Considerations for the transfer of a reference member state

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Abstract
In exceptional circumstances a reference member state (RMS) transfer might become necessary during the lifecycle of a veterinary medicinal product (VMP). Since changing the RMS is not regulated in Directive 2001/82/EC as amended, this article is intended to give an overview of the procedure and the points to be taken into consideration before a change is initiated. This advice is based on the experience gained within the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary (CMDv).

What is an RMS transfer and when is it necessary?

A change of the reference member state (RMS) is a formal procedure undertaken in exceptional circumstances to transfer the responsibility for taking the lead for a procedure from one EU member state to another.

During the lifecycle of a harmonised veterinary medicinal product (VMP) the exceptional situation may occur that the RMS needs to be changed. For example, if a marketing authorisation (MA) in the RMS expires, eg, due to the sunset clause or when a marketing authorisation holder (MAH) decides not to maintain the authorisation in the RMS. In such cases, a new RMS has to be appointed and the lead of the subsequent procedures of the concerned VMP will be transferred to a new RMS. Since it is recommended that the same RMS should be used for different strengths or pharmaceutical forms of a VMP, such a request would also qualify for a change of the RMS.

Another accepted reason for a transfer is the proposed withdrawal from the EU by the RMS following the triggering of Article 50 of the Treaty on the European Union.

This is not an exhaustive list and other reasons for a transfer may be applicable but these would need to be duly justified and discussed with the current RMS which may involve the CMDv in the discussions. However, a request for a change of RMS due to scientific disagreement between the MAH and the current RMS is not acceptable.

In the event that a change of RMS is necessary, it is up to the MAH to decide on the member state taking over the RMS ship, provided this member state agrees.

Announcement and preparatory work for the MAH

The CMDv has published a "Best Practice Guide for changing the Reference Member State" on the CMDv website under Procedural Guidance → Post Marketing Procedures (www.hma.eu/577.html) describing the principles and the process. As a prerequisite, a change of RMS can only be performed if there is no pending or ongoing procedure related to the VMP. Consequently, it is very important that a change of RMS is planned in advance. Ongoing procedures have to be finalised first. Additionally, renewal or variation applications which are to be processed in the near future need to be considered and a discussion with the current and new RMS on the best way to proceed is advisable.

In order to trigger the transfer process, a notification together with a justification should be sent to the current RMS. Also, information on the preferred new RMS should be included. Since the new RMS needs to agree on the MAH's choice it is advisable to inform both parties simultaneously. Clearly, then, it is vital that the current and new RMS are both informed as early as possible. Possible withdrawals from CMS should have been concluded before the change is initiated. This enables the current RMS to update the communication tracking system (CTS) – the EU-wide tracking database for decentralised procedures – in advance of the change.

It should be kept in mind that the national agencies directly involved in the RMS transfer need to consider resource implications in taking on this additional responsibility. This is especially true in the event that the RMS signifies its intent to withdraw from the EU as seen with Brexit. Please see the CMDv document: "Questions

