Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary

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CMDv/BPG/001

BEST PRACTICE GUIDE

for

Veterinary Mutual Recognition Procedure (MRP)

Edition 04

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1. INTRODUCTION

With the entry into force of Directive 2004/28/EC amending Directive 2001/82/EC, the Decentralised Procedure (DCP) is created. Except for cases where the Centralised Procedure is either compulsory or optional, if an applicant/Marketing Authorisation Holder wishes to have a Marketing Authorisation (MA) recognised in more than one Member State (MS), then he will have to use either the Mutual Recognition Procedure (MRP) if the product has a MA in the Community, or the Decentralised Procedure if the product is not authorised in the Community.

2. AIM AND SCOPE

This Best Practice Guide (BPG) has been prepared for use in veterinary MRP by Reference Member States (RMS), Concerned Member States (CMS) as well as the applicant, in order to facilitate a smooth running of the procedure. It does not apply to Repeat Use or Decentralised Procedures, for which specific BPGs exist.

3. REFERENCES AND RELATED DOCUMENTS

- Directive 2001/82/EC[1];
- Notice to Applicants. Volume 6A, Chapter 2 [2];
- TIGes vet guidance on eSubmissions (link)
- Guideline on the definition of a potential serious risk to human or animal health or for the environment[3];

Full list of CMDv documents related to this BPG can be found at the end of the document

4. DESCRIPTION OF THE PROCEDURE

The MRP is divided into three steps: Pre-procedural step; Assessment step and National step. An additional step (referral to CMDv) will occur when agreement on a positive Final Assessment Report of the RMS cannot be reached by all CMS on Day 90.

The RMS may close the procedure at any time point during the procedure, if consensus is reached between MS.

4.1 Pre-procedural phase and general requirements

All communications between RMS and CMS will be sent by email as appropriate in accordance with the relevant guidance documents (see Annex 1).

All competent authorities should maintain CTS (Communication Tracking System) and ensure that the information is updated continuously throughout the procedure.

[1] as amended by Directive 2004/28/EC
[2] Notice to Applicants (Volume 6) is available on the http://ec.europa.eu/health/documents/eudralex/vol-6/index_en.htm website of the Commission.
[3] Guideline available on the website of the Commission: http://ec.europa.eu/health/files/eudralex/vol-6/newdoc/2006_c_132_08_en.pdf

With respect to communications from the applicant, submission of the applicant's responses or other clarification by e-mail, this does not automatically mean that paper copies or electronic submission in an agreed format are not needed. It is the duty of the applicant to check how MS need to receive the documentation. In this respect, useful guidance can be found on the CMDv website, particularly the following documents:

- CMDv-GUI-22 *Format and no. of copies of the dossier for new MAAs via national, MRP or DCP,* doc ref no. EMA/CMDv/299619/2011
- *Member States' additional national requirements for submissions*, doc ref no. EMA/CMDv/691257/2012

Discussion with the intended RMS

The applicant will request the competent authority of the Member State where the product is authorised to act as RMS. The RMS will discuss with the applicant whether the dossier needs updating, if necessary by way of variation/s, prior to initiating the MRP.

The RMS should give regulatory and scientific advice or recommendations to the applicant in order to facilitate the procedure.

At this stage, the RMS should make the applicant aware that in some Member States multi-lingual labels are necessary. Furthermore, in some cases the Applicant may seek to have combined labels in more than one Member State. In such cases, a space restriction might exist and a solution should be sought in trying to fulfil the legal requirements for harmonisation, national legal requirements and the safe use of veterinary medicinal products. The submission of mock-ups reflecting the maximum number of intended languages to be included on multilingual packs or minimum 3 x EN can facilitate this process.

If the package is intended for more than one MS the applicant should also be advised to seek agreement on the name by the CMS*s* affected as early as possible. [4]

Following completion of any necessary variations and the submission of the formal request to act as the Reference Member State with the consolidated dossier, the future RMS will update the Assessment Report (AR) within 90 days. Assessment reports should be written according to the relevant CVMP Guideline.

No more than 4 months before the intended starting date the RMS creates the procedure in the Communication Tracking System (CTS) by allocating a procedure number to the MRP application (in accordance with the numbering system described in Chapter 2, Volume 6A of the NtA and CMDv/SOP/003 - Allocation of the MRP/DCP application number). The RMS will inform the applicant accordingly.

