

**CMDh POSITION PAPER ON
PROCESSING OF GENERIC APPLICATIONS
WHEN THE GENERIC HAS MORE INDICATIONS OR FEWER INDICATIONS
THAN THE REFERENCE PRODUCT IN THE CMS**

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Introduction

The 2005 revision of the pharmaceutical legislation introduced an obligation for CMDh to discuss applications where Member States did not reach an agreement during the MR/DC procedures. The first experience with the so called CMDh referrals highlighted the need for an understanding of how to handle applications where the CMS reference product has more indications or fewer indications than the ones for which the generic has been sought. As long as there are non-harmonised originators on the European market, this will be a common scenario in MR and DC procedures.

When the reference product does not exist at all on a national market, the new legislation gives the opportunity to use the European Reference Product (ERP). This means that a competent authority must accept a reference to a product on another EEA market. The situation discussed in this document is not covered by the ERP because the reference product is or has been on the market in each involved Member State. However the objective with the legislation on ERP is that the individual Member States should rely on evaluation made by other Member States and exchange information on the principles of loyal cooperation and proportionality. This objective should be kept in mind when dealing with non harmonised reference products in MRP/DCP.

The Commission Communication on the Community marketing authorisation procedures for medicinal products (Official Journal C229, 22/7/1998 p.4-17) suggests that Concerned Member States can accept the SmPC of generic medicinal product proposed by the RMS even if it deviates from the reference product in the CMS, except where they have concerns as to the existence of a potential serious risk to public health. Since the introduction of the revised legislation in 2005, the Commission services has confirmed and clarified their interpretation from 1998.

The CMDh supports the Commission view regarding approval of indications for a generic product and has agreed on the following:

Grounds for refusal

In CMD-referrals, the ground for refusing a market authorisation must be based on potential serious risk to public health. The objecting Member State must provide a detailed exposition of these grounds. A deviation in indications (more or fewer) in the generic, not in line with the SmPC of the national reference product, is not considered to be, *per se*, an appropriate reason to refuse licensing.

Documentation for indications missing in the reference product in the CMSs

a) In the case where the Concerned Member State has earlier assessed the data for the indication and refused the indication or if the applicant withdrew the indication, the data is accessible for the Member State. Based on that data, the Member State can then raise a potential serious risk to public health. If the data is the same as earlier refused for the innovator, the MS could come to a positive decision in the light of new scientific development or new or more extensive experience, otherwise additional documentation is most likely to be needed. It is important that the applicant anticipates such issues arising if the indication is missing from the reference product in the CMS, and ensures that early discussion is initiated with the RMS and relevant MS.

b) If the data is not in the possession of the Concerned Member State, the RMS should provide appropriate information. In the case of ERP, this duty is explicitly mentioned in the directive¹. In other situations the duty of the RMS is based on the general principle of the EC Treaty².

In the MRP, when the reference product of the RMS has all indications, the assessment report is sufficient for the CMSs to decide on approval or not. The assessment report of the RMS will include discussions of evidence available to support indications which are not approved in one or more of the CMSs in a procedure. If the applicant has included indications which are not licensed for the reference product in the RMS, the RMS needs more data to reflect the indications in the assessment report.

In the DCP, there is no previous approval and the assessment report of the RMS should cover all applied indications.

Detailed information on the underlying documentation for granting an additional indication should be given if the RMS granted more indications for the reference product than the CMS (see guideline for the Assessment Report in MRP/DCP).

In order for the RMS to be aware of the indications to be covered by the assessment report, the applicant should provide an overview of the product information in CMS(s) (see Notice to Applicants, Volume 2A, Chapter 2, 3.2.2.4). The need for this information should be anticipated by the applicant and should be prepared ahead of submission for early discussion with the RMS.

In any of the above situations, if the RMS or CMSs want access to the underlying data a request should be forwarded to the Member State in possession of the data (involving the RMS for the current procedure in each case). The CMDh has developed a document called *Information to be submitted by the Member State of the European Reference Medicinal Product* (<http://www.hma.eu/211.html>). The principles in this ERP working paper should be used also in the situations where a Member State lacks information on an indication. The request for data could be denied depending on the expiration of the period of data exclusivity in the Member State in possession of the data. But if access to data is denied for legal reasons, the requesting MS may consider refusal of the new indication if it is properly concerned about the risks to public health in the absence of relevant information.

The possibility of requesting data in addition to the assessment report should not be used as a routine but considered only if a Member State has serious doubts on risk to public health.

¹ Article 10.1 (3) – At the request 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.

² Under Article 10, each Member State has an obligation to take measures to ensure the fulfilment of obligations arising out of the Treaty or resulting from action taken by the Community institutions, and must facilitate the achievement of the Community's tasks. This is sometimes referred as giving rise to a duty of 'loyal co-operation' between Community institutions and Member States.