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

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CMDv GENERAL DOCUMENT

MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES

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Contents

1. LEGAL BASIS AND PURPOSE

Information in this CMDv general document "Mutual Recognition and Decentralised Procedures" is transferred from the document Notice to Applicants Volume 6 A Chapter 2 which has been deleted from the European Commission Website https://ec.europa.eu/health/documents/eudralex/vol-6_en. The information in this document, however, has been updated to take into account current practices.

The purpose of this document is to present the summary of general principles of mutual recognition and decentralised procedures. Details of the procedures can be found in the Best Practice Guides and Standard Operation Procedures which are located at the CMDv pages of the Heads of Medicines Agencies (HMA) website http://www.hma.eu/156.html.

The legal provisions covering the mutual recognition procedure and the decentralised procedure for veterinary medicinal products are contained in Directive 2001/82/EC as amended.

Both the mutual recognition procedure (MRP) and the decentralised procedure (DCP) aim at facilitating access to a single market by relying upon the principle of mutual recognition. Thus with the exception of those veterinary medicinal products which are subject to the centralised procedure (see guidance on European Medicines Agency (EMA) website http://www.ema.europa.eu/ema/), a marketing authorisation or the assessment in one Member State (the so-called Reference Member State, RMS) ought in principle to be recognised by the competent authorities of the other Member States (the so-called Concerned Member States, CMS).

If a CMS is requested to recognise a marketing authorisation granted or an application assessed by the reference Member State it can raise grounds that the veterinary medicinal product presents a potential serious risk as defined in the Guideline on the definition of a potential serious risk to human or animal health or for the environment in the context of Article 33(1) and (2) of Directive 2001/82/EC as amended (https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-6/newdoc/2006_c_132_08_en.pdf). Such grounds would have to be fully **justified** in order to ensure that they do not act as an indirect and artificial hindrance to the free movement of goods within the European Economic Area.

2. SCOPE

2.1 Applications eligible for the mutual recognition procedure (MRP) and decentralised procedure (DCP)

The MRP and DCP must be used for applications for marketing authorisation for veterinary medicinal products where an authorisation is sought in more than one Member State unless the application is submitted under the centralised procedure, see section 2.2

Variations of veterinary medicinal products that have been authorised via the mutual recognition or decentralised procedure or are subject to referral procedures under Articles 34 ("Harmonisation referral") and 35 ("Union Interest referral") of Directive 2001/82/EC as amended made *after* 1st January 1995 are required to use the mutual recognition procedure. However, an exception is provided under Article 35(2) of Directive 2001/82/EC: when the referral procedure concerns a range of veterinary medicinal products or a therapeutic class and the EMA may limit the procedure to certain parts of the authorisation (see Chapter 1 of the Notice to Applicants).

According to Articles 21(2) and 22 of Directive 2001/82/EC as amended Member States shall decline to assess national applications for marketing authorisations for veterinary medicinal products when they are informed that another Member State has either authorised a veterinary medicinal product which is the subject of an application for marketing authorisation in this Member State, or that an application for marketing authorisation for the same product is being examined in another Member State. In these cases, mutual recognition or decentralised procedure shall be followed.

Specific scenarios can occure in connection with use of MR/DC principles in Duplicate applications and Informed consent applications. For detailed information, rules and conditions see the relevant CMDv documents:

- CMDv/GUI-010 Recommendation on duplicate applications in mutual recognition and decentralised procedures
- CMDv/BPG/012 BEST PRACTICE GUIDE for Informed consent for MRP and DCP procedures

2.2 Exclusions

The mutual recognition procedure and decentralised procedure will **not be used** in following cases:

Applications for marketing authorisations for:

- products falling under the compulsory scope of the centralised procedure as set out in the Annex to Regulation (EC) 726/2004 i.e.

a) products developed by certain biotechnological processes,

b) medicinal products for veterinary use intended primarily for use as performance enhancers

- products where the company has selected to submit through the centralised procedure according to Article 3(2) and 3(3) of Regulation (EC) 726/2004, irrespective of whether the marketing authorisation was granted, was rejected (negative opinion), or the applicant withdrew his application after an assessment by the EMA of the submitted data.

