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BEST PRACTICE GUIDE
for
The Reference Member State

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1. INTRODUCTION

Articles 31 to 33 of Directive 2001/82/EC¹, sets out the legislative grounds for the Mutual Recognition Procedure, the Decentralised Procedure and also any subsequent referrals to the Co-ordination Group that may arise. The Veterinary Co-ordination Group for Mutual Recognition and Decentralised Procedures (CMD(v)) has prepared this Best Practice Guide (BPG) to help the Reference Member State (RMS) to run the procedures smoothly.

2. AIM AND SCOPE

The RMS has an essential role to play to ensure the smooth and effective operation of the Mutual Recognition Procedure, the Decentralised Procedure and also any product referrals to the CMD(v). The RMS at various times acts as a scientific assessor of the documentation, a regulatory adviser to the applicant and a moderator in the discussion between the applicant and the Concerned Member States (CMS). This BPG describes the role of the RMS in detail, in order to help the RMS fulfil the different duties required from them, and is complimentary to the Best Practice Guides and legislation noted below.

3. REFERENCES AND RELATED DOCUMENT

This Best Practice Guide should be read in conjunction with:

- | | |
|----------------|---|
| CMD(v)/BPG/001 | Best Practice Guide for Veterinary Mutual Recognition Procedure. |
| CMD(v)/BPG/002 | Best Practice Guide for the Decentralised Procedure. |
| CMD(v)/SOP/001 | Standard Operating Procedure Disagreement in Procedures – Referral to CMD(v). |

Guideline on the definition of a potential serious risk to human, animal health or for the environment. (www.ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev5.htm)

- | | |
|----------------|---|
| CMD(v)/SOP/018 | Guidance for Allocation of numbers |
| CMD(v)/GUI/003 | Management of emails during a procedure |
| | SOP for IFAH Questionnaire |

¹ As amended by 2004/28/EC

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4. GENERAL

Abbreviations

RMS	Reference Member State
CMS	Concerned Member State
HMA	Heads of Medicines Agency
AR	Assessment Report
MRP	Mutual Recognition Procedure
DCP	Decentralised Procedure
SPC	Summary of Product Characteristics
VMP	Veterinary Medicinal Product

5. DESCRIPTION OF PROCEDURE

5.1 MUTUAL RECOGNITION PROCEDURE (MRP)

Before the mutual recognition procedure

The applicant should notify the competent authority of the Member State that this Member State will be used as the RMS.

The future RMS should discuss with the applicant whether they should submit variations to update the Marketing Authorisation dossier prior to initiating the MRP.

The RMS should give regulatory and scientific advice or recommendation to the applicant in order to facilitate the planned MRP.

The RMS should remind the applicant that according to Annex I of Directive 2001/82/EC as amended all information which is relevant to the evaluation of the medicinal product concerned shall be included in the application, whether favourable or unfavourable to the product. In particular, all relevant details shall be given of any incomplete or abandoned test or trial relating to the veterinary medicinal product. Moreover, the applicant should be reminded that any information not in the original application, pertinent to the benefit/risk assessment, must be submitted forthwith to the competent authority and be part of the updated dossier.

Special attention should be paid to generic applications. The RMS should remind the applicant that it is the applicant's duty to check the Summary of Product Characteristics (SPCs) of the reference products in the intended CMS to make sure that parts such as the target species, indications, posology, warnings and withdrawal period for the proposed product are compatible with them. The RMS is required to provide information relating to the Reference VMP to any CMS where it is not authorised, in accordance with CMD(v)/GUI/006.

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The future RMS will update the Assessment Report (AR) within 90 days after receipt of a valid application. The AR should be written according to the CVMP guideline of the Preparation of Evaluation Reports. In the AR the RMS should objectively describe the properties of the product and its documentation and present the scientific discussion (including justification of any divergence from existing Guidelines), which led to the granting of the Marketing Authorisation and to the approval of the SPC in the RMS.

During the 90 days of the preparation of the AR, the RMS will approve the English translation of the SPC and labelling/package leaflet text (product information). Content of the SPC should be in accordance with the Notice to Applicants Guideline on SPC. In order to facilitate harmonisation in the MRP, the CMD(v) has agreed that the SPC and product literature headings, as defined in the CMD(v) annotated Quality Review of Documents (QRD) Veterinary Product Information Template should, when applicable, be used in MRP. This template document is available on the HMA-vet website. The English SPC will be included in or annexed to the AR.

Pre validation phase

The RMS should, together with the applicant, set the start date (Day 0) for the Mutual Recognition Procedure. The CMD(v) publishes start dates for MRP on the HMA-vet website. These are adjusted so that the CMD(v) meeting will be on Day 77/78 of the procedure.

