

<p style="text-align: center;"><b>BEST PRACTICE GUIDE FOR DECENTRALISED AND MUTUAL RECOGNITION PROCEDURES</b></p>
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## **Introduction**

1. Competent authorities should ensure that their assessment reports are written according to the CMD guideline on the assessment report for Mutual Recognition and Decentralised Procedures and the agreed templates. For mutual recognition procedures (MRP) they should ensure that their assessment report is updated, if necessary, to be consistent with the dossier whenever possible.
2. For MRP, competent authorities should ensure that assessment reports are released within the required 90 day period. This will be facilitated by good communication between the applicants and the Reference Member State (RMS).
3. Competent authorities should do their best endeavour to avoid delay in the start of the procedure.
4. From 30 October 2005, in accordance with Directive 2001/83/EC as amended, not only the SPC but also the package leaflet (PL) and labelling is part of the MRP and DCP agreement. The applicant should also have considered the need for ‘user consultation’ and undertaken testing as necessary. The RMS should in their assessment report include a comment on which form of ‘user consultation’ of the PL has been performed (a full test or a bridging report) and the acceptability of the level of testing carried out. .
5. When issues have been previously discussed and agreed upon by Member States (MSs) either during DCPs or during MRPs, they should not be reopened for discussion during other DCPs or MRPs including the same MSs, unless new information has become available. The RMS should indicate in the Assessment Report (AR) which other products and procedures the SPC, PL and labelling are based on, and the CMS (Concerned Member State) should be listed. A reference to previous discussions in CMDh should be included in the AR, if applicable. The CMS should also include reference to other agreed MRP/DCP texts in their comments, when applicable. When reference is made to other products, MSs should refer to MRP/DCP numbers.

6. In case of multiple MRP/DCP applications submitted at the same time the RMS should inform the CMS about any differences of the ARs, SPCs and PLs. The RMS should harmonise, whenever possible, the SPCs and PLs of different parallel applications before the start of the MRP or in the Day 70 ARs in case of a DCP, in order to achieve harmonisation.

### **Pre-procedural phase**

7. The applicant has to follow the rules adopted by the MS chosen as the RMS for allocating a timeslot. It is recommended to use the common request form in order to ask a MS to be the RMS in a decentralised procedure (<http://www.hma.eu/91.html>).
8. All incoming MRP applications should be registered and validated within 14 days by CMSs and in case of DCP applications by CMSs and RMS, in accordance with the CMDh document 'Procedural advice: Automatic validation of MR/Repeat-use/DC Procedures' (see <http://www.hma.eu/91.html>).
9. All competent authorities should commit to maintain the CTS database and ensure that the information from each competent authority is updated daily.

### **During the procedure**

10. Emerging potential serious public health issues should be communicated to the RMS and applicant as soon as possible. CMSs should send their position ultimately by Day 50 in MRP, and Day 100 and Day 145 in DCP; delays should be an exception. The CMSs should clearly indicate whether their comment should be regarded as a 'point for consideration' or as a 'potential serious risk to public health'. CMSs should notify the RMS and the applicant, by telephone or e-mail, in case they are not able to send their position on these deadlines. Additional comments should be sent after the deadlines only in exceptional circumstances. All comments should be sent in a single e-mail. If this is not possible, the CMS should mention in the first e-mail that more comments will follow. All CMSs should give details of their 'point of contact' that is available on the crucial days of the procedure.
11. In principle, CMSs should rely on the assessment of the RMS. Potential serious risks to public health and points for consideration should be carefully screened within the national agencies. It is recommended that this screening system should be part of the quality system within the national agencies. If a MS raises a potential serious risk to public health it shall give a detailed exposition of the reasons for this position. The RMS should actively co-ordinate the dialogue between the applicant and the National Competent Authority (NCA) and all efforts should be made to resolve any divergence. All points, with the exception of potential serious risks to public health, which have not been agreed, are to be dropped before Day 90 in MRP and Day 210 in DCP. All unsolved potential serious risks to public health should be referred to the CMDh in accordance with Article 29 of Directive 2001/83/EC as amended.

12. The applicant should circulate their response document so that it reaches all CMSs by day 60 in MRP, and by Day 106 and Day 160 in DCP, in accordance with the CMDh document Applicant's Response Document in Mutual Recognition and Decentralised Procedure – recommended CTD format and the Decentralised Procedure Member States' Standard Operating Procedure (revised December 2009). (see [http://www.hma.eu/fileadmin/dateien/Human\\_Medicines/CMD\\_h\\_/procedural\\_guidance/Application\\_for\\_MA/DCP/CMDh-078-2005-Rev2-clean.pdf](http://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/procedural_guidance/Application_for_MA/DCP/CMDh-078-2005-Rev2-clean.pdf))
13. The RMS should, in all situations, evaluate the response given by the applicant (to the issues raised by the MSs) and circulate a report on the applicant's response to all CMSs before any break-out session or discussion in CMDh takes place. The RMS should indicate in their report the date that the comments from the CMSs are expected. Even in cases when no break-out session or discussion in CMDh is planned, comments from CMSs on the applicant's response should preferably be given within reasonable time, e.g. around day 75 of the MRP and day 145/day 195 of the DCP.