However, if the dossier for a withdrawn veterinary medicinal product or a veterinary medicinal product which has had a negative opinion in the centralised procedure is supplemented with new data based on new pre-clinical studies and tests and clinical trials, the application is considered to be based on a new dossier. For those applications, the applicant can apply again through centralised, mutual recognition or decentralised procedure where applicable, in those cases where a centralised procedure is not compulsory.

- veterinary homeopathic products authorised according to Article 19(2) of Directive 2001/82/EC as amended, as stated in Article 43 of that Directive.

Extension applications:

- introducing in a veterinary medicinal product a proteinaceous component obtained through a biotechnology process listed in the Annex to Regulation (EC) 726/2004.
- of original veterinary medicinal products which have not been

  a) harmonised via national procedures,

  b) subject to referral in accordance with Article 34 or 35 of Directive 2001/82/EC as amended, or

  c) authorised by Member States following Directive 87/22/EEC ("Ex-concertation" procedure)

2.3 Coordination group for mutual recognition and decentralised procedures for veterinary medicinal products – CMDv

According to Article 31 of Directive 2004/28/EC the CMDv group consists of one representative per Member State of the EEA. An observer from the Commission and EMA may participate at the meetings. The EMA provides a secretariat to the CMDv. The group is responsible for the smooth functioning and good outcomes of mutual recognition and decentralised procedures with a mix of regulatory and scientific work.

The Chairperson of the veterinary coordination group shall be elected by and from amongst its members for a period of three years, renewable once. The Vice-Chairperson shall be elected by and from amongst its members for a term of two years

The Coordination group shall consider points of disagreement raised by Member States during mutual recognition or decentralised procedures, in relation to the assessment report, summary of product characteristics, labelling and package leaflet of a medicinal product on the grounds of potential serious risk to human or animal health or to the environment and make every effort to resolve issues to avoid referral to the Committee for Medicinal Products for Veterinary Use (CVMP) for arbitration.

According to the Commission Regulation (EC) No 1234/2008 as amended the Coordination group shall provide recommendations on the classification of unforeseen variations, use their best endeavours to reach agreements in case of Member States disagreements in variation applications and choose a reference authority for worksharing in specified cases of variation procedures.

The Coordination group, as provided for in legislation, shall support worksharing between Member States where appropriate.

Further details on the group's principles of operation can be taken from the Rules of Procedures (CMDv ROP-001).

All publicly available documents related to the work of the CMDv (e.g. Rules of Procedure, Report for Release, recommendations, position papers, Best Practice Guides, Standard Operating Procedures) are published on the website for the Heads of Medicines Agencies http://www.hma.eu/156.html.

3. THE MUTUAL RECOGNITION PROCEDURE (MRP)

3.1 General principles of MRP

The mutual recognition procedure is to be used in order to obtain marketing authorisations in several Member States where the veterinary medicinal product in question has received a marketing authorisation in at least one Member State at the time of application.

As set out in Art. 32 (4) of Directive 2001/82/EC as amended Member States have to approve during the mutual recognition procedure the assessment report of the reference Member State, the summary of product characteristics, the package leaflet and the labelling.

Specific national requirements for items to appear on the product information, for example information on distribution, have to be presented in a so-called "blue box".See also CMDv Guidance GUI-27 Packaging 'blue-box' requirements and

additional information on labelling/package leaflet for products authorised via national, mutual recognition, decentralised or centralised procedures.

The mutual recognition procedure is divided into the following steps:

Pre-procedural phase

- Discussion between the applicant and the intended reference member state
- Update of the dossier via variations, if necessary
- Validation of the dossier by the reference member state
- Update (and translation) of the assessment report by the reference member state
- Validation of the dossier by the concerned member states

Assessment phase

- Comments from the concerned member states regarding the assessment report, the SPC, PL and/or labelling
- Response from the applicant to the list of questions
- Virtual product discussion, if needed
- Conclusion by the concerned member states by day 90
- CMDv referral procedure, if no consensus

National phase

- If agreement has been reached, submission of high quality translations of the final SPC, PL and labelling texts and mock-ups where necessary
- Issuing marketing authorisation once the translations and mock-ups (where necessary) are acceptable

The process of MRP is described in detail in the CMDv/BPG/001 Best Practice Guide for Veterinary Mutual Recognition Procedure (MRP).

