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

BEST PRACTICE GUIDE FOR MUTUAL RECOGNITION PROCEDURE

3 October 1996
Updated July 1998
Updated December 2001
Updated February 2004
Updated: February 2005
Updated December 2005

1. Competent authorities should ensure that their assessment reports are updated, if necessary, to be consistent with the dossier whenever possible, and written according to the MRFG assessment report guideline.

2. 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 RMS.

3. 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 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 whether 'user consultation' of the PL has been performed or the justification for its absence is acceptable.

4. All incoming mutual recognition applications should be registered and validated within 14 days by CMS, in accordance with the CMD(h) document Procedure for Automatic Validation of MR Procedures for New Applications.

5. 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, 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'. CMS are encouraged to use the template for CMS comments, see Annex. CMSs should notify the RMS and the applicant, by telephone or e-mail, in case they are not able to send their position on Day 50. Additional comments should be sent after Day 50 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.

6. Potential serious risks to public health and points for consideration should be carefully screened within the national agencies. If a CMS 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 competent authority 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. All unsolved potential serious risks to public health should be referred to the CMD(h) in accordance with Article 29 of Directive 2001/83/EC as amended).

7. In case of multiple MRP applications submitted at the same time the RMS should inform the CMS about any differences of the ARs and SPCs. The RMS should harmonise, whenever possible, the SPCs of different parallel applications before the start of the MRP, if one CMS is concerned by more than one of the parallel applications in order to achieve harmonisation and to facilitate the work of the CMS.

8. When issues have been previously discussed and agreed upon by MSs either during decentralised procedures (DCP) 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 which other products and procedures the SPC, PL and labelling are based on, and the CMS should be listed. A reference to previous discussions in CMD(h) or MRFG should be included in the Assessment Report, if applicable. The CMS should also include reference to other agreed MRP texts in their Day 50 comments, when applicable. When reference is made to other products, MSs should refer to MRP or DCP numbers.

9. The applicant should circulate their response document so that it reaches all CMS by day 60, in accordance with the MRFG document Applicant's response document in MR – recommended format. The RMS should, in all situations, evaluate the response given by the applicant (to the issues raised by the CMS) and circulate a report on the applicant's response to all CMSs before any break-out session takes place, and by day 68 at the latest. The RMS should indicate in their report the date that the comments from the CMS are expected. Even in cases when no break-out session is planned, comments from CMS on the applicant´s response should preferably be given within reasonable time, e.g. around day 75 of the procedure.

10. 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 of the procedure, but may take place between day 73 and day 80).

11. If the RMS is of the opinion that a break-out session connected to a CMD(h) meeting should take place, the RMS makes a proposal for the timing to be communicated to the CMSs, Chairman of the CMD(h), EMEA and the applicant, in accordance with the Best Practice Guide on Break-out sessions. The Chairman and the EMEA co-ordinate 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 CMD(h), the RMS will give an oral report of the break-out session in CMD(h).

The RMS could also use the meeting of the CMD(h) as an opportunity to discuss major issues that are raised during the procedure and seek assistance in solving the issues.

12. 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 MS. The CMSs should make every effort to send their comments on time and resolve outstanding issues before day 85. Only in exceptional cases should changes to the SPC, PL and labelling be introduced after day 85. In such cases the RMS should actively inform the CMSs about this. The RMS and CMS have the responsibility to ensure full transparency during the procedure.

13. On occasion it may be desirable to have a telephone or video conference around day 85 to reach agreement. To allow for this, it is recommended that CMSs inform the RMS and applicant about any outstanding issues by Day 85.

14. If CMS(s) by Day 90 cannot approve the assessment report, SPC, labelling and PL on the grounds of potential serious risk to public health, the CMS(s) shall notify the RMS, CMSs, the CMD secretariat at the EMEA and the applicant at Day 90 at the latest, preferably before 1.00 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. Even if CMS(s) 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, 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 on Day 90 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. It is not advisable to have day 90 on a Saturday or a Sunday.

15. If consensus is reached by Day 90 with all CMSs, the RMS closes the procedure. The RMS sends the final agreed SPC, PL and labelling to the CMSs and the applicant. The RMS will request the applicant to circulate the agreed finished product specifications at release and end of shelf-life to the RMS and CMSs.

16. If no consensus is reached by Day 90, the RMS will refer the matter to the CMD(h) by circulation of the assessment report, 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 secretariat at the EMEA and the applicant, within 7 days after Day 90. The procedure for the 60-day procedure in CMD(h) is described in the CMD(h) SOP – Disagreement in procedures – referral to CMD(h).