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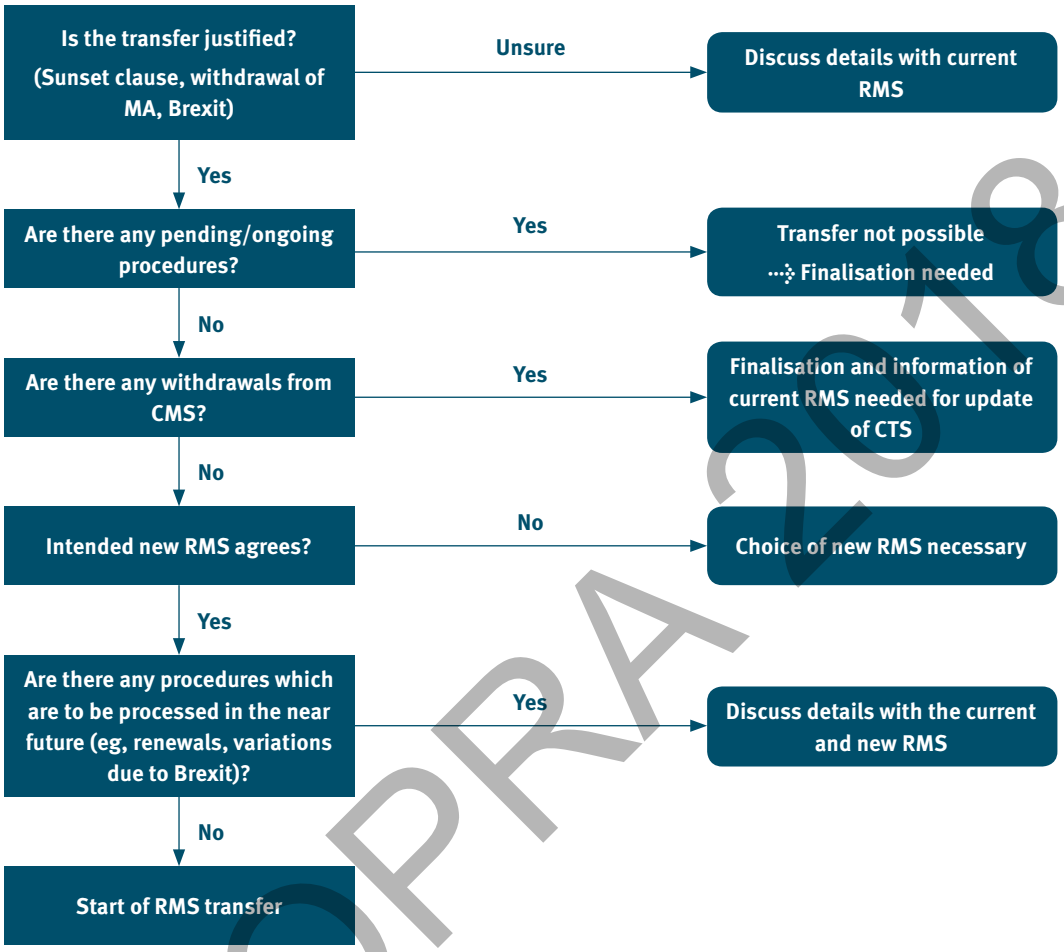
Figure 1: Overview of preparatory work and procedural principles for handling an RMS transfer.



and Answers related to the United Kingdom's withdrawal from the European Union" (www.hma.eu/542.html) which outlines several possible variations that may need to be considered. It is advised with Brexit-driven RMS changes to liaise with the new RMS as soon as possible.

As already outlined above, RMS change is not possible during an ongoing/pending procedure. Therefore, the point in time for the change should carefully be considered together with the current and new RMS.

Implementation of RMS change by original and new RMS

After the current and new RMS have both agreed on the proposed RMS transfer, the new RMS will allocate a new EU procedure number in CTS, which is essential for the current RMS to initiate the change. The current RMS will transfer all relevant documents which are not already in the possession of the new RMS. This will at least comprise the current product information and public assessment report (PuAR) and may be extended to assessment reports or list of questions (LoQs). On request by the new RMS further information and documents might be transferred.

Once the current RMS has initiated the change in CTS and the new RMS has accepted the change in the system, the former EU procedure number is no longer valid and the RMS transfer is finalised. The former RMS will inform all CMS and the CMDv secretariat of the finalisation of the RMS change. Usually, the MAH will also be notified by the new RMS. All future procedures relating to this product will be managed by the new RMS under the new EU procedure number.

In the event that an RMS transfer becomes necessary, please check the points listed in Figure 1. Having considered these points, a formal notification together with a justification of the transfer serves as triggering point for the transfer. The current and new RMS will both inform the MAH when the transfer has been put into effect. Further guidance can be found in the Best Practice Guide mentioned earlier. ■