The RMS creates the procedure in the Communication Tracking System (CTS) as defined in the SOP for allocation of MRP/DCP numbers CMD/(v)SOP/018. CTS should be updated as necessary throughout the procedure. A notification of a future MRP is also notified to CMS via MRNA eudra mailbox. Both RMS and CMS should pay attention to the guidance given on Management of use of e-mail use during procedures (CMD(v)/GUI/003).

The RMS should ensure that the applicant is aware of his responsibilities throughout the procedure, as laid out in Notice to Applicants and the BPG for Mutual Recognition Procedure.

The RMS will confirm the proposed start date and timetable one month before the start date of the future procedure in an email to CMS (and applicant) with a copy to the Secretariat.

The RMS may choose to provide a draft of the AR to the applicant for comment prior to circulating it to the CMS.

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Validation phase

At least 14 days before the proposed Day 0, the RMS will circulate the AR to CMS and applicant via MRNA eudra mailbox and in this e-mail also inform which Member States are involved. A (detailed) timetable for the procedure is included in this mail.

Automatic validation by the CMS will start (see CMD(v) document of Automatic validation of MR procedures (CMD(v)BPG/008) after receipt of both AR and applicant's fax of dossier dispatch.

If a CMS informs the RMS and applicant within the timeframe of automatic validation that the application cannot be validated, the RMS will help the applicant to solve the validation problems. The procedure cannot be started before all validation issues have been clarified and all CMS have validated the application, unless the application is withdrawn for the relevant CMS(s). The CMS(s) who cannot accept the application at the validation stage will update CTS accordingly.

Comments from the CMS (days 0 - 57)

The main duty of the RMS is to facilitate communication between the RMS, the CMS and the applicant, so that such conditions of the clinical use of the veterinary medicinal product may be agreed upon that a safe and rational therapeutic or prophylactic use of the product can be ensured in all CMS.

The CMS, during the MRP, can identify potential serious risks to human or animal health or the environment (major concerns), as well as minor points for clarification and SPC/product literature points for consideration. The CMS will express their concerns in the questions sent to the RMS by day 54 of the procedure (see template 007 CMS comments).

The RMS will forward to the applicant all comments received, without delay, to allow them to start preparing the response as soon as possible. It is the duty of the applicant to produce the response to these questions.

The RMS will collect all the comments sent by the CMS and create a consolidated list of questions (LOQ) using the template 001. The LOQ will be circulated by Day 57 via e-mail (MRNA eudra mailbox to the CMS and open Internet or Eudralink mail to the applicant). The RMS is free to advise the applicant how to deal with these comments.

The RMS has no legal possibility to reject any comments from a CMS received after day 54, but the CMD(v) strongly recommends that all agreed time limits should be adhered to.

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Pre CMD(v) (days 58 =>76)

The RMS should advise the applicant that additional studies are not acceptable during the procedure. However, supplementary data from studies included in the submission can be provided.

The applicant will attach his responses to the LOQ and email the document to the RMS by Day 65. The RMS will circulate the document (Resp-LOQ) including revised SPC/product literature with tracked changes, if any, to all CMS immediately via the MRNA eudra mailbox. The applicant should send to RMS and CMS, to arrive by morning of Day 67, necessary paper copies of attachments and/or documentation as defined in CMD(v) guidance document CMD(v)/GUI/003 Management of email use during procedures and CMD(v)/BPG/001 Best Practice Guide for MRP.

The RMS will assess the applicant's answers and circulate the combined comments-response-assessment document (AR-Resp-LOQ) to the CMS via the MRNA eudra mailbox and to the applicant via open Internet or Eudralink mailbox, by Day 70.

Where any CMS is, after receiving the AR-Resp-LOQ, not in a position to recognise the MA granted by the RMS, the application can be discussed at the CMD(v) meeting on day 78 of the procedure.

The CMS will indicate before the CMD(v) meeting which questions still remain unresolved and send their second comments to the RMS by day 75 of the procedure if possible. In order to help the work of the RMS the original number/s of the unresolved question/s shall remain on this response document. The number/s of the question/s resolved can also be given in the pre CMD(v) comments

It is the duty of the RMS to check the pre CMD(v) comments before the meeting so that only unresolved points are discussed at the meeting.

CMD(v) discussion (Days 77/78)

During the CMD(v) discussion the RMS shall concentrate only on unresolved issues that would lead to referral or arbitration and SPC points. The representative/s of the RMS will coordinate the discussion with the CMS. In the discussion of any particular question, the RMS should include other CMS which have raised similar concerns. Any CMS is entitled to comment on unresolved questions raised by other CMS.

