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Committee on Herbal Medicinal Products (HMPC)

Procedure for the preparation of European Union herbal monographs and European Union list entries and appointment of HMPC rapporteurs and peer-reviewers

Draft

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Executive summary

The purpose of this procedure is to enable a consistent and streamlined process in preparation of all European Union (EU) herbal monographs and European Union (EU) list entries by the Committee on Herbal Medicinal Products (HMPC). This document describes how EU herbal monographs and EU herbal list entries are developed, the roles and responsibilities of those involved in the process and the anticipated timelines.

Through this document the three procedural documents EMEA/HMPC/182320/2005, EMA/HMPC/182352/2005 and EMA/HMPC/57137/2007 and the Standard operating procedure on the establishment of European Union herbal monographs and European Union list entries and related documents (SOP/H/3163) have been merged into one document and the process adapted to the current working methodology for the establishment of EU herbal monographs and EU herbal list entries. In particular, the HMPC Working Party on European Union Monographs and European Union List (MLWP) is no longer a Working Party to the HMPC.

In addition, the 'Procedure for the Appointment by the HMPC of a rapporteur responsible for a scientific evaluation or the establishment of a Community herbal monograph and/or Community list entry', EMEA/HMPC/108877/2005 Rev. 1 and 'Timelines for the establishment of a European Union herbal monograph and/or a European Union list entry' (EMA/HMPC/126542/2005) have been incorporated into this new document. The different roles and responsibilities of the rapporteurs, assessors and peer-reviewers for the preparation of EU herbal monographs and EU herbal list entries have been updated and further details included in this new document. This is also applicable to appointment of HMPC rapporteurs of other guidance documents.

Once finalised, adopted and coming into effect, this procedure replaces/supersedes the following procedural documents:

- EMEA/HMPC/182320/2005
- EMA/HMPC/182352/2005
- EMA/HMPC/57137/2007
- EMEA/HMPC/108877/2005 Rev. 1
- EMA/HMPC/126542/2005
- SOP/H/3163

The templates for the assessment report, monograph and list entry are annexed to this new document and provide detailed information on the compilation of the scientific data/literature and the scientific evaluation leading to the content of the EU herbal monographs and/or EU herbal list entries. These main templates, as well as related supportive templates such as for Overview of comments or List of references, can be updated as necessary without changing the entire procedure that is considered to refer always to the latest template version.

1. Introduction

1.1. Background, scope and objectives

The main tasks of the HMPC is to prepare a draft list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products (hereafter also referred to as 'European Union list' or 'list entry') and to establish European Union herbal monographs (hereafter also referred to as 'monographs') for traditional herbal medicinal products and for well-established herbal medicinal products (Article 16f(1)and Article 16h(3) of the Directive 2001/83/EC (1)).

EU herbal monographs can serve as a basis for the applications of traditional use registration (Article 16a(1) of Directive 2001/83/EC) or well-established use marketing authorisation (Article 10a of Directive 2001/83/EC). If an application for traditional use registration relates to a herbal substance, preparation or a combination thereof contained in the European Union list, the data specified in Article 16c(1)(b)(c) and (d) do not need to be provided (i.e. details of authorisation or registration or refusal to grant authorisation or registration, evidence of long-standing use and bibliographic review of safety data).

According to Article 16c(4) of Directive 2001/83/EC, as amended, the HMPC shall, on the request of a Member State, establish a European Union herbal monograph for a traditional herbal medicinal product that has been used within the European Union for less than 15 years, if the Committee considers it possible.

The structure of monographs has been designed following the Summary of Product Characteristics (SmPC) structure, as established by Article 8(3)j of Directive 2001/83/EC. The SmPC of a medicinal product sets out the agreed position on the medicinal product as distilled during the course of the assessment process. The HMPC, when establishing a specific monograph for herbal substances and preparations with well-established medicinal use (WEU) or traditional use (TU) or drafting a list entry, has to review and assess the available information and documentation of several herbal medicinal products, which contain the related herbal substance/herbal preparation, even though a monograph or a list entry do not correspond to a specific SmPC.

