are sufficient to demonstrate plausible efficacy and pharmacological effects.'

Question 11

What happens when a traditional herbal medicinal product is eligible for simplified registration but has been in medicinal use for less than 15 years in the EU?

Answer 11

When a Member State has determined that a herbal medicinal product is eligible for traditional use registration, but with less than 15 years of medicinal use in the EU, it can refer the matter to the HMPC in accordance with Article 16c(4) of Directive 2001/83/EC.

Guidance on this referral procedure is provided in [Chapter 3 of the Volume 2A](#) in the NtA:

The HMPC is asked to draw up an opinion on whether the herbal medicinal product is eligible for traditional use registration, although it has been used in the EU for less than 15 years.

In addition to issuing this opinion, the HMPC evaluates the possibility of establishing a Community herbal monograph for that herbal substance(s), herbal preparation(s) and/or combinations thereof. When the monograph is established, it should be taken into account by the Member State when taking its final decision to register the product.

Question 12

Which active ingredients can be part of a traditional herbal medicinal product?

Answer 12

Directive 2001/83/EC requires herbal medicinal products to contain exclusively as active ingredients one or more herbal substances or herbal preparations or combinations thereof. Substances of synthetic origin, constituents of animal origin and chemical substances cannot be active ingredients for (traditional) herbal medicinal products.

The HMPC has established guidance on interpretation of the definition of herbal substance and herbal preparation, especially how it relates to some purified compounds of herbal origin.

Such guidance is found in a '[Reflection paper on level of purification](#) of extracts to be considered as herbal preparations' (EMA/HMPC/186645/2008) and in the following questions & answers document:

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/03/WC500104038.pdf

Traditional herbal medicinal products can contain vitamins and minerals if they have an ancillary action. The ancillary action should be justified in the registration dossier. They should fulfil the requirements of the 'Guideline on [summary of requirements for active substances](#) in the quality part of the dossier' (CHMP/QWP/297/97 as revised).

Question 13

What is the value of data on single active ingredients in the assessment of combination products?

Answer 13

The HMPC published a specific guideline on the [quality of combination](#) herbal medicinal products/traditional herbal medicinal products.

The HMPC also published a guideline on the [clinical assessment of fixed combinations](#) of herbal substances/herbal preparations.

The framework for authorisation or registration in the EU is based on one finished medicinal product. It may be a combination of one (or more HS) and one (or more) HP, however evidence must relate to the combination as such.

In order to support an application for a combination, data on the combination are expected. However, it may be possible to include information on the individual substances (literature or actual data), in order to justify the absence of certain specific data on the combination.

For vitamins and minerals, see Q&A 4 and Q&A 12.

Question 14

Does EU legislation have specific requirements for traditional herbal medicinal products, based on non-western medicine systems?

Answer 14

The EU legislation, which establishes the possible reference to 'evidence of 30 years medicinal use' to show that efficacy is plausible, does not introduce a distinction for those products whose traditional use has essentially taken place [outside the EU](#).

The following conditions must be fulfilled for such products to be registered:

- they must comply with the definition of 'traditional herbal medicinal product' (see Q&A 4)
- the medicinal product, or a corresponding product, has been in medicinal use throughout a period of at least 30 years preceding the date of the application
- there must have been at least 15 years of medicinal use in the EU (see Q&A 11).

All requirements apply in the same manner to all 'traditional herbal medicinal products'.

Directive 2001/83/EC introduces some specific requirements to the [labelling](#) of traditional herbal medicinal products, as specified in Article 16g(2). In addition to the requirements of Articles 54 to 65 of Directive 2001/83/EC, any labelling and user package leaflet must contain a statement to the effect that the product is a traditional herbal medicinal product for use in the specified indication(s) exclusively based upon long-standing use. An optional element of the labelling relates to the nature of the tradition: the Directive 2001/83/EC allows a Member State to require that the product's labelling and its user package leaflet state the nature of the tradition in question, for example a reference to the relevant non-western medicine system. This depends on a national decision by the national competent authority in that Member State.