All remaining issues should be addressed and there should be a sincere effort to resolve these issues during the meeting, with input from the Applicant via the RMS where necessary. Therefore, attendees at the CMD(v) meeting from Member States should be able to resolve issues on behalf of their competent authority, if necessary by consultation by telephone, videolink or other means with their authority.

Representatives of all CMSs who raised major issues, which were not solved by the Applicant's answers, should attend the CMD(v) meeting. When a CMS cannot attend the

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meeting, the RMS and CMD(v) Secretariat should be informed, if possible at least one working day before the meeting, and a contact name and telephone number for the CMS should be provided along with any written comments from that CMS.

After CMD(v) (Days 79-90)

The RMS should inform the applicant immediately after the CMD(v) meeting of the views presented by the CMS during the CMD(v) discussion and give guidance on the measures expected of the applicant by the CMS, including amendments to be made to the SPC.

The applicant will make the requested corrections to the SPC, PL and Labelling and send it (using the track changes tool) to the RMS. The RMS will clearly indicate if it accepts the revised documents as proposed by the applicant and circulate the revised SPC, PI and Labelling on day 82 of the procedure. If necessary an updated Assessment Report will also be circulated.

The RMS must always be kept informed of the proposals of the applicant to resolve the outstanding issues during the negotiations between the applicant and the CMS throughout the procedure. The RMS should copy all communications to all CMS.

If modifications to the SPC still are necessary, the RMS will circulate the draft document again on day 85 of the procedure and ask the CMS for their comments or acceptance of the SPC by day 88.

All CMS will confirm their decision by day 90.

The Applicant and RMS should make sure that during the procedure, the complete SPC labelling and leaflet have been agreed, taking into account that in some Member States multi-lingual labels are necessary and that in some cases the Applicant seeks to have combined labels in more than one Member State. In such cases, a space restriction might exist and a solution has to be sought trying to take into account the legal requirement for harmonisation and the national legal requirements and the safe use of veterinary medicinal products.

After issuing the Marketing Authorisation, any changes to the product literature (final SPC, leaflet or labelling) should be considered as a variation.

If no agreement between the Member States can be achieved within the 90 day period, the issue must be referred to CMD(v) in accordance with Article 33 of Directive 2001/82/EC, even if the applicant withdraws the application from the CMS which consider/s that the product would cause potential serious risk to human or animal health or the environment.

Day 90 onward

On day 90 of the MRP, the RMS will notify the completion of the procedure to the CMS and applicant by e-mail.

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In this e-mail the RMS will conclude the outcome of the procedure including a list of CMS where the application was approved/withdrawn. Also information regarding the common renewal date will be included in this e-mail together with final approved SPC, PL, Labelling, Final Assessment Report, Finished Product Specifications and commitments, if applicable.

Once the MRP has been finalised it is the responsibility of the applicant to actively promote the granting of the MA in the CMS by providing correct translations of SPC, PL and labelling, as necessary, within five days of the end of the procedure. The CMS will make their best effort to see that the MA will be issued within 30 days after the CMS has received acceptable translations of the SPC, package insert and labelling.

If, after Day 90, the applicant has problems in reaching the correct contact person in a CMS, the RMS will act as the coordinator between these two and assist in contacting the right person/s.

The RMS will update the CTS database with the outcome of the procedure and will encourage all the CMS also to update the CTS database.

The RMS must initiate a formal referral to the CMD(v) (under Article 33 of Directive 2001/82 as amended) if any CMS was against the opinion of the RMS at Day 90 of the procedure. The referral is to be conducted in accordance with CMD(v) SOP 001

If no agreement is reached during the CMD(v) referral procedure, the RMS must initiate a formal referral to CVMP for arbitration (under Article 36 of Directive 2001/82/EC, in accordance with the EMEA SOP for referrals (EMEA/CVMP/191/96-Final). The RMS will provide the CVMP with a detailed statement of the matter(s) on which the CMS have been unable to reach agreement and the reasons for their disagreement. The CMS and the applicant shall be provided with a copy of this information.

The RMS will complete the CMD(v) – IFAH Europe questionnaire.

The RMS will prepare the public assessment report which will be agreed with the applicant prior to publication, according to SOP 016

The RMS will send the approved final SPC, to the VMRI website.

If commitments are agreed during the MRP, it is the duty of the RMS to ensure that they are fulfilled.

5.2 DECENTRALISED PROCEDURE (DCP)

Before the decentralised procedure

The RMS should discuss the proposed DCP with the applicant at least three months before the intended submission date. The RMS will give regulatory and scientific advice or

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recommendation to the applicant in order to facilitate the planned procedure. The RMS should remind the applicant that according to Annex I of Directive 2001/82/EC as amended all information which is relevant to the evaluation of the medicinal product concerned shall be included in the application, whether favourable or unfavourable to the product. In particular, all relevant details shall be given of any incomplete or abandoned test or trial relating to the veterinary medicinal product.