The clock-start date for the procedure should, after agreement with the applicant, be set according to the agreed list of start dates. The applicant should notify the intended CMS of the intention to submit an application. The RMS will inform the CMS, one month before the start of the procedure, of the proposed start date and timetable.

[4] See also CMDv Q&A nr.130

Submission to CMS

The applicant will submit the application simultaneously to the competent authorities of each of the Member States where a marketing authorisation is to be sought.

The applicant is required to give an assurance, usually in the cover letter accompanying the application that the dossier as submitted is identical in all Member States concerned. A template for this cover letter is available in the CMDv website.

The application should be made in accordance with the legal basis applied for. Guidance on format, appropriate number of copies of the dossier, language requirements, fees etc. can be found in the CMDv website.

In case of electronic submissions the "Guideline on the specifications for provision of an electronic submission (e-submission) for a veterinary medicinal product" also applies.

Text proposals for SPC, PL and labelling in English are acceptable at this stage. The submission of mock-ups reflecting the maximum number of intended languages on multilingual packs is strongly advisable (in any case minimum 3 x EN).

The applicant should notify the RMS and CMS of the dates of dispatch and receipt of the dossier.

It is the duty of all CMS to react immediately if they have not received the application.

Validation

Once the RMS is informed that the application has been submitted to all CMS and dispatch has been completed, the RMS will start the validation period by sending the assessment report via e-mail to all CMS and to the applicant and indicating a proposed timetable for the procedure.

The CMDv has agreed to follow automatic validation procedure for MRP applications as defined in CMDv/BPG/008. The CMS has the duty to update the status of the CTS record continuously to reflect the current (validation) status.
All MS involved in the procedure should validate the application within 14 calendar days.

By day 7 of the validation period the RMS will update the applicant and the CMS with the validation status and inform about the planned start date. The CMS who have not validated, will have 7 days to confirm validation. If no confirmation is received, the RMS will assume the application is valid

Validation issues of an administrative and/or regulatory nature should be notified to the RMS, CMS and applicant by e-mail as soon as possible and within 14 days following the receipt of the application (see also CMDv/GUI/003).

If a CMS has stated that the application is not valid, the clock will not be started until that CMS confirms that the issue(s) has/have been resolved and the application is valid. The CMS must inform the RMS and applicant that the application has become valid immediately after the missing information or fee has been supplied.

If the application is still not considered valid after supplements, the applicant will be advised to withdraw the application in the relevant MS.

In any case, the procedure cannot be started until all validation issues have been resolved, unless the objecting CMS has accepted a suitable commitment to resolve them.

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

At this point the RMS will check and update the information and fill in procedure start date (Day 0) in the CTS.

4.2 Assessment Phase

CMS comments (by Day 54)

As soon as possible, but no later than Day 54, each CMS should identify and communicate to the RMS, other CMS and the applicant (via RMS), any outstanding concerns regarding a potential serious risk to human or animal health or the environment, which, if unresolved, would lead to referral to the CMDv and possible arbitration. Comments would include major issues regarding the Assessment Report, quality, safety or efficacy of the product, or the SPC PL and/or labelling. Any national requirements regarding the product name that would impact on the feasibility of a multi-lingual pack should be raised and discussed during the assessment phase of the procedure, not in the national phase at the end.

The CMSs should present all questions in the agreed format for the Response Report (CMDv/TEM/007) and should include a clear explanation of the grounds for the concern. Other points for clarification together with considerations on the SPC, PL and labelling will also be included in this response report.
All questions should be carefully screened within the national agencies. All CMS comments containing confidential information (for example regarding the restricted part of the ASMF) should be notified (in the title of the e-mail) so that the RMS will be aware of what comments can be sent to the applicant. In such cases, it may be advisable to send two emails, one containing the confidential comments and the other the non-confidential comments.

List of questions (by Day 57)

The RMS should forward the Day 54 comments from each CMS directly to the Applicant as soon as they are received. The RMS will prepare the list of questions (LOQ) according to the agreed format (CMDv/TEM/001) and send this to the Applicant and CMS by Day 57 of the procedure at the latest.