The process for validation of the application dossier is described in the CMDv/BPG/008 Best Practice Guide for automatic validation of applications in the mutual recognition / decentralised procedures.

No agreement could be reached during the MRP

In exceptional circumstances, where a CMS considers that there are grounds for supposing that authorisation of the veterinary medicinal product concerned may present a potential serious risk to human or animal health or for the environment, the Member State shall refer the matter to the CMDv .

See also CMDv/SOP/001 Standard Operation Procedure for Disagreement in procedures, Referral Art. 33(1) to CMDv

Withdrawal in MRP

An application for a marketing authorisation may be withdrawn from a CMS by the applicant at any time during the MRP but this may not prevent a potential serious risk concern being taken forward to a suitable CVMP referral.

3.2 Repeat Use Procedure (RUP)

It is possible to use the MRP more than once for subsequent applications to other Member States in relation to the same veterinary medicinal product (so- called repeat use procedure, RUP). It is recommended that, wherever feasible, the marketing authorisation holder considers involving all Member States where the product is intended to be marketed, in the first use of MRP/DCP (initial application for marketing authorisation).

Each subsequent procedure will be treated as a new MRP including the possibility of new CMS to raise objections based on a potential serious risk to human or animal health or for the environment.

Member States concerned in any repeated mutual recognition procedure shall normally recognise the authorisation granted in the previous procedures. The same principles apply for the repeat use as for the first use of MRP/DCP regarding the cases where there is no agreement and for the withdrawal

The CMDv has released a Best Practice Guide for the Repeat Use Procedure (CMDv/BPG/003) wherin the procedure is detailed.

4. DECENTRALISED PROCEDURE (DCP)

4.1 General principles of DCP

The DCP is to be used in order to obtain marketing authorisations in several Member States where the veterinary medicinal product in question has not yet received a marketing authorisation in any Member State at the time of application.

As set out in Directive 2001/82/EC as amended Member States have to approve during DCP the assessment report, the summary of product characteristics, the package leaflet and the label.

Specific national requirements for items to appear on the product information, for example information on distribution, have to be presented in a so-called “blue box”.

See also CMDv Guidance GUI-27 Packaging ‘blue-box’ requirements and additional information on labelling/package leaflet for products authorised via national, mutual recognition, decentralised or centralised procedures.

The decentralised procedure is divided into the following steps:

Pre-procedural step

- Discussion between the applicant and the intended reference member state
- Submission of the dossier to all member states where marketing authorisation is sought
- Validation of the dossier

Assessment step I

- Circulation of the preliminary assessment report from the reference member state on day 70
- Comments from the concerned member states regarding the preliminary assessment report, SPC, PL and/or labelling and the if necessary, the dossier
- Clock stop
- Response from the applicant to the list of questions

Assessment step II

- Circulation of the draft assessment report from the reference member state on day 120
- Comments from the concerned member states regarding the preliminary assessment report, SPC, PL and/or labelling
- Response from the applicant to the list of questions
- Virtual product discussion, if needed
- Conclusion by the reference and concerned member states by day 210

On day 210 the following options are applicable:

- All CMS agree and RMS assessment is positive → national step
- One or more CMS cannot agree and RMS assessment is positive → CMDv referral
- RMS concludes the benefit-risk balance of the product is negative → application will be refused

National step

- Submission of high quality translations of the final SPC, PL and labelling texts and mock-ups (where necessary)
- Issuing marketing authorisation once the translations and mock-ups (where necessary) are acceptable

The process of DCP is described in detail in the CMDv/BPG/002 Best Practice Guide for Veterinary Decentralised Procedure.

The process for validation of the application is described in the CMDv Best Practice Guide for automatic validation of applications in the mutual recognition / decentralised procedures (BPG-008).

No agreement could be reached during the DCP

In exceptional circumstances, where a CMS considers that there are grounds for supposing that authorisation of the veterinary medicinal product concerned may present a potential serious risk to human or animal health or for the environment, the Member State shall refer the matter to the CMDv.

See also CMDv/SOP/001 Standard Operation Procedure for Disagreement in procedures, Referral Art. 33(1) to CMDv

Withdrawal in DCP

An application for a marketing authorisation may be withdrawn by the applicant from a CMS at any time during the DCP but this may not prevent a potential serious risk concern being taken forward to a suitable CVMP referral.

