EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products

Concept paper on the revision of the "Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in applications for simplified registration"

Agreed by Monograph and List Working Party (MLWP)	June 2016
Adopted by Committee on Herbal Medicinal Products for release for consultation	July 2016
Start of public consultation	2 September 2016
End of consultation (deadline for comments)	30 November 2016

Comments should be provided using this template. The completed comments form should be sent to hmpc.secretariat@ema.europa.eu

Keywords	Herbal medicinal product, non-clinical documentation, traditional use registration, marketing authorisation, genotoxicity, European Union herbal monographs, European Union list entries

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

1. Introduction

In 2006, the “Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in applications for simplified registration” was published. The purpose of the guideline was to harmonize the minimum requirements for non-clinical data for well-established herbal medicinal products in bibliographical applications for marketing authorisations and to provide guidance which non-clinical safety aspects should be addressed in the expert report for the simplified registration of traditional herbal medicinal products and which additional non-clinical safety tests might be necessary to prove safety. The guideline has now been available for approximately 10 years and a considerable practical experience has been gathered during the use of this Guideline in national and European applications and for the preparation of more than 150 monographs.

2. Problem statement

The content of the guideline is still valid, but an update of the document to current standards is required taking into account advances over the last 10 years as well as established practice and legal interpretations. Details in the assessment methodology of genotoxicity have so far been reflected in two separate Guidelines (“Guideline on the assessment of genotoxicity of herbal substances/preparations” (EMEA/HMPC/107079/2007) and “Guideline on selection of test materials for genotoxicity testing for Traditional Herbal Medicinal Products/Herbal Medicinal Products” (EMEA/HMPC/67644/2009)).

3. Discussion (on the problem statement)

Besides a general update of the document and a revision of the text to adequately describe the current practice, there are three major points for consideration:

- Reference to the two above mentioned guidelines (EMEA/HMPC/107079/2007 and EMEA/HMPC/67644/2009) should be added to the Guideline.
- Since these two Guidelines are mainly focussing on the stepwise procedure and the selection of test material, several other specific aspects concerning the testing of multicomponent mixtures in relation to the test design and the evaluation should be included in the Guideline.
- With the new “Guideline ICH S2 (R1) on genotoxicity testing and data interpretation for pharmaceuticals intended for human use” (CHMP/ICH/126642/2008) the concept of genotoxicity testing was extended to an approach which includes two *in vivo* tests. Furthermore a “Guideline on the limits of genotoxic impurities” (CPMP/SWP/5199/02, EMEA/CHMP/QWP/251344/2006) was adopted. A reflection on them should be included in the Guideline.

4. Recommendation

HMPC recommends revising the “Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in applications for simplified registration” as indicated above.

5. Proposed timetable

It is anticipated that a draft of the revised guideline would be available six months after adoption of the concept paper. The draft will be released for public consultation for three months. The revised guideline should be finalised six months after public consultation.

6. Resource requirements for preparation

Two rapporteurs will be involved in drafting the revision. The draft is expected to be discussed at three to four meetings of the MLWP and at one to three meetings of the HMPC.

7. Impact assessment (anticipated)

The guideline is primarily intended for use by NCAs, applicants and interested parties, but it also has a direct impact on the work of the HMPC and MLWP. The marketing authorisations/registrations granted and the monographs prepared according to the guideline will have an impact on public health as it will influence the approval and availability of (T)HMPs in the EU.

8. Interested parties

Before finalisation, the guideline will be made available for comments by interested parties during a period of public consultation. Comments, both on the concept paper but also the draft revised guideline will be taken into account.

9. References

Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in applications for simplified registration EMEA/HMPC/32116/2005

Guideline on the assessment of genotoxicity of herbal substances/preparations EMEA/HMPC/107079/2007

Guideline on selection of test materials for genotoxicity testing for Traditional Herbal Medicinal Products/Herbal Medicinal Products EMEA/HMPC/67644/2009

ICH guideline S2 (R1) on genotoxicity testing and data interpretation for pharmaceuticals intended for human use CHMP/ICH/126642/2008

Guideline on the limits of genotoxic impurities CPMP/SWP/5199/02, EMEA/CHMP/QWP/251344/2006

Questions and answers on the 'Guideline on the limits of genotoxic impurities' EMA/CHMP/SWP/431994/2007 Rev. 3