The main principles for the appointment of rapporteurs, peer-reviewers and assessment teams described in detail in sections 3.2 and 3.3 are also applicable to other HMPC scientific guidance documents/evaluations as appropriate.

This procedure does not describe the steps for the proposal and prioritisation of herbal substances for monograph and list entry establishment (HMPC work programme). Detailed steps for the proposal and identification of priority herbal substances/preparations/combinations to be covered by a monograph /list entry are described in the 'Procedure on management of proposals submitted by Interested Parties for European Union List Entries or European Union herbal monographs' (EMEA/HMPC/328575/2007).

1.2. Responsibilities

This procedure applies to all HMPC rapporteurs/assessors/peer-reviewers for the preparation of monographs for herbal medicinal products with well-established medicinal use or traditional use and/or a list entry. Rapporteurs/assessors/peer-reviewers must ensure the adherence to this procedure and use related templates in the preparation of a monograph for herbal medicinal products with well-established medicinal use or traditional use and/or a list entry.

In general, the rapporteur is responsible for the scientific and the editorial quality of the documents and the peer-reviewer should be the gatekeeper of the scientific and the editorial quality of the documents.

If the rapporteur for various reasons is not able to continue the work, the rapporteur should inform the HMPC secretariat and as necessary, a new rapporteur will be appointed.

It is the responsibility of the HMPC secretariat and the Chairperson of the HMPC to verify that this procedure is adhered to and related templates are used.

1.3. Main principle

The following steps are the main principles of the process in preparation of all monographs and list entries (the details of the procedure are described in the sections below and illustrated in Figure 1).

Step I) HMPC recommends the start of assessment and appoints rapporteur and peer-reviewer

The HMPC decides annually on the prioritisation of new monographs when drafting the work plan for the following year. After adoption of the work plan, the rapporteur and peer-reviewer are appointed by HMPC. In addition, a call for scientific data will be initiated by the HMPC secretariat and a request for a new market overview will be initiated by the rapporteur.

Step II) Assessment of data and drafting of documents for public consultation

The rapporteur together with assessor(s) form the assessment team and assess the available data (including data submitted by interested parties during the call for data) and draft the monograph, assessment report and list of references.

The rapporteur should liaise with the peer-reviewer before discussion(s) and possible adoption for public consultation by the HMPC.

If the data available are insufficient or one or several legal requirements for establishing a monograph are not met , HMPC could decide to cancel the work or a public statement will be drafted and published for public consultation.

Step III) Discussion on comments from interested parties and adoption of finalised documents

If applicable, comments received from interested parties and other stakeholders during the public consultation are discussed and taken into account for the finalisation of the monograph, assessment report and list of references. The comments received on the monograph are presented and evaluated in an overview of comments.

The HMPC voting and publication practice of finalised documents is summarised in Table 1.

When appropriate, a list entry will be developed in parallel, and the Comitology procedure will be followed at the European Commission level after transmission by the EMA.

The EMA secretariat prepares (quality and editorial/linguistic check) the finalised documents for publication on the EMA webpage.

Table 1. HMPC voting and publication practice of finalised documents.

Final documents to be adopted for publication
Monograph (Draft List entry);
Opinion (including voting result and divergent opinions);
Supporting documents (assessment report and list of references) and, if applicable, overview of comments.

2. Step I: HMPC recommends the start of assessment and appoints rapporteur and peer-reviewer

2.1. Principles for recommendation to start the assessment

New proposals for monographs are submitted by interested parties, national competent authorities or HMPC members. The proposals are validated and then discussed, evaluated, and decided upon by the HMPC. The HMPC decides annually on the prioritisation of new monographs when drafting the work plan for the following year. Thereby, the procedure for the preparation of monographs and list entries starts with the adoption of the HMPC annual work plan.