Special attention should be paid to generic applications. The RMS should remind the applicant that it is the applicant's duty to check Summary of Product Characteristics (SPCs) of the reference products in the intended MS to make sure that parts such as the target species, indications, posology, warnings and withdrawal period for the proposed product are compatible with them.

The RMS should notify the future CMSs and the Secretariat of the applicant's intention to submit an application as well as provide an outline timetable. The timetable should be agreed with the applicant, taking into account any delays that might be necessary due to use of a reference product that is not authorised in the RMS. The RMS will allocate a procedure number to the application, inform the applicant and create the procedure in the Communication Tracking System (CTS).

Pre validation phase (Submission)

The RMS on receipt of the application should send an email to all CMSs and to the applicant informing them that the validation period has started.

In the case of a generic application, where the reference product is not authorised in the RMS, the RMS will immediately request the necessary information concerning the reference product from the MS where it is authorised, as defined in the CMD(v) guidance document (006). The start of validation will be postponed until the necessary documentation has been received by the RMS and forwarded to the CMS. Where the reference product is authorised in the RMS but not in all CMS, the RMS must forward the necessary documentation prior to the start of validation.

Validation phase

Automatic validation by the CMS will start (see CMD(v) document of Automatic validation of MR procedures (CMD(v)BPG/008) after receipt of applicant's fax of dossier dispatch.

If a CMS informs the RMS and applicant within the timeframe of automatic validation that the application cannot be validated, the RMS will help the applicant to solve the validation problems. The procedure cannot be started before all validation issues have been clarified and all CMS have validated the application, unless the application is withdrawn for the relevant CMS(s). The CMS(s) who cannot accept the application at the validation stage will update CTS accordingly.

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At the end of the validation phase the RMS will inform the applicant and the CMS of the start date and timetable.

Assessment Step I (Day 0 – 105)

The RMS will start the assessment once the procedure has been started. The AR should be written in English according to the relevant CVMP guideline. The English versions of draft SPC, PL and labelling will follow the CMD(v) annotated QRD template for MRP and DCP.

The RMS will forward a preliminary assessment report (PAR) together with the drafts of SPC, PL and labelling to the CMS within 70 calendar days after the start of the procedure. The PAR will be accompanied by a draft list of questions (LOQ1) as proposed by the RMS. CMS will provide their comments and any additional questions by day 100. The PAR will also be sent to the applicant at Day 70.

Between Days 100 and 105 of the procedure the RMS will compile the LOQ1 for the applicant. During this time the RMS may initiate discussions with any CMS and/or the applicant regarding points and comments that need clarification. Generally the RMS should not identify the source of specific questions. The reports of these discussions should be circulated to all MS concerned. The RMS may choose to leave out of the LOQ1 any comments/questions that are not seen as relevant or have been resolved during the discussions. Similar questions should be combined. On day 105 the RMS will send the LOQ1 to the applicant and CMS and stop the clock accordingly.

Clock Off Period

The clock-off period will be three months for the applicant to prepare his response to the LOQ1 and amend the SPC, package leaflet and labelling as appropriate. If justified and agreed with the RMS, this time period can be extended by an additional three months.

The applicant may submit draft responses to the RMS for pre-assessment. The RMS should agree the date of submission of the final response with the applicant, taking into account the next available start date for Step 2 as published by CMD(v), and the time required for checking and assessment of the response.

The applicant will complete the response to the LOQ by writing the response after each question. This document (Resp-LOQ1) will be sent by e-mail to the RMS, who will immediately forward it by email to the CMS. The applicant will simultaneously send the response by hard copy including any attachments, to the RMS and all CMS.

The RMS check the responses received to ensure all questions have been answered and all attachments present. Then, on day 106, the RMS will advise the applicant and CMS by email that the clock has re-started. An updated timetable will be included.

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From day 106, the RMS has 14 days to provide an assessment of the responses and update the PAR. The resulting Draft AR (DAR), draft SPC, draft PL and labelling must be prepared by Day 120

On day 120 the RMS will circulate to the applicant and CMS the drafts of the Assessment Report (clean copy with no tracked changes), SPC, PL and Labelling together with its recommendation on the product.

Assessment Step II (90 days)

Day 0 will be set to match the published start dates for Mutual Recognition.

CMS comments will be received by day 25. The RMS will forward these immediately to the applicant. The RMS shall prepare the LOQ2 according to the CMD(v) template, with major questions, SPC, labelling/PL points and points for clarification clearly and separately identified, and send this to the applicant and CMS by day 30 of the assessment step II of the procedure.