Question 15

What are the requirements to demonstrate the quality of a traditional herbal medicinal product?

Answer 15

As indicated in the Q&A 5, the quality of a herbal medicinal product is independent of its traditional use. All general quality requirements for herbal medicinal products apply to traditional herbal medicinal products.

Part III of [Annex I to Directive 2001/83/EC](#) lays down specific requirements related to the nature of identified, distinctive types of medicinal products. The section 4 of that Part III gives the specific requirements for herbal medicinal products. These requirements also apply to traditional herbal medicinal products.

Scientific guidelines on quality have been established by the HMPC for herbal medicinal products and traditional herbal medicinal products. They can be found on the website of the EMA at:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000365.jsp&mid=WC0b01ac0580029569

They include a guideline on Good Agricultural and Collection Practices requirements, addressing the collection, cultivation and harvesting of plant material. Preparation of herbal material must also follow [Good Manufacturing Practice](#); in particular [Annex 7](#) provides specific guidance for herbal medicinal products.

The scientific guidelines should be taken into account when preparing applications. Deviations from guidelines must be justified by applicants in their applications.

See also Q&A 12.

Question 16

What are the requirements to demonstrate the safety of a traditional herbal medicinal product?

Answer 16

Applicants must substantiate the safety of the medicinal product by the means of a bibliographic review of safety data together with an expert report, complemented by any necessary data, which the Member State's competent authority may request. The duration of the documented use in humans will be an important element of the evaluation.

The HMPC has established guidance in this field: the guideline on the [non-clinical documentation](#) for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in application for simplified registration (as a traditional herbal medicinal product) (EMEA/HMPC/32116/2005).

It reports that herbal medicinal products are widely used within and outside the EU. This wide use has generated significant amount of bibliographical information relating to non-clinical safety. However, published non-clinical tests for traditional herbal preparations are often incomplete or not in

accordance with today's state of the art. Published toxicological information, well-presented clinical experience (with regard to the length of time and extent of use in humans), epidemiological studies and data as well as post-marketing experience gained by wide spread use in humans may contribute to the avoidance of unnecessary tests in animals (Directive 2001/83/EC, Annex I, Part II (1)b).

General scientific guidelines on non-clinical testing can be found at:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000402.jsp&mid=WC0b01ac0580029571

The specific character of bibliographic data on herbal preparations used over a very long period of time, sometimes over centuries, may require pre-submission discussion/scientific advice between applicants and national competent authorities on how to prepare such applications.

Question 17

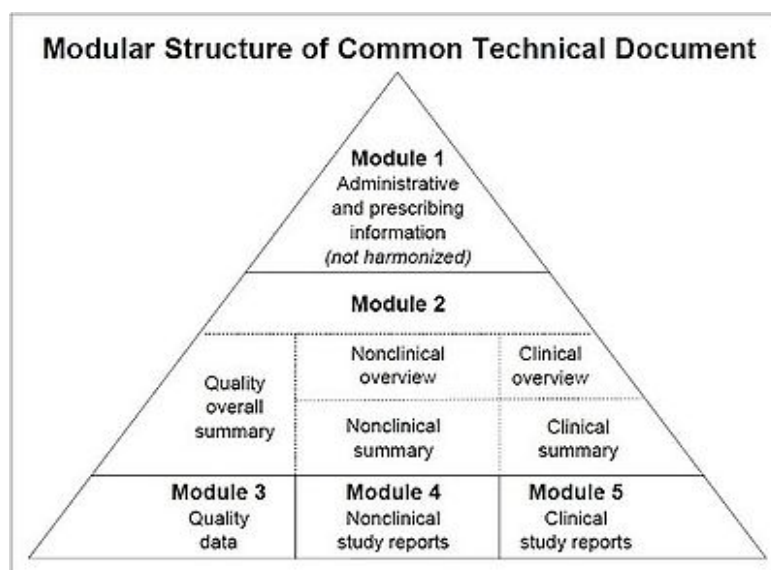
How to present an application for a herbal medicinal product/traditional herbal medicinal product?