For new substance proposals interested parties, national competent authorities or HMPC members have to provide some minimum information as regards data availability and market presence/ medicinal use. This information is verified by the secretariat at the time of validation of the proposal, to allow informed decisions by the committee when adding substances to the work plan and starting the procedure.

Once selected monographs have been included in the work plan and tracked in the Overview of assessment work - Priority list (EMA/HMPC/561868/2021), the HMPC appoints the rapporteur and peer-reviewer.

In addition, a call for scientific data ('Procedure for calls for scientific data for use in HMPC assessment works' EMA/HMPC/1004/2006) will be initiated by the HMPC secretariate and a request for a new market overview ('Template for information exchange for the preparation of the assessment report supporting the establishment of European Union monographs and European Union list entries EMA/HMPC/137093/2006) will be initiated by the rapporteur.

2.2. Principles for the appointment of rapporteur and peer-reviewer

The appointments of rapporteurs and peer-reviewers are made by the HMPC. All HMPC members (including co-opted members) and alternates can act as rapporteur or peer-reviewer. The appointment is made on the basis of objective criteria, which will allow the use of the best available expertise in the EU on the relevant scientific area. The members and alternates' expertise and past experience in the assessment of relevant herbal substance classes are taken into account. Whenever possible, the appointment may also take into consideration other factors such as the wide distribution of rapporteur- and peer-review-ships between HMPC members in line with the 'HMPC Rules of procedure' (EMA/HMPC/139800/2004) fostering active contribution of Committee members.

Members and alternates are invited to express their preferences regarding certain rapporteur or peer-review-ships orally during the HMPC meeting at which rapporteurs and peer-reviewers are appointed, or in writing in advance of the meeting.

If for some reason the rapporteur will not be able to finalise the work in accordance with the general timelines (see section 6), the rapporteur should inform the HMPC. The issue will be discussed at the

following HMPC plenary meeting and it will be decided if a new rapporteur should be appointed. If a new rapporteur should be appointed, the peer-reviewer could be the preferred first option depending on the stage of the ongoing process.

2.3. Principles for including assessor(s) in the assessment team

The rapporteur chooses the assessor(s) who will form the assessment team. The rapporteur is encouraged to involve additional assessor(s) with expertise in areas outside the expertise of the rapporteur and peer-reviewer. However, the assessment team should preferably not include more than 2-3 assessors.

The rules concerning the involvement of external experts in the process (i.e., experts that are not members or alternates of HMPC) can be found in the 'HMPC Rules of procedure' (EMA/HMPC/139800/2004). Importantly, all assessors need to be in the EMA expert database.

3. Step II: Assessment of data and drafting of documents for public consultation

3.1. Compilation of data

The rapporteur is responsible for the compilation of relevant data. Further information on search methodology is included in the assessment report template. Basically, it includes the search in scientific databases using meaningful search strategies and the check of scientific literature for relevant information.

In case that interested parties or other stakeholders have submitted references during the call for scientific data, these data should also be taken into account. However, the rapporteur should check the possibility to use unpublished data. The unpublished data submitted by interested parties or other stakeholders should comply with the requirements stipulated in the 'Procedure for calls for scientific data for use in HMPC assessment works' (EMA/HMPC/1004/2006 Rev.6).

3.2. Assessment of data and drafting of documents

The rapporteur together with the assessment team assess the available data and draft the monograph, assessment report, list of references, and if applicable a list entry, using the latest version of the templates for the documents. The rapporteur is responsible for using the correct version of relevant guidance documents and templates. The scientific guidelines of importance e.g. quality guidelines, non-clinical guidelines, clinical guidelines and guidance on the safety of herbal substance/products can be found on the EMA webpage. Further guidance on assessment and relevant data/information are available in the templates for assessment report and monograph.