The applicant will attach his responses to the LOQ2 and email the document to the RMS by day 50. The RMS will circulate the document (Resp-LOQ2) including revised SPC, PL and Labelling with tracked changes, if any, to all CMS immediately via the MRNA eudra mailbox.

The RMS should advise the applicant that additional studies are not acceptable during this step. However, supplementary data from studies included in the submission can be provided.

Between day 50 and 70 the RMS should evaluate responses given by the applicant to the issues raised by the Member States concerned and communicate this evaluation (AR-Resp-LOQ2) in writing to all CMSs and to the applicant by day 70 at the latest (by e-mail). If the application is to be discussed at a CMD(v) meeting, the evaluation should also be sent at the same time to the CMD(v) Secretariat at the EMEA.

In cases where any CMS is, after receiving the AR-Resp-LOQ2, not in a position to agree to the issue of a marketing authorisation, the application can be discussed at the CMD(v) meeting on day 78 of the procedure.

The CMS will indicate before the CMD(v) meeting which questions still remain unresolved and send their second comments to the RMS by day 75 of the procedure if possible. In order to help the work of the RMS the original number/s of the unresolved question/s shall remain on this response document. The number/s of question/s resolved can also be given in the pre CMD(v) comments

It is the duty of the RMS to check the pre CMD(v) comments before the meeting so that only unresolved points are discussed at the meeting.

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CMD(v) discussion (Days 77/78)

During the CMD(v) discussion the RMS shall concentrate only on unresolved issues that would lead to referral to CMD(v), SPC points and disagreements on product literature and the assessment report. The representative/s of the RMS will coordinate the discussion with the CMS. In the discussion of any particular question, the RMS should include other CMS, which have raised similar concerns. Any CMS is entitled to comment on any unresolved questions raised.

All remaining issues should be addressed and there should be a sincere effort to resolve these issues during the meeting, with input from the Applicant via the RMS where necessary. Therefore, attendees at the CMD(v) meeting from Member States should be able to resolve issues on behalf of their competent authority, if necessary by consultation by telephone or other means with their authority.

Representatives of all CMSs who raised major issues, which were not solved by the Applicant's answers, should attend the CMD(v) meeting. When a CMS cannot attend the meeting, the RMS and CMD(v) Secretariat should be informed, if possible at least one working day before the meeting, and a contact name and telephone number for the CMS should be provided along with any response report from that CMS.

After CMD(v) (Days 79-90)

The RMS should inform the applicant immediately after the CMD(v) meeting of the views presented by the CMS during the CMD(v) discussion and give guidance on the measures expected of the applicant, including amendments to be made to the SPC, PL and Labelling.

The applicant will make the requested corrections to the SPC, PL and Labelling and send it (using the track changes tool) to the RMS. The RMS will clearly indicate if it accepts the revised SPC, PL and Labelling as proposed by the applicant and circulate the revised SPC, PL and Labelling on day 82 of the procedure.

The RMS must always be kept informed of the proposals of the applicant to resolve any outstanding issues during any negotiations between the applicant and the CMS. The RMS should copy all communications to all CMS.

If modifications to the SPC, PL and Labelling still are necessary, the RMS will circulate the SPC, PL and Labelling again on day 85 of the procedure and ask the CMS for the acceptance of the SPC, PL and Labelling by day 88.

All CMS will confirm their decision by day 90.

The Applicant and RMS should make sure that during the procedure, the complete SPC labelling and leaflet have been agreed, taking into account that in some Member States multi-lingual labels are necessary and that in some cases the Applicant seeks to have combined labels in more than one Member State. In such cases, a space restriction might exist and a solution has to be sought trying to take into account the legal requirement for

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harmonisation and the national legal requirements and the safe use of veterinary medicinal products.

After issuing the Marketing Authorisation, any changes to the product literature (final SPC, leaflet or labelling) should be considered as a variation.

If no agreement between the Member States can be achieved within the 90 day period, the issue must be referred to CMD(v) even if the applicant withdraws the application from the MS which consider/s that the product would cause risk to human or animal health or the environment.

Day 90

On day 90 after the RMS will circulate an e-mail to all CMS and the applicant.

The following information should be included:

- A list of MS accepting or disagreeing
- The common renewal date
- The final SPC, PL and labelling
- The finished product specifications
- Any agreed commitments

If all MS agree to accept the product, MS concerned will proceed nationally to grant a marketing authorisation. If not, issues of concern will be referred to CMD(v).

If there is consensus that the product is not approvable, no national step, or referral to, CMD(v) will follow.

If one or more MS agree to approve the application but others do not, the matter will be referred to the CMD(v) for the 60 day referral process (see document for Disagreement in procedures Referral to CMD(v), CMD(v)/SOP/001). The reasons for non-acceptance from MS will be stated clearly to the RMS when applicable, the other CMS and to the applicant. The RMS will refer these parts of disagreement to the CMD(v) without delay.