17. At the level of CMD(h), all MSs concerned shall use their best endeavours to reach agreement on the action to be taken within 60 days after the start of the CMD(h) procedure. If consensus is reached, the RMS records the agreement and closes the procedure at Day 150. The RMS sends the final agreed SPC, PL and labelling to the CMSs and the applicant. The RMS will request the applicant to circulate the agreed finished product specifications at release and end of shelf-life to the RMS and CMSs.

18. If no consensus is reached at the level of CMD(h), the RMS informs the EMEA on Day 60 of the CMD(h) 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 EMEA 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 EMEA. 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.

19. No pre-authorisation post day 90 commitments should be requested by MSs. Any post-marketing commitments should be exceptional and full justification should be given by the requesting CMS.

20. The National Competent Authority of each CMS shall adopt a national decision within 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 no later than 5 days after the procedure is closed. CMSs 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 package leaflet will be permissible and should be taken into account when finalising the national translations.

21. All competent authorities should commit to maintain the mutual recognition database and ensure that the information from each competent authority is updated daily (CTS).

FLOW CHART FOR THE MUTUAL RECOGNITION PROCEDURE

Approx. 90 days before submission to CMS	Applicant requests RMS to update Assessment Report (AR) and allocate procedure number.
Day -14	Applicant submits the dossier to CMS. RMS circulates the AR including SPC, PL and labelling to CMSs. Validation of the application in the CMSs.
Day 0	RMS starts the procedure
Day 50	CMSs send their comments to the RMS and applicant
Day 60	Applicant sends the response document to CMSs and RMS
Until Day 68	RMS circulates their assessment of the response document to CMSs and applicant.
Day 75	CMSs send their remaining comments to RMS and applicant. A break-out session can be organised between day 73 – 80).
Day 85	CMSs send any remaining comments to RMS and applicant.
Day 90	CMSs notify RMS and applicant of final position (and in case of negative position also the CMD secretariat of the EMEA). If consensus is reached, the RMS closes the procedure. If consensus is not reached, the points for disagreement submitted by CMS(s) are referred to CMD(h) by the RMS within 7 days after Day 90.
Day 150	For procedures referred to CMD(h): If consensus is reached at the level of CMD(h), the RMS closes the procedure. If consensus is not reached at the level of CMD(h), the RMS refers the matter to CHMP for arbitration
5 days after close of procedure	Applicant sends high quality national translations of SPC, PL and labelling to CMSs and RMS.
30 days after close of procedure	Granting of national marketing authorisations in the CMSs subject to submission of acceptable translations.

All days mentioned in this document should be regarded as calendar days.

ANNEX: CMS COMMENTS - MUTUAL RECOGNITION PROCEDURE

1 DAY XXX COMMENTS FROM THE XXX

Product name:	**XXX**
Procedure No.:	XXX
Dosage form and strength:	XXX
Date:	XXX

The XXX agrees with the overall conclusion of the RMS and is therefore prepared to grant a marketing authorisation for XXX.

alt:

The XXX is of the opinion that there are potential serious risks to public health related to the use of this product (see below) and is, at present, not prepared to grant a marketing authorisation.

2 POTENTIAL SERIOUS RISK TO PUBLIC HEALTH

2.1 SPC, PL and labelling

XXX

2.2 Module 3 – Quality

XXX

2.3 Part III/Module 4 – Non-clinical

XXX

2.4 Part IV/Module 5 – Clinical

XXX

3 POINTS FOR CONSIDERATION

3.1 Module 1 – Application related comments and SPC, PL and labelling

XXX

3.2 Module 3 – Quality

XXX

3.3 Part III/Module 4 – Non-clinical

XXX

3.4 Part IV/Module 5 – Clinical

XXX

4 PRACTICAL INFORMATION TO THE APPLICANT:

Please note that any responses that are submitted by email should be sent to our general email address XX@XX and not to any personal email addresses. The size limitation for emails is 2 Mb. A hard copy should also be sent to the following address: XXX. *(to be adapted according to the requirements for each CMS)*

Name of the project manager/
contact person in the CMS

☎
💻

Names of the assessors (if applicable):

Quality (Module 3):

☎
💻

Non-clinical (Part III/Module 4):

☎
💻

Clinical (Part IV/Module 5):
Pharmacokinetics

☎
💻

Efficacy and Safety

☎
💻