European Medicines Agency

London, 15 July 2008
Doc. Ref. EMEA/HMPC/315413/2008

COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

DRAFT

CONCEPT PAPER ON SELECTION OF TEST MATERIALS FOR GENOTOXICITY TESTING FOR TRADITIONAL HERBAL MEDICINAL PRODUCTS/ HERBAL MEDICINAL PRODUCTS[1]

AN ANNEX TO
Guideline on the Assessment of Genotoxicity of Herbal substances/preparations (EMEA/HMPC/107079/2007)

AGREED BY HMPC QUALITY DRAFTING GROUP	June 2008
ADOPTION BY HMPC FOR RELEASE FOR CONSULTATION	3 July 2008
END OF CONSULTATION (DEADLINE FOR COMMENTS)	15 October 2008

Comments should be provided to hmpc.secretariat@emea.europa.eu
Fax +44 20 7418 7051

KEYWORDS	herbal medicinal products; traditional herbal medicinal products; herbal substances; herbal preparations; extracts; HMPC; genotoxicity testing

[1] The proposed guideline will be an Annex to the 'Guideline on the assessment of genotoxicity of herbal substances/preparation **(**EMEA/HMPC/107079/2007)

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20)
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

1. INTRODUCTION

The 'Community list of herbal substances , preparations and combinations thereof for use in traditional herbal medicinal products' (Community list) is established by the Committee on herbal medicinal products (HMPC), in accordance with Directive 2001/83/EC, as amended. The Community list is being developed gradually through entries of structured information relating to individual herbal substances or preparations.

Inclusion in the Community list of a herbal substance/preparation represents a significant advantage to applicants seeking registrations for traditional herbal medicinal products. This is because once a herbal substance/preparation is included in the Community list an applicant will not be required to provide evidence of the safe and traditional use of a medicinal product for which he seeks a traditional use registration if he demonstrates that the proposed product and related claims in the application comply with the information contained in the Community list.

2. PROBLEM STATEMENT

Once a herbal substance/preparation is included in the Community list competent authorities will not have the legal basis to require additional data to assess the safety and the traditional use of the product. In view of this, the HMPC has concluded that where data on genotoxicity are inadequate or absent it will not be possible to include the herbal substance/herbal preparation in the Community list.

As a result progress with the development of Community list is being hampered by the absence of genotoxicity data. Experience to date confirms that many well known traditional herbal substances/preparations, already widely available within the Community, will be excluded from the Community list solely as a consequence of absence of genotoxicity data and thus any potential benefits of the Community list to applicants will be lost.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

In view of the difficulties encountered, the HMPC has encouraged interested parties, industry and potential applicants to address the deficiencies in genotoxicity data to enable the Community list to be populated.

To assist applicants the HMPC has developed the 'Guideline on the assessment of genotoxicity of herbal substances/preparation' (EMEA/HMPC/107079/2007) which describes a general framework and practical approaches on how to assess or to test the potential genotoxicity of herbal substances/preparations and how to interpret the results. The stepwise approach described in this guideline sets out a pragmatic approach to address both scientific aspects of genotoxicity testing and the special needs of herbal medicinal products within the current regulatory framework applicable to these products.

In principle, genotoxicity testing should be carried out by individual applicants on their specific materials and it is recognised that this represents a major task and considerable duplication of effort particularly for applicants seeking registrations for traditional herbal medicinal products. Industry has therefore been encouraged to consider undertaking collaborative research on genotoxicity and such a study is understood to be under discussion within some Member States.

The HMPC is of the view that consideration should also be given to the development of guidance on what types of extracts should be subjected to testing for genotoxicity bearing in mind that different extracts may have different toxicological profiles. The HMPC considers that the concept of adopting a 'bracketing/matrixing' approach to the test materials should be explored with the aim of testing a representative range of extracts rather than requiring individual manufacturers to undertake their own testing on specific extracts. It may be possible to agree on a standard range of extraction solvents, of varying polarities, as the test materials for the genotoxicity testing. Using the 'bracketing' concept, only samples on the extremes of certain design factors, in this case, solvent polarity, would be tested. However, it is considered that testing of an extract of intermediate polarity may also be appropriate.

'Bracketing and matrixing' principles should be discussed with a view to achieving consensus on a standard range of test materials which could be considered to be representative of the herbal substances/preparations intended for the Community list.

A similar approach could be applied to herbal ingredients of herbal products which fall within the well-established use category of herbal medicinal products.

4. RECOMMENDATION

Further guidance should be developed on a standard range of test materials for genotoxicity testing which could be considered to be representative of the herbal substances/preparations intended for the Community list.

This additional guidance would form an Annex to the recently adopted 'Guideline on the assessment of genotoxicity of herbal substances/preparation' (EMEA/HMPC/107079/2007).

The guidance would be of significant benefit to industry groups considering collaborative work on genotoxicity testing as currently encouraged by HMPC. Furthermore, it is envisaged that a similar approach could be applied to herbal ingredients of herbal products which fall within the well-established use category of herbal medicinal products.

5. PROPOSED TIMETABLE

It is anticipated that a draft guideline could be available 6 months after the adoption of the concept paper. The draft will then be released for external consultation for 6 months. The guideline could be finalised within 6 months after external consultation.

6. RESOURCE REQUIREMENTS FOR PREPARATION

The Rapporteur will prepare a draft guideline. Member States are invited to provide comments via their Committee and/or working party members.

7. IMPACT ASSESSMENT (ANTICIPATED)

Industry attributes great importance to the development of the Community list which offers significant advantages to applicants. Further guidance on materials for genotoxicity testing will assist in collaborative studies to ensure the development of the Community list. A similar approach could also be applied to herbal ingredients of herbal products which fall within the well-established use category of herbal medicinal products and thus the guidance would also be of value to applicants for products in this category as well.

8. INTERESTED PARTIES

Comments from interested parties could be integrated during the development of the guideline, should they wish to submit comments at this stage.

9. REFERENCES TO LITERATURE, GUIDELINES ETC

'Guideline on the assessment of genotoxicity of herbal substances/preparation' (EMEA/HMPC/107079/2007)