The applicant can withdraw the application at any stage of the procedure, but this will not prevent the CMD(v) referral phase in the case of disagreement between MS based on potential serious risk.

If commitments are agreed during the DCP, it is the duty of the RMS to ensure that they are fulfilled.

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Post Day 90

The RMS will also be responsible for completing the following tasks post day 90.

- The RMS will complete the CMD(v) – IFAH Europe questionnaire.
- The RMS will prepare a copy of the public assessment report which will be agreed with the applicant and CMS prior to publication In accordance with SOP016.
- The RMS will send the approved final SPC, PL and Labelling to the VMRI website.

5.3 CMD(v) 60-DAY REFERRAL PROCEDURE

The Referral to CMD(v) will take place in accordance with SOP 001. Within 7 days of the end of the procedure for Mutual Recognition or the Decentralised Procedure where divergent positions have not been resolved, the Secretariat, after agreement with the RMS and the CMD(v) Chairperson will send the timetable and accompanying letter for the referral procedure to all members of CMD(v) by email and to the applicant.

The RMS will circulate copies of the latest assessment report, SPC, PL and Labelling and the grounds for referral provided by the dissenting CMS(s) to all members of the CMD(v).

At the next CMD(v) meeting after the end of the procedure, the RMS will lead the discussion focussing only on those areas of disagreement.

The RMS will then convey the outstanding areas of disagreement to the applicant using the agreed template.

The applicant prepares a response to these areas of disagreement and the RMS copies this to all CMD(v) members.

The RMS leads the discussion at the second CMD(v) meeting of the referral.

After the close of the referral procedure the RMS will notify the applicant of the outcome within 5 days. The RMS will also notify the EMEA Secretariat if any subsequent referral to CVMP for arbitration is necessary.

Where a consensus is reached, the RMS records agreement, closes the procedure and notifies the applicant and CMSs.

5.4 BREAKOUT SESSIONS

Product discussions can at times be very involved however time is often short. Usually only 45 minutes are allocated per product. It is therefore vitally important that the RMS can

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manage and focus discussions on the key issues in order to seek to achieve agreement between the RMS and CMS. This will mean that the RMS would have ideally discussed the questions and negotiating positions with the applicant prior to the CMD(v) meeting.

The RMS responsibility in conducting the breakout sessions are referred to in previous paragraphs. Nevertheless the following principles should be followed for each breakout discussion:-

- At the start of the session introduce the product, its active substance and legal basis on which the application is made.
- Detail those CMSs who have already notified their acceptance, those with outstanding areas of serious concern and those who have provided no feedback.
- Using the numbered LOQ move through the major unresolved questions. It is not necessary to talk about those which have already been resolved.
- Facilitate the discussions inviting CMS to contribute as appropriate.
- Summarise any agreements.
- Once the major questions have been discussed then move to discuss the SPC.

The Chair will conclude the discussion with a 'tour de table' in order to confirm CMS positions.

6. List of documents

CMD(v)/Tem/001	LOQ.
CMD(v)/Tem/006	CMD(v) Annotated QRD Template.
CMD(v)/Tem/011	Notification to EMEA of Failure to Reach Agreement.
CMD(v)/Tem/002	Reasons for Referral to CMD(v)
CMD(v)/Tem/007	CMS Comments
CMD(v)/SOP/016	Standard Operating Procedure for Production and Publication of Public Assessment Reports.
CMD(v)/BPG/003	Best Practice Guide on Repeat Use of the MR Procedures.
CMD(v)/SOP/009	Standard Operating Procedure on VMRI Procedure.

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CMD(v)/BPG/008 Best Practice Guide on Automatic Validation of Applications in Mutual Recognition Procedures.

CMD(v)/GUI/006 Documentation to be Submitted by a Member State When Reference Medicinal Product is Not Authorised in the RMS.

CMD(v)/BPG/009 Best Practice Guide on Processing SPC, Labelling and Packaging Provided in Support of Mutual recognition and Decentralised Applications.

Articles 31 to 33 of Directive 2001/82/EC.

Volume 6a, Chapter 2 of the Notice to Applicants.