Answer 17

Applications have to be submitted in the format referred to in [volume 2B](#) in the NtA.

Application dossiers for medicinal products for human use should follow the structure of the Common Technical Document (CTD), divided into five modules:

1. Administrative and prescribing information
2. Overview and summary of modules 3 to 5
3. Quality (pharmaceutical documentation)
4. Non-clinical (Pharmacology/Toxicology)
5. Clinical – efficacy and safety (Clinical Trials)



For simplified registration of traditional herbal medicinal products, the HMPC has established specific guidance, including a table of concordance: the guideline on the [use of the CTD format in the preparation of a registration application](#) for traditional herbal medicinal products (EMA/HMPC/71049/2007).

Guidance on Module 2.3 and Module 3 as described in the guideline is also relevant for applications for marketing authorisations for herbal medicinal products.

3. Type and role of monographs in the European framework (Q&A 18-21)

Question 18

What monographs exist in the EU regulatory framework that need to be taken into consideration for (traditional) herbal medicinal products?

Answer 18

Under the EU regulatory framework, there are two distinctive types of monographs that need to be taken into consideration for (traditional) herbal medicinal products:

- pharmacopoeial monographs established at European or national level
- Community herbal monographs established at the EMA.

Pharmacopoeial monographs at European level

The European Pharmacopoeia (Ph. Eur.) is a single reference work for the quality control of medicines in the signatory states of the Convention on the Elaboration of a European Pharmacopoeia. It is a collection of standardised specifications on the quality of pharmaceutical preparations, their constituents or their containers. These specifications are laid down in either general Ph. Eur. monographs or specific monographs. The official standards published by the Ph. Eur. provide a legal and scientific basis for quality control during the development, production and marketing processes.

They concern the qualitative and quantitative composition and the tests to be carried out on (herbal) medicines, on the raw materials used in production of (herbal) medicines and on the intermediates of synthesis. All producers of (herbal) medicines and/or (herbal) substances for pharmaceutical use must therefore apply these quality standards in order to market their products in the signatory states of the Convention.

The work on the Ph. Eur. is carried out at the European Directorate for the Quality of Medicines & HealthCare (EDQM), in Strasbourg, France. <http://www.edqm.eu>

At the EDQM, three working groups are dedicated to the development of monographs for herbal substances; one of them exclusively prepares monographs for herbs used in Traditional Chinese Medicine.

Pharmacopoeial monographs at national level

Likewise, some Member States have a national pharmacopoeia officially in use.

Community herbal monographs

Community herbal monographs established by the HMPC have the objective of facilitating the marketing of HMP and THMP. Indeed, when monographs have been established, they shall be taken into account by the Member State when examining an application. Accordingly, even though the Member States are not obliged to follow the monograph, any decisions not to accept the content of the monograph as adopted by the HMPC should be duly justified taking into account the important role of monographs to bring harmonisation to this field.

Other monographs

Worldwide, several international or national bodies have also established monographs on the medicinal uses of plants and herbal preparations, for example monographs in the Pharmacopoeia of the People's Republic of China (PPRC), monographs in the Ayurvedic Pharmacopoeia of India, WHO herbal monographs or monographs established by the International Standardization Organization (ISO) regarding traditional herbal medicines. They can be part of the documentation used to demonstrate the medicinal use outside the EU within the dossier to support an application for traditional use registration.

Guidance is found in the Annex I to Directive 2001/83/EC, clarifying how to use these other monographs when they provide specifications² on HS/HP in the absence of a monograph in the Ph. Eur. or in the pharmacopoeia of a Member State. See also Q&A 15.

Question 19

How does the Ph. Eur. monographs relate to the Community herbal monographs?

Answer 19

The Community herbal monographs describe the medicinal uses (and all related conditions for a safe use) of herbal substances/preparations. Ph. Eur. monographs provide the quality specifications for these herbal substances and herbal preparations.