When drafting the documents, the rapporteur should consider the harmonisation with other monographs in the same therapeutic area in regards the wording of the various sections or of previous HMPC decisions (e.g. new or revised thresholds for constituents of concern e.g. thujone, pulegone).

If the available data are insufficient or one or several legal requirements for establishing a monograph are not met, a public statement will be drafted. The reasons not being able to establish a monograph as listed in the public statement should be substantiated and transparent by publishing the supporting assessment report and list of references. If the rapporteur discovers in the early stage of the process

that there are insufficient data available or other issues that preclude the establishment of a monograph, the HMPC may decide that the work should be cancelled. The reasons to cancel an assessment should be made transparent in the public meeting report. These steps are further described in the 'Procedure on the publication of HMPC public statements when Community herbal monographs on herbal substances, preparations and/or combinations thereof are not established' (EMA/HMPC/84530/2010).

3.3. Discussion(s) on draft documents

The rapporteur is responsible for the communication with the peer-reviewer before submitting documents to HMPC for discussion. Preferably, the issues for discussion during HMPC plenary should be presented by the rapporteur in a Reader's Guidance. The peer-reviewer should contribute to the scientific discussion(s) on the draft documents.

For issues which are not within the expertise of the rapporteur or the assessment team, the rapporteur is advised to consult additional expertise, for example a HMPC member/alternate with that particular expertise. If needed, HMPC may also consult another EMA Scientific Committee, working party or other expertise within the EU Regulatory Network. Draft documents should be discussed 1-3 HMPC meetings before included in the HMPC agenda for possible adoption for public consultation.

3.4. Quality assurance of documents and adoption for public consultation

A thorough peer-review by the peer-reviewer should be performed before possible adoption for public consultation by the HMPC. The rapporteur and peer-reviewer should agree upon a reasonable timetable for the peer-review process. Importantly, the rapporteur is responsible for the communication with the peer-reviewer. The peer-reviewer should check the quality of the documents, from a scientific and editorial point of view.

After the HMPC adoption for public consultation, the documents are published on the EMA webpage and interested parties and other stakeholders are invited to submit comments on the draft monograph.

While the HMPC secretariat performs a complete check of draft monographs before public consultation, supporting draft assessment report including draft list of references undergo only a rough editorial check to not hamper the process at this stage. A disclaimer is added to the documents as provided by the rapporteur that clarifies the nature and intermediate state of these supporting draft documents and refers to the completion for finalisation.

4. Step III: Discussion on comments from interested parties and adoption of finalised documents

4.1. Comments received and finalisation of documents

The HMPC secretariat receives comments from the interested parties and other stakeholders during public consultation and forwards them to the rapporteur and peer-reviewer. The rapporteur, together with the assessment team, should discuss the comments received during the public consultation and take them into account for the finalisation of the draft monograph/list entry, assessment report and list of references. The comments received on the monograph are presented and evaluated using the 'Template for overview of comments received on a draft European Union herbal monograph or

European Union list entry' (https://www.ema.europa.eu/documents/template-form/template-overview-comments-received-draft-european-union-herbal-monograph-european-union-list-entry_en.doc).

The set of full text references used in the assessment as reflected in the final List of references should be provided by the Rapporteur the latest at the time of final adoption and made transparent in the meeting documents. These references are considered an essential part of a final monograph/ list entry package for adoption and have to be archived at EMA to be available for any request or future rapporteurs, peer-reviewers, reviews and revisions.

All documents should be rediscussed 1-2 HMPC meetings before included in the HMPC agenda for possible final adoption. The rapporteur is responsible for the communication with the peer-reviewer before submitting documents to HMPC for discussion. Preferably, the issues for discussion during HMPC plenary should be presented by the rapporteur in a Reader's Guidance. The peer-reviewer should contribute to the scientific discussion(s) on the draft documents.

