EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

28 January 2015
EMA/HMPC/124695/2011 Rev. 1
Committee on Herbal Medicinal Products (HMPC)

Procedure for the systematic review of European Union herbal monographs and/or European Union list entries and supporting documents

Final

Draft agreed by Organisational Matters Drafting Group (ORGAM DG)	October 2010 February, April, June 2011
Draft agreed by Working Party on European Union Monographs and European Union List (MLWP)	May 2011
Adoption by HMPC for release for consultation	12 July 2011
End of consultation (deadline for comments)	15 November 2011
Agreed by ORGAM DG	December 2011
Adoption by HMPC	24 January 2012
Draft revision 1 agreed by ORGAM Drafting Group	December 2014
Adoption revision 1 by HMPC	28 January 2015

Keywords	HMPC; European Union herbal monographs; systematic review; revision

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1. Introduction (background and scope)

1.1. Systematic review

The systematic review (assessment of the need for revision) by the Committee on Herbal Medicinal Products (HMPC) of its European Union herbal monographs is laid down in section 3.2 of the 'Reflection paper on the reasons and timelines for revision of final European Union herbal monographs and European Union list entries' (EMA/HMPC/326440/2007 current Rev.4). The need for a revision will be considered every 5 years in order to ensure that European Union herbal monographs remain up-to-date (scientific state of the art).

This procedure addresses the scope, timelines and documenting aspects of the review and possible subsequent revision. The purpose of this document is to enable a consistent process for all monographs adopted by the HMPC.

When a list entry exists, revision of an EU herbal monograph can have consequences for relevant changes in the existing list entry as well. The need for revision of the list entry following the revision of an EU monograph should be carefully assessed, on a case by case basis, taking into account the nature of the changes and the presence of any safety concern. Minor changes in wording (e.g. wording of existing therapeutic indications, contraindications, interactions, undesirable effects) without safety implications should not trigger a revision of the European Union list entry.

When appropriate, the revision of European Union list entries will take place in parallel to or shortly after the revision of related monographs. When a European Union list entry is revised according to Article 16f(3) of Directive 2001/83/EC as amended, the Comitology procedure will be followed at the European Commission level after transmission by the EMA.

1.2. Legal basis

As outlined in the above-mentioned 'Reflection paper on the reasons and timelines for revision of final European Union herbal monographs and European Union list entries'.

1.3. Responsibilities

The Rapporteur is responsible for undertaking a systematic review of a monograph/list entry but this may not always lead to a revision of the scientific and regulatory content of the monograph/list entry and/or supporting documents. The Rapporteur is supported by HMPC and MLWP in prioritization of the selection of monograph/list entries to be revised, with the help of the HMPC secretariat.

2. Scope of the revision

2.1. Scientific revision

To determine whether a revision of the scientific content of the monograph/list entry is required, the Rapporteur shall examine:

- scientific literature published since the finalisation of the monograph and supporting documents
- scientific decisions taken by the HMPC when adopting other monographs/list entries or other types of scientific recommendations since the finalisation of the monograph/list entry. For example, the

HMPC may have adopted guidelines and public statements that should be taken into account, e.g. the 'Public statement on the use of herbal medicinal products containing thujone' (EMA/HMPC/732886/2010).

The new literature search should be carried out in accordance with recommendations laid down in section 1.3 of the 'Template for HMPC AR for the development of European Union herbal monographs and European Union list entries' (EMA/HMPC/418902/2005 current Rev.5).

2.2. Regulatory revision

2.2.1. Adjustment to situation in the Member States

The review of a monograph/list entry is an opportunity to improve the relevance of the monograph/list entry to industry and National Competent Authorities. The Rapporteur shall consider the overview of traditional herbal medicinal products registered in all Member States, which is to be published on the EMA website and updated every 6 months. The Rapporteur will consider the need to obtain from HMPC members a full market overview covering registered and authorised herbal medicinal products marketed in the Member States, having regard to the cut-off date of the latest published overview. The Rapporteur may consider relevant information related to the products whose marketing is not based on marketing authorisation or traditional use registration in the Member States. Information from use in countries outside the European Union will also be considered.
When regulatory activities in the Member States justify it, the monograph/list entry shall be revised to adjust it to the real market situation.

2.2.2. Additional preparations eligible for TU registration

By the end of the deadline for systematic review, 5 years since the initial adoption/last revision will have passed. This 5-year period of time may allow the herbal substance and/or some herbal preparations thereof that did not meet the requirement for at least 30 years documented medicinal use or the requirement for 15 years of use in the European Union to now be eligible for inclusion in the monograph/list entry.
The Rapporteur shall reconsider the eligibility of the herbal substance and/or any herbal preparation thereof which were previously rejected on those grounds and the monograph/list entry shall be revised accordingly.

2.3. Editorial revision

The Rapporteur should pay attention to the existing list entry and the nature of editorial changes intended. Editorial revision of a list entry is only to be started when safety concerns are involved. Minor changes in wording of a list entry regarding consistency or compliance with EMA templates should not trigger a Comitology process at the European Commission.