Therefore both types of monographs are complementary.

In summary:

- the specifications for quality are found in Ph. Eur. monographs (or national Pharmacopoeia monographs)
- the HMPC conclusions on efficacy and safety are found in the Community herbal monographs.

Question 20

What information is found in Community herbal monographs?

Answer 20

A **Community herbal monograph** comprises the scientific opinion of the HMPC on safety and efficacy data concerning a herbal substance and preparations thereof intended for medicinal use. The HMPC evaluates scientifically all available information including non-clinical and clinical data but also documented long-standing use and experience in the EU and, if available, outside the EU. Community herbal monographs are divided into two columns:

- the left column describes the conclusions on the herbal preparations that fulfil the well-established use requirements (marketing authorisation)
- the right column describes the conclusions on the herbal preparations that fulfil the traditional use requirements (simplified registration). See Q&A 5 and Q&A 6.

Each **herbal preparation** is assessed individually as available information may vary from one preparation to another. As a result some preparations will appear in the well-established use section of

² For definitions, please refer to the HMPC 'Guideline on test procedures and acceptance criteria for HS, HP and HMP/THMP'

the monograph and others will be in the traditional use section. Some preparations might not be included if data are insufficient. A monograph reflects the view of the HMPC on all information necessary for the use of a medicinal product containing the herbal substance/preparation(s) described in the monograph:

- What the herbal product is used for,
- Who the herbal product is intended for (e.g. adults only or children as well, in pregnant and lactating women, etc.),
- Safety information such as details of undesirable effects and interaction with other medicines.

The monographs are published with other documents including an assessment report containing reviews of all available data relevant for the medicinal use of the herbal substance/preparations.

When the HMPC prepares a draft Community herbal monograph, it is released for public consultation on the EMA website for a period of three months. Comments received are subsequently evaluated and discussed and the final version of the monograph is published on the Agency website.

Question 21

How can the work on a monograph be initiated, and how can I find information on which monographs are established or are under development?

Answer 21

The work on Community herbal monographs by the HMPC at the EMA is supported by the 'HMPC secretariat' in London. The progress of the work on monographs is publicly accessible via two documents on the EMA website.

In the *Overview of assessment work – Priority List (EMA/HMPC/278067/2006)*, the status of each monograph is maintained during the process of evaluation. This [Priority List](#) is regularly updated and can be found on the EMA website.

The *Inventory of herbal substances for assessment (EMA/HMPC/494079/2007)* gives a full overview of all herbal substances, including those which are proposed for a Community herbal monograph by an interested party. This [Inventory](#) is regularly updated and can be found on the EMA website.

The procedure which is applicable for the submission of new proposals is described in detail in the 'Procedure on management of [proposals submitted by interested parties](#) for Community list entries³ or Community herbal monographs' (EMA/HMPC/328575/2007). This document also presents links to guidance how to submit scientific data in support of the assessment work on herbal monographs at the EMA.

³ Please refer to the information available on the EMA website under:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000213.jsp&mid=WC0b01ac0580033a9b

4. Advice, procedures and relevant institutions (Q&A 22-24)

Question 22

Where can I get scientific support and advice for (traditional) herbal medicinal products?

Answer 22

Before considering seeking advice from the HMPC, companies are reminded of the following other options to obtain guidance on herbal medicinal products:

- Scientific and regulatory advice can be obtained from the national competent authorities in the Member States of the EU,
- Scientific advice can be obtained from the Scientific Advice Working Party (SAWP) established by the CHMP. In particular, the SAWP can be contacted for advice on herbal medicinal products other than traditional herbal medicinal products. The SAWP will liaise with the HMPC where appropriate.