5. CMDv PROCEDURE ON DISAGREEMENT ON POTENTIAL SERIOUS RISK TO HUMAN OR ANIMAL HEALTH OR FOR THE ENVIRONMENT AND ARTICLE 33(4) REFERRAL ('MUTUAL RECOGNITION AND DECENTRALISED REFERRAL')

5.1. CMDv 60 day procedure

Where one or more CMS cannot approve the assessment report, the SPC, labelling or PL on grounds of a potentially serious risk to human or animal health or for the environment the points of disagreement shall be referred to the CMDv. It is the duty of the RMS to submit a notification of a referral under article 33(1) of Directive 2001/82/EC as amended.

All involved Member States shall use their best endeavours to reach agreement within 60 days following the notification of disagreements at the level of the CMDv. During the 60-day procedure no clock-stop is foreseen.

During the 60-day procedure, the applicant shall be allowed by CMDv to make their point of view known, orally or in writing. Whether a written procedure or a hearing is the most appropriate way to reach an agreement has to be decided in consultation with the applicant.

During this phase Member States that have approved the assessment report, the

SPC, labelling and PL are not allowed to issue a marketing authorization.

The CMDv/SOP/001 Standard Operation Procedure for Disagreement in Procedures Referral Art.33(1) to CMDv should be followed.

5.2. End of CMDv referral procedure

If, within 60 days CMDv referral procedure, Member States reach an agreement (consensus), the RMS shall record the agreement, close the procedure in accordance with the CMDv BPG for relevant procedure and inform the applicant and CMDv accordingly.

If Member States fail to reach an agreement within the 60-day period, the RMS shall immediately inform the EMA, with a view to the application of the procedure under Articles 36, 37 and 38 of Directive 2001/82/EC as amended. The EMA shall be provided with a detailed statement of the matters on which the CMS have been unable to reach agreement and the reasons for their disagreement. A copy shall be forwarded to the applicant.

Any matter dealt with by the CMDv in a previous mutual recognition procedure or decentralised procedure may not be raised again in any subsequent procedure except for justified reasons. Matters dealt with in an arbitration in a previous mutual recognition procedure or decentralised procedure may not be raised again in any subsequent procedure.

Member States that have approved the assessment report, the draft SPC, the labelling and package leaflet of the RMS may, at the request of the applicant, grant the marketing authorization for the veterinary medicinal product without waiting for the outcome of the procedure laid down in Article 36 of Directive 2001/82/EC as amended. In that case, the authorisation granted shall be without prejudice to the outcome of that procedure.

5.3. Article 33(4) Mutual Recognition and Decentralised referral procedure

In the case of unsolved disagreement in the CMDv procedure, the RMS will refer the matter to the EMA/Committee for Medicinal products for Veterinary Use (CVMP) for arbitration with a detailed reasoning for the disagreement.

During the referral procedure all members of the CVMP are involved in the evaluation and opinion taking process. The Commission decision following the referral procedure shall be addressed to all Member States. Those Member States where the veterinary medicinal product is authorised or where an authorisation is pending shall be required to take action following the Commission decision on arbitration within 30 days. Member States in which an application has not been submitted are bound by the decision in the event that an application is subsequently submitted.

However, in such cases of repeat use of the mutual recognition procedure, Member

States can raise issues which they consider grounds of a potential serious risk to human or animal health or for the environment provided these grounds were not already covered in the earlier referral. In case such grounds are raised in the RUP, they will lead to a new discussion in the CMDv and, possibly, to a new referral procedure by EMA/CVMP.

CMDv has published guidance for actions after an opinion from an article 33 CVMP referral to describe the actions that will follow the opinion of the CVMP in case of negative or positive opinion for the referral (CMDv/GUI/009 GUIDANCE for Actions after an opinion from an article 33 CVMP referral).

Further details on the referral procedure are contained in Chapter 3 of the Notice to Applicants Volume 6A.

6. PROCEDURE AFTER THE FINALISATION OF A MRP or DCP

6.1 Changes to the marketing authorisation in the RMS after finalisation of the MRP

Where, in the course of the MRP, the RMS and CMS agree that changes to the current authorisation in the RMS are necessary in order for MRP to take place, the marketing authorisation holder/applicant and RMS will introduce these using the appropriate (national) procedures.