2.3.1. Consistency

When reviewing a monograph/list entry, the Rapporteur shall consider its degree of harmonisation with other monographs/list entries in the same therapeutic area as regards the wording of the various sections. The evolution of the wording chosen by the HMPC results from the adoption of these monographs/ list entries at different points in time. Inconsistencies might be identified especially in monographs/list entries adopted in the early years of establishment of the committee. Inconsistencies

in wording that can be further harmonised across related monographs/list entries shall be distinguished from true differences justified by the data that were assessed. Where relevant, the monograph/list entry shall be revised.

Revision of a list entry for reason of consistency with other monographs/list entries is only to be started when safety concerns are involved.

2.3.2. Compliance with EMA templates

The documents should be checked against the latest templates. Even if the package is scientifically up-to-date, the Rapporteur needs to make sure that documents comply with the latest templates, in liaison with the HMPC secretariat. Beyond the EMA identity features (logo, font, etc.) and the inclusion of the herbal substance common name in all EU official languages, attention should be paid to new elements of the templates that may trigger revision, such as new headers (e.g. monograph's section 4.6 on Fertility, pregnancy and lactation) and new sections (e.g. benefit/risk statements in the AR's overall conclusions). Where required, the monograph/list entry and supporting documents will be revised.

3. Timelines

The following timelines are agreed for the various steps towards the systematic review and subsequent revision when required. All times are given in months relative to the 5-year anniversary of the monograph's/list entry´s adoption, expressed as day zero (D 0).

D -12 months The HMPC secretariat will systematically issue a call for scientific data, using the template 'Call for scientific data for the systematic review of the monograph on'. To avoid receiving data and comments similar to those submitted on the draft monograph, a recommendation to consult the overview of comments received on the draft monograph and the list of references is included in the call.
The Rapporteur shall consider latest information on the TU registrations granted in the Member States and to ask for an up-to-date market overview from HMPC members.

D -9 months Deadline for interested parties to submit data to the HMPC secretariat for transmission to the Rapporteur. At this point the Rapporteur is expected to go through the received material as well as perform a new literature search.

D -8 months The Rapporteur informs the MLWP whether he recommends a revision of the content of the monograph and, where appropriate, additionally of the list entry and/or the supporting documents beyond the adaptation to the EMA identity features. He shall present the intended scope of the revision. The agenda for the forthcoming MLWP meetings will include the monograph/draft list entry and supporting documents for discussion. Otherwise, the package of documents adapted to the latest templates is scheduled for adoption by the MLWP and subsequently by the HMPC.
Taking into account the volume of scientific literature to be assessed and the workload of the MLWP/HMPC, a timetable beyond the 5-year anniversary of adoption can be agreed. This timetable shall include a 3-month public consultation by interested parties if deemed necessary according to the nature/extent of the changes.

D -6 months The revised monograph/draft list entry (± revised supporting documents) is(are) discussed by the MLWP.

D -4 months The revised monograph/draft list entry (± revised supporting documents) is(are) adopted by the MLWP.

D 0 At this point the revised documents should have been adopted by the HMPC and published.
Additional steps for revision of European Union list entries:
The revised draft list entry is translated in all EU official languages (HMPC). Subsequently, the revised draft European Union list entry together with the HMPC opinion on the draft revised list entry, the AR and list of references are transmitted to the European Commission followed by the publication of the link to the European Commission page where to access the Commission Decision on the EMA website.

4. Documenting the review/revision

The extent of the revision undertaken shall be transparent in every document.

Assessment report and list of references

The AR will systematically be updated to reflect that the need for revision was assessed and readopted.

As a minimum, the section 1.3 *Search and assessment methodology* shall be updated to reflect the new literature search carried out.

When one or several section(s) of a monograph are modified, the relevant parts of the AR shall contain the new data and accompanying explanation/justification for the changes introduced in the monograph and, where appropriate, additionally of the list entry.

When the AR is modified extensively throughout all sections, the Rapporteur will consider inserting a summary of the major modifications under a section "1.4 Major changes introduced in the <*first*><*number as appropriate*> revision".

Monograph

The monograph will systematically be readopted, showing the date of the review under section 7 *Date of compilation/last revision* and on the covering page.

When one or several section(s) of a monograph are modified, this shall be clearly indicated on the covering page; the justification(s) shall be found in the AR.

List entry

When a European Union list entry is revised according to Article 16f(3) of Directive 2001/83/EC as amended, the Comitology procedure will be followed at the European Commission level after transmission by the EMA.

HMPC Opinion

A new HMPC opinion will systematically be adopted.

Overview of comments

Upon publication for 3-month public consultation of a revised monograph and, where appropriate, additionally of the list entry, comments from interested parties shall be collected and assessed. An overview of comments received during the public consultation shall be prepared accordingly.

5. References

1. Reflection paper on the reasons and timelines for revision of final European Union herbal monographs and European Union list entries (EMA/HMPC/326440/2007 current Rev.4)
2. Procedure for calls for scientific data for use in HMPC assessment works (EMA/HMPC/1004/2006 current Rev.4 *Corr.* [1])
3. Template for assessment report for the development of European Union herbal monographs and European Union list entries (EMA/HMPC/418902/2005 current Rev.5)
4. Timelines for the establishment of a European Union herbal monograph and/or a European Union list entry (EMA/HMPC/126542/2005 Rev.2 *Corr.*[1])