<http://www.emea.europa.eu>

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Annex A

CHECK LIST for the REFERENCE MEMBER STATE FOR MUTUAL RECOGNITION PROCEDURE		
Before day -14	Update AR	
Before day -14	Allocate procedure number	
Before day -14	Create procedure in CTS	
Before day -14	E-mail CMS proposed start date	
-14 days – Automatic validation	E-mail CMS with AR confirming start of automatic validation	
Day 0	E-mail CMS timetable	
Day 0	Update CTS with start date	
Day 54	Comments from CMS send to applicant	
Day 57	Send CLOQ to applicant and CMS	
Day 65	Send applicants response to CMS	
Day 70	Circulate RMS response to applicant, CMS and CMD(v) secretariat.	
Day 75	Send CMS pre-CMD(v) comments to applicant and CMDv secretariat.	
Day 77/78	CMD(v) for discussion	
Day 79 +	Inform applicant of CMD(v) outcome	
Day 82	Send Day 82 SPC, PL & Labelling to CMS	
Day 85	Send Day 85 SPC, PL & Labelling to CMS	
Day 89	Send SPC, PL & Labelling to CMS and Applicant	
AGREEMENT REACHED		
Day 90	Send final e-mail close procedure	
Day 90 **	Update CTS	
Day 90	Send SPC to VMRI database	
Day 95	Receive mock ups	
Day 120	Grant national marketing authorisation	
Day 120	Complete IFAH questionnaire	
NO AGREEMENT – REFERRAL		
Day 90 + 7	Complete CMD(v) TEM/011 referral form	
Day 90 + 7	E-mail form, AR, SPC, Labelling to CMS and CMDv secretariat	
Day 120	E-mail draft list of concerns to all MS	
Day 120 +	CMD(v) meeting	
Day 120 (15)	E-mail applicants response to all CMD(v)	
Day 120 (45)	e-mail assessment of applicant response	
Day 120 (-60)	Second CMD(v) meeting	
Day 120 (-60)	Agreement reached e-mail final SPC, Labelling to CMS (follow steps from **)	
If no agreement reached inform EMEA and refer to CVMP		

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Annex B

CHECK LIST for the REFERENCE MEMBER STATE FOR MUTUAL RECOGNITION PROCEDURE WHERE RVMP IS NOT AUTHORISED IN RMS		
Before day -14	Request details of RVMP using Annex 1 CMD(v) GUI/006	
Before day -14	Update AR	
Before day -14	Allocate procedure number	
Before day -14	Create procedure in CTS	
Before day -14	E-mail CMS proposed start date	
-14 days – Automatic validation	E-mail CMS with AR confirming start of automatic validation	
Day 0	E-mail CMS timetable	
Day 0	Update CTS with start date	
Day 54	Comments from CMS send to applicant	
Day 57	Send CLOQ to applicant and CMS	
Day 65	Send applicants response to CMS	
Day 70	Circulate RMS response to applicant, CMS and CMD(v) secretariat.	
Day 75	Send CMS pre-CMD(v) comments to applicant and CMD(v) secretariat.	
Day 77/78	CMD(v) for discussion	
Day 79 +	Inform applicant of CMD(v) outcome	
Day 82	Send Day 82 SPC, PL & Labelling to CMS	
Day 85	Send Day 85 SPC, PL & Labelling to CMS	
Day 89	Send SPC, PL & Labelling to CMS and Applicant	
AGREEMENT REACHED		
Day 90	Send final e-mail close procedure	
Day 90 **	Update CTS	
Day 90	Send SPC to VMRI database	
Day 95	Receive mock ups	
Day 120	Grant national marketing authorisation	
Day 120	Complete IFAH questionnaire	
NO AGREEMENT – REFERRAL		
Day 90 + 7	Complete CMD(v) TEM/011 referral form	
Day 90 + 7	E-mail form, AR, SPC, PL, Labelling to CMS and CMD(v) secretariat	
Day 120	E-mail draft list of concerns to all MS	
Day 120 +	CMD(v) meeting	
Day 120 (15)	E-mail applicants response to all CMD(v)	
Day 120 (45)	e-mail assessment of applicant response	
Day 120 (-60)	Second CMD(v) meeting	
Day 120 (-60)	Agreement reached e-mail final SPC, PI, Labelling to CMS (follow steps from **)	
If no agreement reached inform EMEA and refer to CVMP		