### **Break-out sessions, teleconferences and discussion at CMDh**

14. If potential serious risks to public health are identified, a break-out session may be arranged. The occasion, format and the timing of this should be determined by the RMS (current experience has shown that this is often best around day 75/Day 195 of the procedure). The RMS could also use the meeting of the CMDh as an opportunity to discuss major issues that are raised during the procedure and seek assistance in solving the issues.
15. If the RMS is of the opinion that a break-out session connected to a CMDh meeting should take place, the RMS makes a proposal for the timing to be communicated to the CMSs, Chairman of the CMDh and European Medicines Agency (EMA), in accordance with the Best Practice Guide on Break-out sessions. The Chairman and the Agency coordinate the proper timing in case several break-out sessions have to take place. Parallel meetings should not be excluded. If further discussion is needed in CMDh, the RMS will give an oral report of the break-out session in CMDh.
16. If the RMS is of the opinion that a discussion in the CMDh meeting should take place, the RMS should liaise with the Agency to place it on the agenda, and should inform all CMDh members in advance of the meeting on the issues to be discussed.
17. It may be desirable to have a Vitero or telephone conference around day 75-85/day 195-205 to reach agreement. To allow for this, it is recommended that CMSs inform the RMS and applicant about any outstanding issues before the date indicated by the RMS.

## **Finalisation of the procedure**

18. It is advised to introduce any major amendments to the SPC, PL and labelling during an early stage of the procedure in order to allow proper discussion in each MSs. The CMSs should make every effort to send their comments on time and resolve outstanding issues before day 85 in MRP and day 205 in DCP. Only in exceptional cases should changes to the SPC, PL and labelling be introduced after day 85 and day 205 in MRP and DCP, respectively. In such cases the RMS should actively inform the CMSs about this. The RMS and CMSs have the responsibility to ensure full transparency during the procedure.
19. No post day 90/210 commitments that can hinder the granting of a national marketing authorisation should be requested by MSs. Any post-authorisation requirements should be exceptional and full justification should be given by the requesting MS.
20. If consensus is reached by Day 90/Day 210 with all MSs or if at Day 210 in DCP the RMS concludes that the product is not approvable, the RMS closes the procedure. If consensus is reached that the product is approvable, the RMS sends the final agreed SPC, PL and labelling to the CMSs and the applicant. If the RMS concludes that the product is not approvable, the RMS includes information in the FAR on the remaining outstanding issues at the end of the procedure. No referral to CMDh will follow. The procedure continues with the national step.

## **CMDh referral**

21. If a CMSs by Day 90/210 cannot approve the AR, SPC, labelling or PL on the grounds of potential serious risk to public health, the CMSs shall notify the RMS, CMSs, the CMDh Secretariat at the EMA and the applicant at Day 90/Day 210 at the latest, preferably before 4.00 pm CET. The notification shall include a detailed exposition of the reasons for the negative position. This also applies in case the applicant has withdrawn the application in a CMS based on potential serious risk to public health raised by this CMS, unless it concerns a withdrawal of an application via DCP before the DAR is sent. Even if CMSs earlier in the procedure have informed that they are of the opinion that there are potential serious risks to public health with the application, they need to confirm their final position on Day 90/Day 210, so that it is clear to all parties involved, whether the issues have been resolved or not by the applicant's response. It is encouraged to stop an MRP or DCP on Day 90/Day 210 at 4.00 pm CET. It is recommended that the CMSs give their final position according to the timelines given above so that the procedure can be closed on day 90/day 210. A notification to the CMDh of a referral cannot be submitted later than day 90/day 210. It is not advisable to have day 90/day 210 on a Saturday or a Sunday.

22. If no consensus regarding a positive RMS AR is reached by Day 90/Day 210, the RMS will refer the matter to the CMDh by circulation of the AR, proposed SPC, PL and labelling and the explanation of the grounds for referral from the disagreeing CMSs to all CMDh members, CMDh chair, the CMDh Secretariat at the Agency and the applicant, within 7 days after Day 90/Day 210. The procedure for the 60-day procedure in CMDh is described in the CMDh SOP – Disagreement in procedures – referral to CMDh.
23. At the level of CMDh, all CMSs shall use their best endeavours to reach agreement on the action to be taken within 60 days after the referral to the CMDh. If consensus is reached, the RMS records the agreement and closes the procedure at Day 150/Day 270. The RMS sends the final agreed SPC, PL and labelling to the CMSs and the applicant.
24. If no consensus is reached at the level of CMDh, the RMS informs the EMA immediately after Day 60 of the CMDh discussion period, with a view to the application of the procedure under Articles 32, 33 and 34 of Directive 2001/83/EC as amended. The RMS provides the EMA with a detailed statement of the matters on which the MSs have been unable to reach agreement and the reasons for their disagreement. A copy shall be forwarded to the applicant and CMSs by the RMS. The procedure described in Chapter 3 of the Notice to Applicants should be followed using the appropriate form to notify the EMA. MSs that have approved the assessment report, SPC, PL and labelling may, at the request of the applicant, authorise the medicinal product without waiting for the outcome of the procedure laid down in Article 32 of Directive 2001/83/EC as amended. In that event, the authorisation granted shall be without prejudice to the outcome of that procedure.

### **National implementation**

25. The NCA of each MS shall adopt a national decision 30 days after the RMS closes the procedure, subject to submission of acceptable translations. The applicant submits high quality national translations of the SPC, PL and labelling and mock-ups, if necessary, no later than 5 days after the procedure is closed. MSs may introduce linguistic changes only to the SPC, PL and labelling and must ensure their national version of the product information is a faithful translation of the final harmonised position. The ‘blue box concept’ for adequate national information on the label and PL will be permissible. In case the procedure ended with a decision that the product is not approvable, all MSs need to take a final decision at national level, unless the applicant withdraws the application.