

|   |
|---|
| <p><b><u>CMDv/SOP/001</u></b></p> <p><b>Standard Operating Procedure</b></p> <p><b>for</b></p> <p><b>Disagreement in procedures</b></p> <p><b>Referral Art. 33(1) to CMDv</b></p> <p><b>Edition number: 03</b></p> <p><b>Edition date: 12/11/09</b></p> <p><b>Implementation date: 01/01/2010</b></p> |
|---|

| EDITI<br>ON | DATE           | Page/secti<br>on        | REASON FOR CHANGE  |
|-------------|----------------|-------------------------|--|
| 01          | 27/10/<br>2006 | 3, 5, 6, 8              | Addition of Appendix - Guidance on Oral Explanations<br>References specified, References to templates for referral to the CMDv and the CVMP, respectively, added, The RMS to circulate an assessment of the Applicant's response (instead of an updated AR) around day 45.<br>Day 60 should be within 10 working days after the 2 <sup>nd</sup> CMDv meeting (instead of 5 working days)   |
| 02          | 15/05/<br>2008 | 3, 4, 5, 6,<br>7, 8, 10 | Update of the link to Heads of Agencies website and the Potential Serious Risk to human or animal health document<br>Clarification regarding the duty of the RMS to refer the application to CMDv referral<br>Clarification regarding the possibility to finalise the CMDv referral procedure if consensus is reached within the group earlier than day 60.<br>Deletion of the part "applicant should provide 30 hard copies of the handouts to CMDv secretariat". |
| 03          | 21/10/<br>2009 | 3,4, 5, 6, 8            | Update of the document to comply with the f the Variations Regulation (Commission Regulation (EC) 1234/2008)<br>Addition of variation to the CMDv referral and deletion of information when RMS has negative opinion. Update of Day 0 and deletion of 1 <sup>st</sup> CMDv meeting in the Annex I.   |

|  |  |  |
|--|--|--|
| <u>Prepared by:</u><br>Alenoosh Abedi (SE) | <u>Reviewed by:</u><br>Alenoosh Abedi (SE) | <u>Approved by:</u><br>Esther Werner (Chairperson) |
|--|--|--|

|   |              |
|---|--------------|
| <b>STANDARD OPERATING PROCEDURE</b><br><br><b>For</b><br><br><b>Disagreement in procedures – Referral to CMDv</b> | CMDv/SOP/001 |
|   | Ed: 03       |
|   | Page 2/10    |

## **TABLE OF CONTENTS**

- 1. AIM**
- 2. SCOPE**
- 3. REFERENCES AND RELATED DOCUMENTS**
- 4. GENERAL**
- 5. THE REFERRAL**
- 6. WITHDRAWAL**
- 7. PROCEDURE AND TIMETABLE**
- 8. OUTCOME OF THE PROCEDURE**
- 9. HOMEOPATHIC MEDICINAL PRODUCTS**
- 10. DATA SUPPORT**

### **ANNEXES**

- 1. Flow chart – Day 60 procedure**
- 2. Guidance on oral explanations to CMDv**

|   |              |
|---|--------------|
| STANDARD OPERATING PROCEDURE                  | CMDv/SOP/001 |
| For   | Ed: 03       |
| Disagreement in procedures – Referral to CMDv | Page 3/10    |

## 1. AIM

The aim of this document is to describe the procedure to be followed in case of disagreement between Member States in a particular Mutual recognition, Decentralised procedure and type II variations and those variations (including groupings) that are subject to the worksharing procedure.

## 2. SCOPE

The procedure covers applications for marketing authorisations (including repeat use procedures), renewal applications, extensions, type II variations according to Article 10(4) of the Variations Regulation and those variations (including groupings) that are subject to the worksharing procedure according to Article 20(8) of the Variations Regulation (EC) No 1234/2008 ) to existing authorisations.