For issues not within the expertise of the rapporteur or the assessment team, the rapporteur is advised to consult additional expertise, for example a HMPC member/alternate with that particular expertise. If needed, HMPC may also consult another EMA Scientific Committee, working party or other expertise within the EU Regulatory Network.

The peer-reviewer should check the quality of the documents, from a scientific and editorial point of view. The rapporteur and peer-reviewer should agree upon on a reasonable timetable for the peer-review process. Importantly, the rapporteur is responsible for the communication with the peer-reviewer.

4.2. Adoption of documents and HMPC opinion

The HMPC voting and publication practice of finalised documents is summarised in Table 1. Further information on HMPC voting and adoption of documents is available in the 'HMPC Rules of Procedures' (EMA/HMPC/139800/2004). Briefly, whenever possible, scientific opinions or recommendations of the Committee shall be taken by consensus. If such a consensus cannot be reached, the scientific opinion or recommendation will be adopted if supported by an absolute majority of the members of the Committee. The divergent positions and the names of the members expressing the divergent positions in the scientific evaluation are included in the HMPC opinion, and mentioned in the minutes of the respective Committee meeting. Members having divergent positions shall clearly state the reasons on which they are based and provide the draft already to the secretariat latest one week before final adoption for transparency before voting on the complete package. Final divergent opinions are to be submitted by the close of the meeting. They will be appended to the opinion. The reasons for the divergent opinions shall be publicly available together with the document made publicly available.

After HMPC final adoption, the HMPC secretariat prepares (including quality and editorial/linguistic check) the documents for publication on the EMA webpage. If after the regulatory and scientific consistency check issues are detected that require clarification, rapporteur and peer reviewer will be contacted by the secretariat. Only in case of major issues or necessary changes to the monograph or draft list entry, the Chairperson will be informed to decide on post-adoption corrections or re-adoptions at the next committee meeting.

If a draft list entry is proposed, the EMA secretariat prepares the translations in cooperation with the 'Centre de traduction des organes de l'Union européenne' in Luxemburg (CdT) and national competent authorities, and the complete draft list entry package is submitted to the European Commission. The

Comitology procedure will be followed at the European Commission level. Once adopted, the HMPC is informed and a link to the extended EU list on the Commission website is provided under the corresponding substance page on the EMA website.

If the data available are insufficient or one or several legal requirements for establishing a monograph are not met, a public statement will be published in accordance with 'Procedure on the publication of HMPC public statements when Community herbal monographs on herbal substances, preparations and/or combinations thereof are not established' (EMA/HMPC/84530/2010).

5. Timelines

The estimated timelines for the procedure for the preparation of monographs and list entries are illustrated in Figure 1.

1. Call for scientific data

When a herbal substance has been included in the HMPC work plan after decision by HMPC, the HMPC secretariat issues a call for scientific data with 3 months deadline.

2. Discussion at HMPC and peer-review before public consultation

Once peer-reviewed and agreed by the majority of HMPC members (preferably 1-3 HMPC meetings), the draft monograph/list entry and the draft supporting documents are included in the HMPC agenda for adoption for public consultation. The time between the end of the call for scientific data until public consultation should preferably not exceed 12 months.

3. Adoption by HMPC for public consultation

The draft monograph/list entry and the draft supporting documents are adopted for public consultation during the HMPC meeting.

4. Public consultation

The draft monograph/list entry and draft supporting documents are published for 3 months public consultation.

5. Discussion at HMPC and peer-review after public consultation

After public consultation, the received comments will be summarised in the Overview of comments by the rapporteur and discussed at HMPC (preferably 1-2 meetings). After peer-review, the draft monograph/draft list entry and draft supporting documents are included in the HMPC agenda for final adoption.

6. Final adoption by HMPC

The monograph/draft list entry and draft supporting documents are adopted by the HMPC during the following HMPC meeting.

7. Publication of finalised documents

After HMPC final adoption, the HMPC secretariat prepares the documents for publication on the EMA webpage. For draft European Union list entries, the Comitology procedure will be followed at the European Commission level.