6.2 Maintenance of identical dossiers

Having the benefit of MRP/DCP also carries through the life of the veterinary medicinal product. Thus, variations to a veterinary medicinal product which has benefited from mutual recognition or a referral in accordance with Articles 34 or 35 of Directive 2001/82/EC as amended are required to use the mutual recognition procedure. In this way, the SPC, package leaflet and labelling of the marketing authorisation, which has been harmonised, continues to be consistent and identical in all Member States where the veterinary medicinal product is authorised.

6.3 Renewals

In accordance with Article 28 of Directive 2001/82/EC as amended the marketing authorisation shall be renewed after 5 years on the basis of a re-evaluation of the risk/benefit balance by the competent authority of the Member States where it is authorised. Once renewed, the marketing authorisation shall be valid for an unlimited period unless the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal.

The guidance and procedure for renewal procedures can be found from Guidelines on Processing of Renewals in the Mutual Recognition and Centralised procedures (NtA Volume 6C) and the CMDv BPG-007 Best Practice Guide for Handling Renewals in the Mutual Recognition and Decentralised Procedure.

6.4 Extension application

Extensions to marketing authorisations for veterinary medicinal products can be made, provided that the conditions reflected in Annex I of Regulation (EC) No 1234/2008 as amended are met.

6.5 Product Index and public assessment report

The MRP and DCP are based on the principle that veterinary medicinal products are approved or assessed by the RMS followed by a 90/210- days period where the CMS(s) consider the RMS's assessment report.

The RMS shall prepare the publicly available assessment report according to Article 25(4) of Directive 2001/82/EC as amended.

In order to manage the 90/210-days procedure Members States operate a Communication and Tracking System (CTS) where the RMS updates the product information. The RMS and CMS update all events during the 90/210-days period.

The Veterinary Mutual Recognition Product Index (VMRI) includes all veterinary medicinal products authorised in the Member States following MRP or DCP. The particulars (product name, name of marketing authorisation holder, pharmaceutical form, species, strength, active substance(s), RMS and CMS, type of application) are automatically transferred from the Communication and Tracking System (CTS) into the VRMI. In the Product Index the final SPC is published together with the public assessment report (when available). The maintenance of the Product Index is a decentralised responsibility, which means that the competent authority acting as RMS or CMS is responsible for keeping the product index up to date.

The product index is located on http://mri.cts-mrp.eu/veterinary/

7. NUMBERING SYSTEM FOR THE PROCEDURES FOR MRP and DCP

Each veterinary medicinal product authorised through MRP or DCP is characterised by a unique and specific number for unambiguous identification (so-called procedure number). The principle of the system is as follows:

The RMS is responsible for allocating the number for all MRP/DCP i.e. marketing authorization application and and post-authorisation applications.

The number for a specific procedure is a unique combination of seven sections

CC/V/nnnn/sss/Y/vvv/g

The information in the sections are:

CC: Country code (2 digits) of the Reference Member State

AT: Austria	IT: Italy
BE: Belgium	LV: Latvia
BG: Bulgaria	LI: Liechtenstein
CY: Cyprus	LT: Lithuania
CZ: Czech Republic	LU: Luxemburg
DE: Germany	MT: Malta
DK: Denmark	PL: Poland
EE: Estonia	NL: The Netherlands
EL: Greece	NO: Norway
ES: Spain	PT: Portugal
FI: Finland	RO: Romania
FR: France	SK: Slovakia
HR: Croatia	SI: Slovenia
HU: Hungary	SE: Sweden
IE: Ireland	UK: United Kingdom
IS: Iceland	

V: medicinal product for veterinary use

nnnn: the 'Medicinal Product Number' characterising the medicinal product, related to an active principle and to an applicant or "xxxx" as placeholder for specific variations

sss: the 'Speciality Number' characterising the strength and/or pharmaceutical form and/or target species.

Y: the type of application to the veterinary medicinal product:

- MR for Mutual recognition Procedure
- DC for Decentralised Procedure
- IA for Type IA Notifications
- IB for Type IB Notifications
- II for Type II Variations
- R for Renewals
- E for Repeat-use Procedures
- X or DX for line extensions procedures
- WS Workshare variation

vvv: the chronological number for notifications/variations,

renewals, repeat use or line extensions procedures.

g: grouped variations qualifier (G)