## 3. REFERENCES AND RELATED DOCUMENTS

- Rules of Procedure of CMDv, CMDv/ROP/001
- Directive 2001/82/EC as amended by Directive 2004/28/EC
- Commission Regulation (EC) No 1234/2008
- Guideline on the definition of a potential serious risk to human or animal health or for the environment. <http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev6.htm>
- SMP for The role and responsibilities of the chairperson, vice chairperson and secretariat of the CMDv, CMDv/SMP/002
- BPG for Veterinary Decentralised Procedure, CMDv/BPG/002
- BPG for the Veterinary Mutual Recognition Procedure, CMDv/BPG/001
- BPG for Repeat Use of the Mutual Recognition Procedure, CMDv/BPG/003
- BPG for Handling Renewals in the Mutual Recognition and Decentralised Procedure, CMDv/BPG/007
- BPG for the Reference Member State, CMDv/BPG/010
- Meeting dates for CMDv, <http://www.hma.eu/CMDv.html>
- Template for referral to the CMDv, CMDv/TEM/002
- Template for notification of referral by the RMS to the EMEA/CVMP, CMDv/TEM/011
- CMDv letter to company with referral timetable Day 60 CMDv/TEM/020
- Timetable – CMDv referral Art. 33 – Day 60 CMDv/TEM/021
- Letter to company with referral list of concerns CMDv/TEM/022

## 4. GENERAL

When an application for a marketing authorisation is submitted according to the MRP or DCP the Member States concerned shall approve the draft (DCP) or updated (MRP) assessment report, the SPC and the labelling and PL within 90 days from receipt of the relevant documents according to Article 32(4) in the above-mentioned directive. In case of variation procedure the Member States concerned shall approve the final variation assessment report (FVAR) in accordance to the time lines mentioned in the Variations Regulation (EC) No 1234/2008.

|   |              |
|---|--------------|
| STANDARD OPERATING PROCEDURE                  | CMDv/SOP/001 |
| For   | Ed: 03       |
| Disagreement in procedures – Referral to CMDv | Page 4/10    |

Where one or more of the Member States concerned cannot approve the draft/updated assessment report, the FVAR, the SPC, labelling or PL, the points of disagreement shall be referred to the CMDv. The reasons for disagreement shall be on grounds of potential serious risk to human or animal health or to the environment and explained in detail by the disagreeing Member State(s).

#### 4.1 Abbreviations

|      |  |
|------|--|
| BPG  | Best Practice Guide  |
| CMDv | Co-ordination group for Mutual Recognition and Decentralised Procedures (vet)                      |
| CMS  | Concerned Member State   |
| CTS  | Communication and Tracking System for the mutual recognition procedure and Decentralised Procedure |
| CVMP | Committee for Medicinal Products for Veterinary use  |
| DCP  | Decentralised Procedure  |
| EMA  | European Medicines Agency  |
| FVAR | Final Variation Assessment Report  |
| MRP  | Mutual Recognition Procedure   |
| PL   | Package Leaflet  |
| RMS  | Reference Member State   |
| SPC  | Summary of Product Characteristics   |

## 5. THE REFERRAL

The Member State(s) that cannot approve the documents mentioned above shall provide a detailed statement of their reasons (using TEM-002) to the RMS, the other CMS, the CMDv secretariat at the EMA and the applicant on Day 90/210 at the latest in case of MRP and DCP or at the completion of the timetabled variation or worksharing procedure for variation procedures. It is the duty of the RMS to submit a notification of a referral under article 33(1) to the CMDv via/and CMDv secretariat.

The secretariat will propose a timetable for the 60-day referral procedure to the Chairperson of CMDv and the RMS within 3 working days after day 90/210<sup>1</sup>. Following their approval or in case no comments are received within 3 working days the CMDv secretariat sends this timetable with a notification letter in hardcopy and by e-mail to the applicant and by e-mail to all Members of CMDv.

The RMS should provide the Member States not previously concerned by the procedure with the final (latest) assessment report or FVAR, proposed SPC, labelling and PL and the explanation of the grounds for referral from disagreeing Member State/s. In addition, the applicant has the opportunity to provide its latest position. On request, other relevant information may be provided by the RMS.

<sup>1</sup> The starting date should be set close to Day 90/210 in order not to prolong the procedure but the dates of the CMD meetings have to be kept in mind.

|   |              |
|---|--------------|
| STANDARD OPERATING PROCEDURE                  | CMDv/SOP/001 |
| For   | Ed: 03       |
| Disagreement in procedures – Referral to CMDv | Page 5/10    |

## 6. WITHDRAWAL

The applicant can withdraw the application at any point in time. However, depending on the procedure and/or the actual day during the procedure when the question is raised, a withdrawal shall not prevent an issue of disagreement based on potential serious risk to human or animal health or to the environment from being referred to the CMDv. From the legislation it is clear that a referral to CMDv should be made if a Member State cannot approve the assessment report, the SPC, the labelling and the package leaflet within the time period laid down in article 32(4). The time period in Article 32(4) is the 90-day procedure of the mutual recognition procedure and the 90-day period following the submission of the draft documents referred to in Article 32(3), i.e. Assessment step II in the decentralised procedure. In the case of an MRP, the potential serious risk issue leading to a withdrawal of an application will automatically be referred to the CMDv. In the case of a DCP, a referral will only take place if the application is withdrawn after the draft documents have been sent to the concerned Member States, normally on day 120 of the procedure. In both cases mentioned it is the duty of the RMS, if the reason for withdrawal is based on a potential serious risk to human or animal health or to the environment raised by a CMS, to refer the matter to the CMDv for discussion.