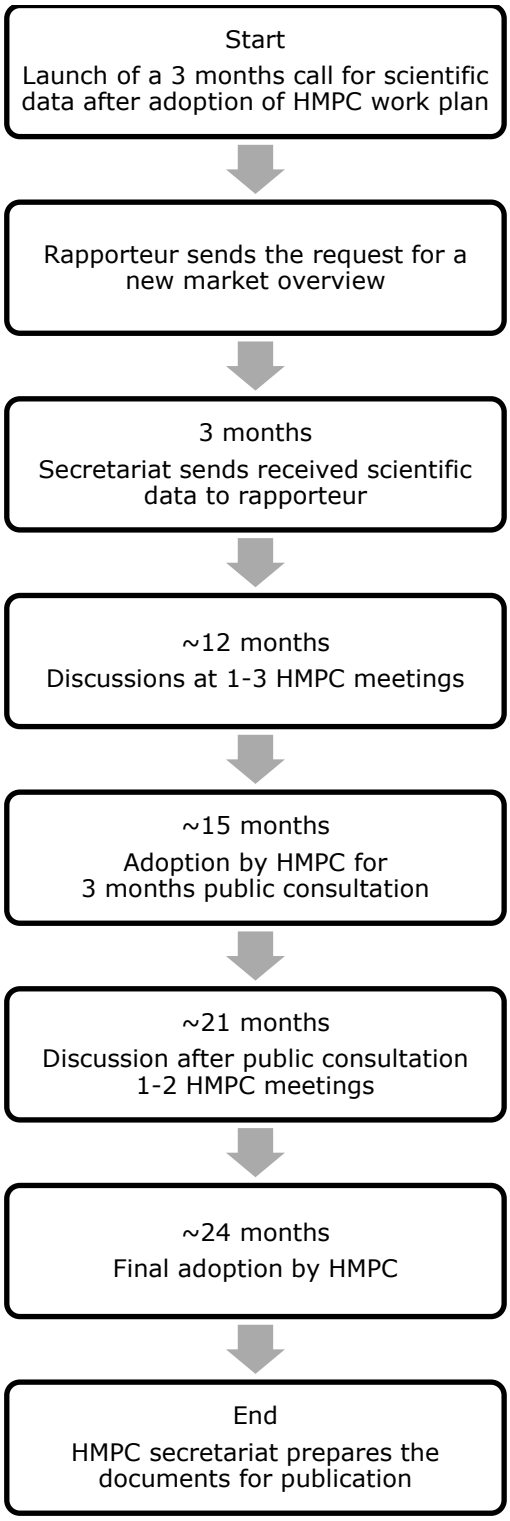

Figure 1. Main steps of the procedure and anticipated timelines for the preparation of European Union herbal monographs and European Union list entries.

6. References

Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 relating to medicinal product for human use

Procedure on management of proposals submitted by Interested Parties for European Union List Entries or European Union herbal monographs' (EMEA/HMPC/328575/2007)

Overview of status of HMPC assessment work – Priority list (EMA/HMPC/561868/2021)

Procedure for calls for scientific data for use in HMPC assessment works (EMA/HMPC/1004/2006)

Template for information exchange for the preparation of the assessment report supporting the establishment of European Union monographs and European Union list entries (EMA/HMPC/137093/2006)

HMPC Rules of Procedures (EMA/HMPC/139800/2004)

Procedure on the publication of HMPC public statements when Community herbal monographs on herbal substances, preparations and/or combinations thereof are not established (EMA/HMPC/84530/2010)

Template for overview of comments received on a draft European Union herbal monograph or European Union list entry (https://www.ema.europa.eu/documents/template-form/template-overview-comments-received-draft-european-union-herbal-monograph-european-union-list-entry_en.doc)

Annex 1 –Assessment report template

Annex 2 – Monograph template

Annex 3 – List entry template