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Annex C

CHECK LIST for the REFERENCE MEMBER STATE FOR DECENTRALISED PROCEDURE		
- 3 months	Allocate procedure number	
- 3 months	Create procedure in CTS	
- 3 months	E-mail CMS/secretariat	
Before day -14	Receipt of dates of dispatch/receipt	
- 14 days	E-mail CMSs/applicant start of validation	
- 2 days	E-mail CMSs confirm validation	
Day 0	E-mail CMS start date and timetable	
Day 0	Update CTS with start date	
Day 70	Send PAR & drafts to CMS and applicant	
Day 70	Update CTS	
Day 100	Received CMS comments	
Day 105	Send LOQ to applicant	
Day 105	Update CTS	
CLOCK OFF PERIOD		
Day 106	Received applicant's response	
Day 106	Update CTS	
Day 120	Update AR	
Day 120	E-mail second phase timetable CMSs & applicant	
Day 120 (0)	Update CTS	
Day 120 (0)	Circulate AR / PL / Labelling/SPC to CMSs	
Day 145 (25)	Receive CMS comments	
Day 150 (30)	Circulate LOQII	
Day 170(50)	Applicant's response	
Day 70	Circulate RMS response to applicant, CMS and CMDv secretariat.	
Day 75	Send CMS pre-CMD(v) comments to applicant and CMD(v) secretariat.	
Day 77/78	CMD(v) for discussion	
Day 79 +	Inform applicant of CMD(v) outcome	
Day 82	Send Day 82 SPC, PL & Labelling to CMS	
Day 85	Send Day 85 SPC, PL & Labelling to CMS	
Day 89	Send AR, SPC, PL & Labelling to CMS and Applicant	
AGREEMENT REACHED		
Day 90	Send final e-mail close procedure	
Day 90 **	Update CTS	
Day 90	Send SPC to VMRI database	
Day 95	Receive mock ups	
Day 120	Grant national marketing authorisation	
Day 120	Complete IFAH questionnaire	

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NO AGREEMENT – REFERRAL		
Day 90 + 7	Complete CMD(v) TEM/011 referral form	
Day 90 + 7	E-mail form, AR, SPC, PL, Labelling to CMS and CMD(v) secretariat	
Day 120	E-mail draft list of concerns to all MS	
Day 120 +	CMD(v) meeting	
Day 120 (15)	E-mail applicants response to all CMD(v)	
Day 120 (45)	e-mail assessment of applicant response	
Day 120 (-60)	Second CMD(v) meeting	
Day 120 (-60)	Agreement reached e-mail final SPC, Labelling to CMS (follow steps from **)	
If no agreement reached inform EMEA and refer to CVMP		

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Annex D

CHECK LIST for the REFERENCE MEMBER STATE FOR DECENTRALISED PROCEDURE WHERE RVMP IS NOT AUTHORISED IN RMS		
- 3 months	Allocate procedure number	
- 3 months	Create procedure in CTS	
- 3 months	E-mail CMS/secretariat	
Before day -14	Receipt of dates of dispatch/receipt	
Before day -14	Request details of RVMP using Annex 1 CMD(v) GUI/006	
- 14 days	E-mail CMSs/applicant start of validation	
- 2 days	E-mail CMSs confirm validation	
Day 0	E-mail CMS start date and timetable	
Day 0	Update CTS with start date	
Day 70	Send PAR & drafts to CMS and applicant	
Day 70	Update CTS	
Day 100	Received CMS comments	
Day 105	Send LOQ to applicant	
Day 105	Update CTS	
CLOCK OFF PERIOD		
Day 106	Received applicant's response	
Day 106	Update CTS	
Day 120	Update AR	
Day 120	E-mail second phase timetable CMSs & applicant	
Day 120 (0)	Update CTS	
Day 120 (0)	Circulate AR / PL / Labelling / SPC to CMSs	
Day 145 (25)	Receive CMS comments	
Day 150 (30)	Circulate LOQII	
Day 170(50)	Applicant's response	
Day 70	Circulate RMS response to applicant, CMS and CMD(v) secretariat.	
Day 75	Send CMS pre-CMD(v) comments to applicant and CMD(v) secretariat.	
Day 77/78	CMD(v) for discussion	
Day 79 +	Inform applicant of CMD(v) outcome	
Day 82	Send Day 82 SPC, PL & Labelling to CMS	
Day 85	Send Day 85 SPC, PL & Labelling to CMS	
Day 89	Send AR, SPC, PL & Labelling to CMS and Applicant	
AGREEMENT REACHED		
Day 90	Send final e-mail close procedure	
Day 90 **	Update CTS	
Day 90	Send SPC to VMRI database	
Day 95	Receive mock ups	
Day 120	Grant national marketing authorisation	

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Day 120	Complete IFAH questionnaire	
NO AGREEMENT – REFERRAL		
Day 90 + 7	Complete CMD(v) TEM/011 referral form	
Day 90 + 7	E-mail form, AR, SPC, Labelling to CMS and CMD(v) secretariat	
Day 120	E-mail draft list of concerns to all MS	
Day 120 +	CMD(v) meeting	
Day 120 (15)	E-mail applicants response to all CMD(v)	
Day 120 (45)	e-mail assessment of applicant response	
Day 120 (-60)	Second CMD(v) meeting	
Day 120 (-60)	Agreement reached e-mail final SPC, Labelling to CMS (follow steps from **)	
If no agreement reached inform EMEA and refer to CVMP		