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COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

GUIDANCE ON DOCUMENTATION TO BE PROVIDED BY MEMBER STATES AND APPLICANTS/MAHs IN SUPPORT OF A SIMPLIFIED REGISTRATION REFERRAL UNDER ARTICLES 16c(1)c AND 16c(4)

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TABLE OF CONTENTS

INTRODUCTION:

Community pharmaceutical legislation has created a binding Community arbitration mechanism for traditional herbal medicinal products, which may be invoked on the basis of the following articles:

This proposal concerns:

1. Article 16c(1) c of Directive 2001/83/EC as amended ("Traditional use >15 years referral")
2. Article 16c(4) of Directive 2001/83/EC as amended ("Traditional use <15 years referral")

This document intends to address the following aspects related to the start of a referral procedure:

- Validation of referral notification
- Documentation to be submitted to HMPC by referring member state
- Identification of MAHs/Applicants (if applicable)
- Who to rely on for contact details of MAHs/Applicants (if applicable)
- Initial timetable
- Documentation to be submitted by applicants/MAHs to HMPC List of Questions (LoQ)/List of Outstanding Issues (LOI)

I – VALIDATION OF REFERRAL NOTIFICATION

Draft Referral notification form

The notification forms for triggering a referral are annexed to the HMPC ORGAM proposal for inclusion of "Simplified registration referrals for traditional herbal medicinal products" into Chapter 3 of NtA – Community Referral.

- When referral is triggered by a Member State

1. In advance of triggering a referral, a draft letter of referral should be sent to the EMEA at least two weeks in advance of a HMPC meeting.

   The draft letter of referral should include precise questions referred to the HMPC for consideration together with a summary of background information and, if applicable a draft List of Questions (LoQ) to be addressed by the applicant (prepared by the MS triggering the referral to start the discussion during HMPC where a final LoQ (if applicable) will be adopted) and a table of the traditional herbal medicinal product(s) and/or corresponding products, when applicable, in the referring MS.

2. Once the EMEA receives the draft letter of referral the HMPC Secretariat (incl RA/Legal) should discuss any issues related to the draft referral letter or possible problems with the procedure, in particular the legal basis of the referral and, if needed, the timeframe of the national procedure in which the referral was triggered. The HMPC Chair could be consulted, if required.
   The EMEA checking time is 3 days.

3. The check performed by the HMPC Secretariat should take into consideration the following aspects:

   - Legal basis
   - Concerned products (invented name/herbal substance/herbal preparation or combination thereof); medicinal product authorised/pending in the referring MS (or held by the MAH/Applicant).
   - Content of the letter (scope/grounds)

Scope is clearly defined: adequacy of evidence on long-standing use of the product in the proposed indication(s), or a corresponding product (clear and concise identification of the question(s) referred to the HMPC).

Official notification of a referral to HMPC - Final referral letter

- Once the check of the draft referral notification has been completed, HMPC Secretariat sends comments to the Member State who triggered the referral.

- A final, signed dated letter of referral should be sent to the EMEA within 2 days after the receipt of comments.

- In case the EMEA receives straight away a signed referral letter, the HMPC Secretariat should send, if necessary, the EMEA comments within 3 days and request the MS to send a revised signed letter clearly stating that the latest one supersedes the previous letter and that the previous one is void.

- Once the final letter is received, HMPC Secretariat checks if the EMEA comments have been implemented and if the letter is dated and signed. In case comments have not been implemented the HMPC Secretariat has to liase with EMEA Legal and RA sectors.

  Once the procedure is started the HMPC Secretariat sends the referral notification together with the LoQ (if applicable) to the MAH (see also section III).

Documentation to be submitted to the HMPC by the referring MS before the start of the referral:

- Complete dossier as submitted by the applicant, preferably in electronic format, including responses to LoQ raised by the referring Member State during the evaluation of the application
- Updated assessment report in English (after assessment of the responses to the LoQ) compiled by the referring Member State which focus primarily on the main scope of the referral
- Description of the remaining issues and clear and concise identification of the question(s) referred to the HMPC
- Draft LoQ to be addressed by the applicant/MAH, if applicable
- Latest version of the proposed Product Information (English version with track changes), if applicable

II – IDENTIFICATION OF APPLICANTS/MAHs AND PRODUCTS CONCERNED

The major issues, which needed to be addressed here, are:
- Identification of Contact points in the MS to provide information.
- Timeframes for submission of information.
- Reliability of data provided.

Inclusion of MAHs and Applicants for Simplified registration referrals

For Articles 16c(1)c and 16c(4) referrals, only registrations/applications which are part of the national or MRP should be included.

Contact points in the MS

A list of contact points in the MS to provide the information required when starting a referral is to be made available by the National Competent Authorities. This information should be updated regularly. It is proposed that the HMPC Secretariat will be responsible for the maintenance of an updated list of contact points for simplified referrals.

Identification of Applicants/MAHs and information on traditional herbal medicinal products

The following timeframe/actions are proposed in relation to the request of information on the Applicants/MAHs and products concerned by a simplified registration referral procedure:

1. As soon as official notification of referral is received (at the latest one week in advance of the HMPC week, HMPC Secretariat sends a fax and e-mail to contact points in MS including Norway and Iceland, requesting the respective information. A table to be filled in by the contact points with the information required is annexed to such fax/e-mail. Companies will need to subsequently identify a contact point (See below 2).
2. HMPC Secretariat to prepare a final table to be sent to the MAHs/Applicants concerned, contact points in MS and included in the HMPC post-mail for information.

III – START OF PROCEDURE / TIMETABLE

The timetable for referral procedures is the same for all referrals and is clearly defined in volume 2A, Chapter 3 of NtA.

Day 0 – Notification of a referral to the HMPC (day of receipt of the signed letter of referral)

Day 1- First meeting of the HMPC following the referral notification to:

- Discuss the question(s) referred to the HMPC (possibility for EMEA/HMPC to refuse the start of the referral if one of the legal conditions are not fulfilled)
- The appointment of the Rapporteur/Co-Rapporteur, where appropriate
- Adoption by the HMPC of the LoQ to be addressed by the applicant, if applicable
- Deadline for answer the LoQ adopted by the HMPC

Day 1 will be Thursday of HMPC week. The official notification letter of the start of the referral procedure should be sent rapidly by the HMPC Secretariat to MAHs on Friday of the HMPC week, if possible.

The content of the letter should include:
- Identification of Rapporteur/Co-Rapporteur
- Deadline to answer LoQ, number of copies to be provided and general format to be followed for the responses
- Request to provide contact points within the companies and check the information provided in the tables annexed to the letter.

The following should be annexed to the letter:
- Final notification of referral (with the detailed explanation of the issue raised attached
- LoQ, if applicable
- Tables of Applicants/MAHs and medicinal products concerned.
- Timetable (active days should be mentioned)

The period for answering the first LoQ should not normally exceed 6 months.

IV – WRITTEN ANSWERS TO THE HMPC LoQ/LOI (If applicable)

The MAHs should send the written answers to the HMPC LoQ/LOI in accordance to the following requirements (these requirements will be mentioned in the initial notification letter sent to the MAHs):

Part I – Introduction, written summary answering each question, conclusion, proposed SPC, Labelling and Package Leaflet (if applicable)

Applicants/MAHs should be requested (in the HMPC LoQ/LOI) to provide in this Part I, a table listing all the publications and data referred to in the answers. For unpublished data it should be clearly stated if the results of such study could be released (i.e. mentioned/discussed in HMPC Assessment Report) in the framework of the referral procedure.

Part II – Supportive documentation (as applicable)