The RMS should also inform the applicant in case questions on the closed part of the ASMF have been forwarded to the ASMF holder, indicating whether these relate to potential serious risk issues and/or points for clarification.

Applicant's response (Day 65)
In accordance with the agreed format the applicant should send the response (Resp-LOQ) by Day 65 at the latest by email to the RMS, who will forward this to all the CMS. Applicants must ensure that necessary paper /electronic copies, as published on the CMDv website, arrive by Day 67 at the latest in all CMS. All changes to the SPC, PL and labelling proposed by the Applicant must be done using the 'track changes' tool in the originally proposed versions in order to record changes made throughout the procedure The applicant should note that changes to the proposed product name initiated by the applicant or by a Concerned Member State during the procedure should be clearly and immediately communicated by the applicant to

the CMS affected by the proposed change in a separate mailing, copying the Reference Member State. An updated exchange page of the application form and annex 5.18 will have to be submitted to the NCA if a new name is agreed during the procedure.

RMS assessment of applicant's response (Day 70)
The RMS should evaluate responses given by the applicant to the issues raised by a CMS and communicate this evaluation (AR-Resp-LOQ) in writing to all CMS and to the applicant by Day 70 at the latest (by e-mail).

CMS comments (Day 75)
All CMS should send their remaining issues by Day 75 at the latest to the RMS, the other CMS and the applicant (via the RMS), in order for the RMS to prepare for a consultation with CMS as to whether a virtual product discussion is necessary.

At the CMDv meeting (Day 77)
The RMS will consult CMS in order to agree whether a virtual product discussion is necessary. This meeting will be held during the following week; usually on the Monday/Tuesday (i.e. on Day 81/82*)*.
At the request of the RMS/CMS the product discussion may, where deemed necessary/appropriate, be held during the CMDv plenary meeting. In these special cases the RMS is required to liaise with the secretariat as soon as possible.

Procedure-related, outstanding major questions that are considered to be of a principal nature may also be highlighted and presented by RMS/objecting CMS at the CMDv plenary meeting.

If there are no issues of potential serious risk to resolve, it is not necessary for the application to be discussed unless the decision to hold a discussion has been agreed by the member states concerned. The RMS will announce cancellations at the CMDv plenary meeting and by e-mail communicate the same information via the List V-CMD, List V-MRNA and CMDv@ema.europa.eu. In principle, applications with only one CMS are not discussed. However, discussion to resolve any points of disagreement relating to the AR, draft SPC, PL and labelling is to be encouraged, i.e. via the List V-MRNA.

Representatives of all CMS (including experts where possible) should be available by telephone, fax or e-mail (in addition to Eudramail) between Day 77 and 90 of the procedure.

Virtual Product Discussion (Day 81/82)

Issues of potential serious risk, together with issues concerning the AR, SPC, PL and labelling, should be scheduled for virtual discussion, by default, on Day 81/82 of the procedure

All issues should be resolved as far as possible during the virtual product discussion. (See also CMDv/GUI/021 – GUIDANCE Virtual CMDv product discussions).

Representatives of all CMS who raised potential serious risk (PSR) concerns, which were not solved by the Applicant's answers, should participate in the virtual product discussion and should be able to resolve issues on behalf of their competent authority (See also CMDv Rules of Procedure). It is strongly recommended that the national expert(s) raising PSR issues participate(s) in the discussion..

When the representative from the CMS which raised a PSR issue cannot attend the discussion,

the RMS and CMDv Secretariat should be informed, if possible at least one working day before the discussion is due to take place. In this case, a contact name and telephone number for the CMS should be provided along with a response report from that CMS.

The RMS should actively co-ordinate the dialogue between the participants and all efforts should be made to resolve any outstanding issues.

After the virtual product discussion

The RMS should inform the applicant immediately after the virtual product discussion of the views presented by the CMS during the CMDv discussion and give guidance on the measures proposed by the CMS and/or RMS, including amendments to be made to the SPC, PL and labelling.