For the variation and worksharing procedures the CMDv referral can be avoided when the variation application has been withdrawn from RMS and CMS.

## 7. PROCEDURE AND TIMETABLE

### 7.1 Parties involved

All members of the CMDv have the right to take part in the discussions in the CMDv. All Member States concerned by the application shall use their best endeavours to reach agreement on the action to be taken. This includes all the Member States where the application has been submitted even if the application is withdrawn in the MRP or after the draft documents have been sent to the concerned Member States, normally on Day 120 (in Assessment step II) in the DCP (see section 6).

The RMS will lead the scientific discussions in the CMDv. There will be discussions in two CMDv meetings if necessary, see below.

### 7.2 Procedure

The CMDv secretariat coordinates the procedure whilst the RMS remains responsible for the handling of matter(s) of disagreement.

- The secretariat proposes and sends the timetable agreed by the chairperson and the RMS (see section 5).
- RMS and disagreeing CMS should agree on a list of concerns/questions and forward this to the CMDv secretariat. The secretariat sends the agreed list of concerns/questions to the applicant and the members of CMDv. The secretariat informs at the same time the applicant of the possibility of an oral hearing and the date by which confirmation should be received.

|   |              |
|---|--------------|
| <b>STANDARD OPERATING PROCEDURE</b><br><br><b>For</b><br><br><b>Disagreement in procedures – Referral to CMDv</b> | CMDv/SOP/001 |
|   | Ed: 03       |
|   | Page 6/10    |

- The applicant is expected to prepare a response document and send it to the RMS. The RMS will immediately forward the responses to all CMDv members. No new studies from the applicant will be allowed unless otherwise agreed by the RMS and CMS. After receipt of the responses the RMS should circulate an assessment of the Applicant's response to all CMDv members.
- All members of CMDv should preferably state their view on the response document in writing at least 3 working days before the second CMDv meeting, by email to all CMDv members.
- The main scientific discussion including, if applicable, the applicant's hearing, will normally take place at the second CMDv meeting after the start of the procedure. The members of CMDv can be accompanied by relevant national experts. Preferably the experts should be others than those taking decisions in the CVMP but it is up to the individual Member States to decide on participation. The participation of the RMS assessor/s or their substitute is mandatory. The participation of the assessor/s (or their substitute) from the CMS raising issues of potential serious risk is also mandatory. The views from the applicant, presented orally or in writing, should be taken into account. To ensure the efficiency of the procedure, the Member States' representatives taking part in the discussion should have the proper mandate to make it possible to reach an agreement in principle during the meeting according to Article 33 of the Directive.
- Before day 60, all CMS must confirm their position to the RMS and to the applicant. However, in Article 33 of the Directive 2001/82/EC, as amended the time period given to CMDv to solve a disagreement is expressed as 'within 60 days'. By this wording it follows that the procedure could be ended earlier than Day 60 if agreement is reached. In these cases the RMS shall ensure that all CMSs have been provided the opportunity to state their final opinion until the end of the given timeline.

## **8. OUTCOME OF THE PROCEDURE**

There are only two possible outcomes of the procedure for MRP and DCP. Either there is consensus between the Member States where the application was submitted (including those where the application was withdrawn), on approving or refusing the application, or the matter should be referred to the EMEA for an arbitration procedure in accordance with Articles 36 - 38.

The possibility to withdraw the variation application is only applicable for type II variation or worksharing procedure.

If the Member States reach an agreement within the 60-day referral procedure, the RMS shall record the agreement, close the procedure and inform immediately the applicant, the members of CMDv and the secretariat of the outcome and finalise the AR. Subsequently the Member States shall adopt the decision in conformity with the agreed SPC, labelling and PL within 30 days after reaching the agreement. To obtain an approval in any Member State where the application has been withdrawn, a repeat use procedure will be necessary.