Scientific support and advice specifically for traditional herbal medicinal products can be requested from the HMPC. There is a fee for single areas e.g. questions concerning quality *or* safety *or* long-standing use and experience, and a fee for questions on multiple areas i.e. a combination of single issues. The fee must be paid to the EMA in accordance with the 'Rules for the implementation of Council Regulation (EC) No 297/95 on fee payable to the European Medicines Agency and other measures' (EMA/MB/112878/2013):

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000327.jsp&mid=WC0b01ac0580024596

The scientific support and advice given by the HMPC is not legally binding to national competent authorities with regard to any future simplified traditional use registration application. However these authorities should take into consideration any HMPC advice as a result of a request for scientific support and advice.

Requests for scientific support and advice have to be submitted to the secretariat of the HMPC (email: hmpc.secretariat@ema.europa.eu). The procedure for submitting such requests is described in detail in the [guidance for companies seeking scientific support and advice](#) on traditional herbal medicinal products.

Question 23

Are the Mutual Recognition Procedure (MRP) and the Decentralised Procedure (DCP) possible for traditional herbal medicinal products?

Answer 23

Yes, both are possible. According to Article 16d of Directive 2001/83/EC, Mutual Recognition Procedure (MRP) and Decentralised Procedure (DCP) applies by analogy to THMP registrations:

- provided that a respective Community herbal monograph exists,

- provided that the THMP submitted for registration consists of herbal substances, herbal preparations or combinations thereof contained in the Community List⁴.

If the registration of a THMP as described above is intended in a single Member State the respective national procedure is applicable. According to Article 16d of Directive 2001/83/EC, if the registration of a THMP as described above is intended in more than one Member State, DCP is recommended. If a THMP as described above is already registered in a Member State and the applicant intends registration in further Member States, MRP applies by analogy. The applicant however, should be aware of any divergent positions on the Community herbal monograph.

The CMDh has established a [Q&A document on traditional herbal medicinal products](#).

The MRP/DCP is also possible for registration of THMPs on a voluntary basis even if neither a Community list entry nor an Community herbal monograph exists provided that adequate and sufficient documentation for traditional use and safety is enclosed in the dossier submitted. However, it should be clarified that the use of MRP/DCP is the decision of the Member State. Discussion with Member States intended to be included in any procedure, is recommended before submission of an application. This also applies to traditional herbal medicinal products, based on non-western traditions.

⁴ Please refer to the information available on the EMA website under:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000213.jsp&mid=WC0b01ac0580033a9b

Question 24

Where are decisions taken and advice given in the European regulatory framework?

Answer 24

Final decision regarding:	Authority:	Location:
Marketing authorisation for a product falling under the scope of the centralised procedure	European Commission	Brussels, Belgium
Marketing authorisation for a herbal medicinal product authorised nationally	Competent Authority of a Member State	Competent Authority of the Member State
Registration for a traditional herbal medicinal product	Competent Authority of a Member State	Competent Authority of the Member State
Scientific or regulatory advice for herbal medicinal products	Scientific Advice Working Party of CHMP or Competent Authority of a Member State	European Medicines Agency, London or Competent Authority of the Member State
Scientific support and advice for traditional herbal medicinal products	Competent Authority of a Member State or Committee on Herbal Medicinal Products (HMPC)	Competent Authority of the Member State European Medicines Agency, London
Community herbal monograph	Committee on Herbal Medicinal Products (HMPC)	European Medicines Agency, London
Community list entry (see footnote 3 on page 17)	European Commission	Brussels, Belgium
Referral procedure on “adequacy of evidence of long-standing use” according to Article 16c(1)c)	Initiated by Member State leading to an opinion of the HMPC	Competent Authority of the Member State (taking into account the HMPC opinion adopted at EMA in London)
Referral procedure on “period of traditional use less than 15 years in EU” according to Article 16c(4)	Initiated by Member State leading to an opinion of the HMPC	Competent Authority of the Member State (taking into account the HMPC opinion adopted at EMA in London)
Monographs on herbal substances in the European Pharmacopoeia	European Pharmacopoeia Commission	European Directorate for the Quality of Medicines and HealthCare, Strasbourg