Within 48 hours of the conclusion of the virtual meeting, the RMS should forward to the CMDv Secretariat a brief summary note of the outcome of the meeting (position of MS and major issues possibly leading to referral), with a copy to the List V-CMD and List V-MRNA .(

As soon as possible after communication of the virtual product discussion, the RMS will receive from the applicant a revised draft SPC, PL and labelling with track changes, incorporating all of the agreed changes. The RMS will check this draft SPC, PL and labelling and circulate them to all CMS involved in the procedure, by Day 83 at the latest. If necessary an updated AR is circulated as well. If agreed with the Member State concerned the applicant can submit draft translations in order to expedite issue of the national authorisations.

If a further modification of the SPC, PL and labelling is then still necessary, a new draft of these should be circulated on Day 85 and commented on by Day 88. By Day 90 the CMS should confirm their final position in respect of granting a marketing authorisation. All points must be agreed on regarding the SPC, PL and labelling on or before Day 90.

Any request for post authorisation commitments must have been put forward to the applicant by 13:00 on day 88, at the latest. (see point 4.6)

Day 90

On Day 90 the procedure is closed preferably at 13:00 GMT. The RMS will circulate an e-mail to all CMS and the applicant indicating the final outcome of the procedure.

- A list of CMS agreeing or disagreeing with the final conclusion of the RMS
- If all Member States are prepared to grant a marketing authorisation - the Common Renewal Date and
- List of any agreed commitments (see 4.6 below)
- PSUR submission cycle.
- The final SPC, PL and labelling texts (in English)

The following should also be circulated as soon as available

- The finished product specifications (at release and at the end of shelf life)

If all CMS agree to grant a marketing authorisation for the product, CMS will proceed nationally to grant a marketing authorisation (see 4.4). The RMS will update CTS accordingly and upload the final SPC to the system.

If one or more CMS cannot agree to accept the product the matter will be referred to the CMDv for the 60 day referral process (see 4.3). The reasons for non-acceptance from CMS will be circulated to the RMS, the other CMS and to the applicant, using template CMDv/TEM/002a (RMS) and CMDv/TEM/002b (CMS).

The applicant can withdraw the application from a CMS at any stage of the procedure, but this will not prevent the CMDv referral phase in the case of disagreement between MS based on potential serious risk.

4.3 CMDv referral procedure

If any issues of potential serious risk are not solved by Day 90, the CMDv referral procedure will apply as detailed in the CMDv/SOP/001.

At Day 90 the Member States concerned will give detailed reasoning for their disagreement to the RMS, other CMSs and the applicant according to the agreed format. The RMS will refer these points of disagreement to the CMDv without delay.

The CMS will use their best endeavour to reach an agreement. If agreement is reached during this referral procedure, the RMS closes the procedure and informs the applicant accordingly. The procedure continues with the national step leading to issues of national authorisations. If no agreement is reached the matter will be referred to CVMP (see point 4.7).

4.4 National Step – granting of the Marketing Authorisation

If agreement is reached at the conclusion of the procedure (Day 90), within 5 days, the applicant will send high-quality national translations of final SPC, PL and labelling to all MS concerned.

The granting of the MA is linked with the reception of high-quality translations. Please refer to the CMDv's best practice guide (no. 017) for the submission of high-quality national translations (doc ref. no. EMA/CMDv/68043/2013)[5].

National translations will be submitted in accordance with the CMDv template for product information for MRP and DCP. Additional nationally required information in the PL and labelling will be included in the "blue box". These are published on the CMDv website.

Templates for product information in all languages have been published on the HMA/ CMDv website.

Competent authorities should ensure that authorisations are granted within 30 days after the conclusion of the procedure, provided that acceptable translations are submitted (i.e. correct translation of the SPC, PL and labelling in the language(s) of the MS and mock-ups, as required).

4.5. RMS Conclusion

[5] Foreseen to publish this document later in Q3 2013

The RMS should also prepare the publicly available assessment report in accordance with the CMDv/BPG/010 and CMDv/SOP/016

4.6 Commitments

In principle, commitments should not be requested of the Applicant by competent authorities during the assessment of the application. Any post procedure commitment, which will be binding for all involved Member States, should be exceptional and must be requested by the RMS on behalf of the CMS. CMS who request such a commitment should provide full justification to the RMS.

Commitments should be made in a written format, an official signed letter from the Applicant clearly stating the time limits for the submission of data. Documentation from the applicant relating to completion of commitments must be sent to the RMS and all CMS simultaneously.

