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

BEST PRACTICE GUIDE FOR THE REFERENCE MEMBER STATE IN THE MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES

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The Reference Member State (RMS) is the Member State, which evaluates the marketing authorisation application dossier and prepares the assessment report on behalf of the Concerned Member States in Mutual Recognition Procedure (MRP) and Decentralised Procedure (DCP). RMS has an essential role in both MR and DC procedures; the RMS acts as a scientific assessor of the documentation, as a regulatory advisor to the applicant, and as a moderator in the discussion between the applicant and the Concerned Member States (CMS).

In this Best Practice Guide, the role of the RMS is described in detail. This Best Practice Guide is complementary to the procedural guidance given in the Best Practice Guide for the Mutual Recognition Procedure and Decentralised Procedure Member State's Standard Operating Procedure.

1. The RMS may give regulatory advice and recommendation (e.g. on the SPC for generics, the choice of the reference product, legal basis of the application, update of the dossier if relevant) to the applicant to facilitate the planned procedures. All information available regarding the procedures, science and regulation, should be taken into account by the RMS and the applicant. If needed, the issues related eg. on the legal basis of the applications can be discussed in the meeting of the Co-ordination Group for Mutual Recognition and Decentralised Procedures (CMD(h)) prior to the start of the procedure, initiated by the RMS. After the agreement on starting the procedures the RMS will allocate the procedure numbers for the applications.

2. The competent authority, in the role of the RMS, should scientifically assess the documentation submitted by the applicant. The Assessment Report (AR) of this evaluation should be written according to the guidelines and using the templates agreed by the CMD(h). In the AR together with the summary of products characteristics, package leaflets and labellings, the RMS should objectively describe the properties of the product and its documentation and describe the scientific discussion (including justification of divergence from existing Guidelines), which lead to the granting of the marketing authorisation in the MRP or which is the basis for the discussion in the DCP.

3. The competent authority, in the role of the RMS, should together with the applicant agree on the timetables for the MR or DC procedures. The RMS should include the procedures in the Communication Tracking System and follow the validation phase of the application, informing the applicant of any deficiencies notified by the CMS. In case of an invalid notification by a CMS, the procedure cannot start until that CMS confirms with the RMS that the issue has been resolved and indicates in the CTS that the application is valid.

4. If the CMS, during the MRP, identifies emerging potential serious risk to public health with the use of the medicinal product with respect to quality, safety and/or efficacy (ref. to Commission guideline on the definition of a potential serious risk to public health), including issues related to the SPC, package leaflets and labellings, it is the duty of the applicant to produce the responses to the comments and questions presented by the CMS. The RMS should also evaluate the responses given by the applicant and clearly indicate within the defined timeframe, if the responses are acceptable to the RMS. If necessary, the RMS can give additional clarification on the issues where there is disagreement between the RMS and the CMS.

5. During the MRP and DCP the RMS will act as the central point between the Concerned Member States and the applicant. All dialogue between the parties involved should be channeled through the RMS. The main duty of the RMS is to facilitate the dialogue between the RMS, CMS and the applicant so that such conditions of the clinical use of the medicinal product could be agreed upon that a safe and rational therapeutic use of the product can be ensured in all CMS.
   If needed, the RMS consults with the CMSs to discuss the issues raised with the aim of reaching consensus, however, it is not the duty of the RMS to give a full evaluation of the comments of the CMS and the RMS is not in the position to classify the comments and questions with respect to their significance (i.e. if any of the comments could be ignored). The RMS is free to advise the applicant how to deal with these comments. RMS has no legal possibility to reject any comments from a CMS provided after the agreed deadlines (eg. day 50), but the CMD(h) strongly recommends that all agreed time limits should be adhered to.

6. In order to facilitate the discussion of the potentially serious risk to public health by Concerned Member States during the MRP or DCP a break out session can be arranged. The RMS will liaise with the CMS and the applicant to determine the need for the break out session and agree its timing with the EMEA CMD(h)-secretariat.
   The break out session should be chaired and conducted by the RMS as stated in the Best Practice Guide on Break-Out Sessions for Mutual Recognition and Decentralised Procedures. In addition the RMS could also use the CMD(h)-meetings as an opportunity to discuss the major issues and seek assistance in solving the issues.

7. The RMS should inform the applicant of the views presented by the CMS at the breakout session. RMS will give the applicant the minutes of the breakout session, and give guidance of the measures expected by the CMS of the applicant.

8. The RMS must always be kept informed of the proposals of the applicant to resolve the out-standing issues during the procedure. The RMS must clearly indicate if it accepts the responses, revised SPC, PL and labelling as proposed by the applicant and if the product is approvable or not.

9. If no agreement between the member states (MSs) can be achieved within the 90 day period (MRP or assessment step II of the DCP) and one or more member states cannot approve the AR, SPC, PL and the labelling, the points of disagreement shall be referred to the CMD(h). It is the duty of the RMS to refer the matter to the CMD(h) by circulating the AR, proposed SPC, PL and labelling and the explanation of the grounds for referral from the disagreeing CMS(s) to all CMD(h) members, CMD(h) chair, the CMD(h) secretariat at the EMEA and the applicant within 7 days after day 90/210. The 60-day referral procedure

is described in detail in the CMD(h) SOP – Disagreement in procedures – Referral to CMD(h).

After starting the procedure the RMS circulates the proposal for the list of questions to all Member States. Based on the discussion with the MSs the RMS finalises the list of questions to the applicant. After receiving the applicant's responses, the RMS evaluates the responses and prepares and circulates the updated assessment report to the Member States.

The RMS will lead the scientific discussion during the CMD(h) meeting and possible oral explanation from the company in order to concentrate on the remaining major issues and seek consensus between the disagreeing Member States and the applicant. After the CMD(h) meeting the RMS should inform the applicant accordingly on the outcome of the discussion.

If agreement is reached the RMS should record the agreement, close the procedure and inform the applicant accordingly.

If no agreement is reached during CMD(h) referral procedure, the RMS should immediately inform the EMEA and the applicant and provide a detailed statement of the unresolved issues and the reasons for the disagreement according to article 29(4) of Directive 2001/83/EC, as amended.

10. After the MR/DC procedure or the positive outcome of the CMD(h) referral, the RMS will notify the completion of the procedure and circulate the final, dated SPC, PL and labelling to the CMSs. In addition the RMS will request the applicant to circulate the agreed specifications for the drug substance and product to the RMS and CMSs.

    It is the responsibility of the RMS to compile a Final Assessment Report, which will describe the events of the MR/DC procedure. The RMS is also responsible for preparing the public assessment report, which will be published on the Heads of Medicines Agency website in accordance with the Best practice guide for the public assessment report in the decentralised and mutual recognition procedures.