

## **CMD(h) PROCEDURAL ADVICE ON CHANGING THE REFERENCE MEMBER STATE**

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### **INTRODUCTION**

In **exceptional** circumstances, a Marketing Authorisation Holder (MAH) may request a change of the Reference Member State (RMS). The change may be needed when a MAH or a subsidiary responsible for the communication on behalf of the MAH has been closed in the RMS, or when a medicinal product has more than one RMS for the different pharmaceutical forms of the medicinal product, or, subject to clear justification, due to the sunset clause in the RMS. These are examples and other reasons might be justified.

A request for the change of RMS based on scientific disagreement between the MAH and the current RMS (expressed e.g., as a negative recommendation of a variation application by the RMS, where Community interests are involved) is not acceptable. The competent authority of a Member State (MS) may decide upon other reasons of non-acceptance.

Resource implications will be considered when a request to change the RMS has been received by the authorities.

A change of RMS cannot take place during a pending procedure. Before accepting a change of RMS, the MAH should in cooperation with the RMS close all the procedures in the current RMS even if they have not yet started and confirm to the new RMS that no procedure is being examined in the current RMS.

This position has been agreed by the CMD(h) to facilitate the process for a MAH, if such an exceptional situation should arise.

### **LEGAL FRAMEWORK**

Change of RMS is not regulated in the present pharmaceutical legislation cf. Articles 18 and 28 of Directive 2001/83/EC as amended. The present legislation does not impede the possibility of change of the Reference Member State during the life-cycle of a medicinal product: Article 18 does not contravene the opportunity that more than one Reference Member State could be chosen and Article 28 gives the possibility to use the Mutual Recognition Procedure (MRP) and the Decentralised Procedure (DCP) more than once as the MAH may request one or more MS(s) to mutually recognise an authorisation granted by the RMS.

## ADVICE TO THE MARKETING AUTHORISATION HOLDER

If a MAH considers a request for change of RMS, or if a change of RMS is needed due to the sunset clause ~~as~~ the MA in the RMS will cease to exist, the MAH should approach the current RMS and the chosen future RMS well in advance to discuss the situation before any further steps are taken.

It is the obligation of the MAH to ensure that both the current RMS and the future RMS accept the change of RMS. According to MS interpretation of the present legislation, a withdrawal of the marketing authorisation in the current RMS without any appointed new RMS will have an indirect impact on the granted MA(s) in all CMS(s), as the RMS has the lead position during PSUR-, variation- and renewal procedures. In cases with only one remaining CMS in the MRP or the DCP, the MS concerned will automatically become the new RMS as the MS cannot deny being RMS even if there has not been any prior agreement.

### *Important to notice:*

According to the CMD(h) interpretation of the legislation the Mutual Recognition (MR) rules still apply for variations (cf. Commission Regulation (EC) 1084/2003 Article 1 Subject matter) and for renewals in the situation where only one MS remains in the MRP or in the DCP as the medicinal product has benefited from the MR procedure.

## THE CHANGE OF RMS INITIATED BY THE AUTHORITIES

In a situation where an acting RMS and one of the CMS's are planning to change RMS for a particular procedure the final decision cannot be taken without agreement of the MAH.

Due to resource implications, it is recommended only to have one RMS ~~only~~ for a medicinal product, as the same variations ~~are~~ often are foreseen for different pharmaceutical form(s)/strength(s) of a medicinal product.

## THE CHANGE OF RMS REQUIRED BY THE RMS

The RMS cannot force any of the CMS's to become the new RMS. Any change needs to be based on full acceptance between the MAH, the current RMS and the potential RMS.

If only one MS remains in the procedure this MS cannot deny being the new RMS.

## **IF THE RMS IS UNABLE TO ACT AS RMS FOR A FURTHER VERSION OF THE MEDICINAL PRODUCT DUE TO CLASSIFICATION REASONS**

If a MAH wishes to seek reclassification from Prescription only to Non-Prescription or opposite of a medicinal product which is DCP/MRP approved and the RMS has no possibility to accommodate this request the MAH may after discussion with the current RMS apply for a further license using one of the CMS as their RMS for this new additional application.

The CMDh wishes to underline that a proper justification has to be submitted and discussed with the current RMS before the MAH approaches one of the CMS.

## NOTIFICATION OF THE CHANGE

The MAH must notify

Both the ~~change of RMS to all CMS(s) before the change of the RMS takes effect.~~

~~The original~~ **and new** RMS must record the change of the RMS in the procedure tracking system, CTS, for internal use by the MS(s) and for statistical purposes. In the current version of the procedure tracking system this is done ~~in the header section of all pharmaceutical form(s)/strength(s) of~~ **by initiating a RMS-Change from** the product ~~information~~ sheet **via the “File-RMS Change” menu-item.** The ~~new RMS will manually create a~~ product ~~information~~ sheet **for will remain in a transition phase (displaying a status of “RMS pending”) until the new RMS takes over the ownership of** the product **by invoking the “RMS-change” item from the “File” menu.**

~~The following information~~ **The change of RMS should be given:**

<i>Example</i>	<b>“Outgoing RMS”</b>	<b>New RMS</b>
<b>Field</b>		
<b>MA Holder</b>	<b>New RMS</b> Proc. No. DE/H/372/01	<b>Former RMS</b> Proc. No. DK/H/136/01
	<b>Name and address of the MAH</b>	<b>Name and address of the MAH</b>

~~The new RMS also has~~ **communicated by the** responsibility to ensure that updated information **new RMS to the remaining CMS after the transfer is** available in the MRI ~~Product Index~~ **concluded.**

## NUMBERING SYSTEM IN CASE OF CHANGE OF RMS

The numbering of variations/renewal in the new RMS will start with the next sequential number for the variation/renewal.

## TRANSFER OF DOSSIER/ASSESSMENT REPORTS AND OTHER RELEVANT MATERIAL TO THE NEW RMS

When the change has been agreed with the MAH it is the responsibility of the MAH to supply to the new RMS if anything is missing or by any reason not already in possession of the new RMS.

Upon request from the new RMS it is also the obligation of the previous RMS to assist in providing the relevant information from previous procedure(s). However, the previous RMS should

proactively send the Word-file of the Public Assessment Report to the new RMS- if the procedure has been performed according to the provisions as given in Directive 2004/27/EC of 31 March 2004 amending Directive 2001/83/EC- to give them the opportunity to update and publish this report accordingly.

It has been agreed that the transfer of dossier/assessment reports and other relevant material to the new RMS should be sent within 30 days from the request. The new RMS will only be able to start any new procedure when the requested documentation has been received.