The RMS will provide the CMS with an assessment of the documentation by email with details of the timetable for comments.

If time limits are exceeded or data are insufficient, the matter will be brought back to CMDv for discussion.

4.7 Referral to CVMP

If CMDv has not reached agreement at day 60 of the referral procedure, the RMS should notify the EMA/CVMP in the agreed format (using template CMDv/TEM/011a and include the CMS reasons for disagreement (CMDv/TEM/011b) in the notification)

ANNEX 1

LIST OF RELATED DOCUMENTS

EMA/TIGes/VET	Guideline on e-submission for Veterinary Products
CMDv/ROP/001	CMDv Rules of Procedure
CMDv/SOP/001	Disagreement in Procedures – referral to CMDv
CMDv/SOP/003	Allocation of the MRP/DCP application number
CMDv/SOP/006	Production and Publication of Public Assessment Reports
CMDv/BPG/003	Repeat use of the MRP and DCP
CMDv/BPG/008	Automatic Validation of Mutual Recognition Procedures
CMDv/BPG/009	Processing of SPC, Labelling and Packaging provided in support of Mutual Recognition and Decentralised Applications
CMDv/BPG/010	Reference Member State
CMDv/BPG/017	Submission of high-quality national translations[6]
CMDv/GUI/003	Management of e-mail use during procedures and standardisation of Subheadings
CMDv/GUI/006	Guidance for exchange of documentation relating to RVMP between MS
CMDv/GUI/015	CMDv Guidance for CTS Minimum data input
CMDv/TEM/006	QRD veterinary product information annotated template (EN and translations)
CMDv/TEM/018	Cover letter for new MA application
CMDv/TEM/ 007	Template CMS Comments MRP/DCP
CMDv/TEM/001	Template for the consolidated List of Questions (LOQ)
CMDV/TEM/003	Publicly Available Assessment Report for a Veterinary Medicinal Product
CMDv/TEM /2a	RMS referral notification to CMDv
CMDv/TEM/ 2b	CMS reason for CMDv referral
CMDv/TEM/11a	RMS Notification to the EMA/CVMP
CMDv/TEM/11b	CMS annex to RMS Notification for art 33(4) referral

[6] Foreseen to publish this document in Q3 2013

ANNEX 2

FLOW CHART

FLOW CHART for the MUTUAL RECOGNITION PROCEDURE	
Before day -14	Applicant discusses the application with RMS RMS will • Update the AR • Allocate procedure number • Create procedure in CTS • Inform CMS of proposed start date Submission of the dossier to the RMS and CMS
-14 Days	Circulation of the AR to CMS and applicant Automatic validation of the application
Day 0	Start of the procedure
Day 54	CMS send comments to RMS and applicant (via RMS)
Day 57	RMS circulates LOQ to the applicant and CMS
Day 65	Applicant sends response to LOQ
Day 70	RMS circulates assessment of response to LOQ to applicant and CMS
Day 81/82	CMDv virtual product discussion RMS informs applicant of outcome of discussions immediately after the meeting and sends brief summary note to CMDv Secretariat.
Day 83	Applicant sends new drafts of SPC, PL and labelling to RMS Translations may be included if agreement reached on the product information. RMS immediately forwards this to CMS
Day 84	CMS comments on SPC, PL and labelling
Day 85	If necessary, final drafts of SPC, PL and labelling
Day 88	CMS send final comment to RMS, including requests for commitments by 13:00 at the latest
Day 90	If consensus is reached, the RMS will close the procedure and circulate to CMS and Applicant, the Common Renewal Date, PSUR cycle, final SPC, PL and labelling, finished product specifications and a list of any agreed commitments. – if consensus not reached, referral to CMDv
National step	
5 days after close of procedure	Applicant sends high-quality translations to all member states concerned and mock-ups, if required.
30 days after close of the procedure	Granting of national MAs (subject to the submission of acceptable translations and, where required, mock-ups) if no referral to the CMDv.
30 days after close of CMDv referral procedure	Granting of national MAs in RMS and *all* CMSs if positive outcome of CMDv referral (i.e. no onward referral to the CVMP), subject to the submission of acceptable translations and, where required, mock-ups.