Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human

CMD(h) WORKING DOCUMENT - INFORMATION TO BE SUBMITTED BY THE MEMBER STATE OF THE EUROPEAN REFERENCE MEDICINAL PRODUCT

January 2006

Abbreviations

AR	Assessment Report
CMD(h)	Coordination Group for Mutual Recognition and Decentralised Procedure (human)
CMS	Concerned Member State
DCP	Decentralised Procedure
ERP	European Reference Product
MAH	Marketing Authorisation Holder
MRP	Mutual Recognition Procedure
MS	Member State
PrAR	Preliminary Assessment Report
RMP	Reference Medicinal Product
RMS	Reference Member State
SPC	Summary of Product Characteristics

Introduction

Following the implementation of Directive 2004/27/EC and in connection with the authorisation of generic medicinal products, a 'Generic' is not any longer based on the 'Originator' but on the Reference Medicinal Product (RMP) as defined in Directive 2001/83/EC, as amended. In the case of a RMP never authorised in the chosen Reference Member State (RMS) or the chosen Concerned Member State(s) (CMS), a RMP authorised by another national competent authority or by the European Commission can be chosen. This RMP is the so-called European Reference Product (ERP).
The ERP should be carefully selected by the applicant and the possible implications of this choice be discussed at the prefiling-meeting with the RMS. Where the ERP is only applicable for CMS, a discussion between the applicant and this CMS is recommended. As already mentioned, the ERP can only be used, if the RMP was not authorised in the Member State (MS) in which the application is submitted.

Extracts from Directive 2001/83/EC, as amended

Article 10
"1. By way of derogation from Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests and of clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised under Article 6 for not less than eight years in a Member State or in the Community.

The first subparagraph shall also apply if the reference medicinal product was not authorised in the Member State in which the application for the generic medicinal product is submitted. In this case, the applicant shall indicate in the application form the name of the Member State in which the reference medicinal product is or has been authorised. At the request of the competent authority of the Member State in which the application is submitted, the competent authority of the other Member State shall transmit, within a period of one month, a confirmation that the reference medicinal product is or has been authorised together with the full composition of the reference product and if necessary other relevant documentation."

Scope

The purpose of this document is to give guidance on the necessary information, as stated in Directive 2001/83/EC, to be submitted by the MS of the ERP, especially to give guidance with regard to the term '… other documentation.'
The information given in this document is of primary importance for the Decentralised Procedure (DCP), as the Mutual Recognition Procedure (MRP) is based on an already authorised medicinal product in the RMS. In this case arising problems with the ERP in the RMS have been solved during the national marketing authorisation process and should be addressed in the Assessment Report (AR) of the RMS.
This guidance is complementary to the information given in the Notice to Applicants.

Necessary information

In order to ensure that the information concerning the ERP passed from one MS to another is sufficient for assessing a generic application, the Coordination Group for Mutual Recognition and Decentralised Procedure (human) (CMD(h)) has agreed on the necessary minimum of information to be passed by the competent authority of the MS where the ERP is, or has been, authorised to the competent authority of the MS where the MA application is submitted.

In order to facilitate the process and to save resources, the RMS will ask the MS of the ERP on behalf of all MS concerned by the application, to provide the necessary information as specified in the Annex II by the CMD(h) and in line with the current legislation. This information shall be sent by the MS of the ERP to the RMS and distributed by the RMS without delay to all CMS involved in the procedure. It will also be an integral part of the Preliminary Assessment Report (PrAR) to be prepared by the RMS.

The minimum of information to be provided is:

- confirmation of current or past authorisation of the ERP:
    - date of authorisation
    - date of expiry, withdrawal of the authorisation by the MAH, or withdrawal by the MS
    - if the authorisation has expired or been withdrawn, confirmation that MA of the ERP has not been withdrawn or lapsed due to safety reasons or a change in the risk/benefit ratio
- full composition (qualitative and quantitative) of the ERP

This minimum of information as defined in the legislation is deemed to be necessary for the start of the procedure by the RMS.

'… other documentation.'

Before asking the MS of the ERP for additional information, MS will do their best to try to solve the outstanding questions first on an internal basis (e.g. a similar medicinal product is approved in this MS, the SPC of the ERP is publicly available, there is common scientific knowledge available …).
If the information provided in the SPC of the ERP (e.g. indications, contraindications, warnings) is different or even unknown in the RMS, a scientific dialogue should be initiated by the RMS with the MS of the ERP to try to solve this question (e.g. the MS of the ERP may act as 'co-RMS' for specific parts of the AR). This should be successfully finished before the PrAR is distributed on Day 70 to the CMS.
This outlined way, is brought forward by the CMD(h) as the preferred option to define the term '… other documentation' and will avoid the necessity to review and exchange 'old documentation' which might be available only in a national language. The intention is to save valuable resources, both for the MS of the ERP and the MS involved in this application for a generic. It will provide the possibility to solve outstanding issue on a high scientific level, while increasing the mutual understanding in the authorisation of medicinal products between MS.

The guidance of the CMD(h) given in this paper is the preferred option, but without prejudice to any CMS requesting in special cases additional information (e.g. assessment report - if available). However, it is strongly recommended that such request for additional information is channelled through the RMS.

Annex I: Case Study

Case 1: RMS with RMP; CMS rely on ERP
All information is available to the RMS and will be addressed in the AR. The SPC of the RMP in the RMS is the basis of the application

Case 2: RMS rely on ERP; CMS with RMP
The RMS will ask the MS of the ERP for information

Case 3: RMS rely on ERP; CMS rely on ERP
A careful discussion between all MS and the Applicant is necessary if the ERP is nationally authorised. In the case the ERP is authorised by the European Commission, no additional information is deemed necessary by the MS.

Annex II: Standard form for information

Annex II

Standard form to be sent by the RMS to the MS of the ERP

[Before sending the request, the RMS will complete the form with the information available to him]

RMS	
Contactpoint projectteam leader (name/E-mail/phone)	☎ 💻
Date of request	
MRP/DCP-Number of the Application referring to the ERP	
CMS where application is submitted	

Information on the ERP

MS of the ERP	
Name of ERP	
MAH of ERP	
MA-Number of the ERP	
Date of initial authorisation and any renewals	
Authorisation valid? If not, expiry date	
Withdrawal reason?	
Full composition of RMP	see Annex
Other information	