If the Member States fail to reach an agreement during the 60-day period, the RMS should immediately inform the EMEA and the applicant and provide a detailed statement from each

|   |              |
|---|--------------|
| <p style="text-align: center;">STANDARD OPERATING PROCEDURE</p> <p style="text-align: center;">For</p> <p style="text-align: center;">Disagreement in procedures – Referral to CMDv</p> | CMDv/SOP/001 |
|   | Ed: 03       |
|   | Page 7/10    |

of the objecting CMS of the unresolved issues/concerns and the reasons for the disagreement. The procedure described in the EMEA SOP on arbitrations should be followed.

According to article 33(6), the Member States that have approved the assessment report, the draft SPC and the labelling and package leaflet may, at the request of the applicant, grant an marketing authorisation at any point of time after the end of the CMDv referral procedure without waiting for the outcome of the CVMP arbitration procedure laid down in Article 36.

## 9. HOMEOPATHIC MEDICINAL PRODUCTS

For homeopathic veterinary medicinal products eligible for registration according to Article 16, Articles 32 and 33 (1) to (3) apply. However, Article 33 (4), (5) and (6) shall not apply (See article 43). This means that the procedure used for other veterinary medicinal products should be followed except for the possible referral to the CVMP. If the discussions in CMDv do not solve the disagreements the matter shall not be referred to the CVMP.

## 10. DATA SUPPORT

The CMDv secretariat keeps track of the procedures referred to CMDv. The RMS and CMS should fill in the required information in the CTS.

|   |              |
|---|--------------|
| <b>STANDARD OPERATING PROCEDURE</b><br><br>For<br><br>Disagreement in procedures – Referral to CMDv | CMDv/SOP/001 |
|   | Ed: 03       |
|   | Page 8/10    |

## ANNEX 1

### Flow chart – Day 60 procedure

|   |   |
|---|---|
| <b>Day 90/210 of MRP/DCP</b>                  | The disagreeing Member State(s) <u>shall provide</u> a detailed exposition of the reasons for their position. This is sent to RMS, CMS(s), including MS(s) where the application has been withdrawn in the MRP and DCP (if the withdrawal has been made after the draft documents have been sent by the RMS), CMDv Secretariat and the applicant. The RMS submits to the CMDv a notification of a referral under article 33(1).   |
| <b>Within 7 days</b>                          | <p>The RMS initiates the referral by sending the final (latest) assessment report, proposed SPC, labelling and package leaflet and the explanation of the grounds for referral from disagreeing Member State(s) to <u>all</u> CMDv members, CMDv chair, CMDv secretariat and the applicant. The RMS is encouraged to discuss with the applicant before the first CMDv meeting. The Secretariat puts the item on the next CMDv agenda, for information. The Secretariat and CMDv Chairperson decide on a starting date.</p> <p>The RMS shall circulate a draft list of concerns to be finalised via written procedure by the CMSs.</p> |
| <b>Day 0 (within 30 days from Day 90/210)</b> | The secretariat will forward the final list of concerns to the applicant and starts the procedure.  |
| <b>Within 15 days</b>                         | <p>The applicant to send a response document to the RMS.</p> <p>The RMS to forward the response immediately to all CMDv members</p>   |
| <b>Around Day 45</b>                          | RMS to circulate an assessment of the Applicant's response to all CMDv members and the applicant.   |
| <b>Second CMDv meeting</b>                    | Scientific discussion, possible hearing and decision. Members of CMDv should preferably state their view on the response document to all members 3 working days before the meeting. Agreement to be reached in principle.   |
| <b>Before day 60</b>                          | <p>All CMS to confirm their position to the RMS and applicant.</p> <p><u>The procedure can be finalised earlier than day 60 if a consensus has been reached within the group to approve the application</u></p>   |
| <b>Day 60</b>                                 | If agreement has been reached the RMS should record the agreement, close the procedure, inform the applicant, the members of CMDv and the secretariat and finalise the AR. Failing consensus, the RMS should immediately inform the EMEA and the applicant and provide a detailed statement of the unresolved issues and the reasons for the disagreement and refer the procedure to the CVMP.  |

|   |              |
|---|--------------|
| <b>STANDARD OPERATING PROCEDURE</b><br><br>For<br><br>Disagreement in procedures – Referral to CMDv | CMDv/SOP/001 |
|   | Ed: 03       |
|   | Page 9/10    |

## ANNEX 2

### Guidance on oral explanations to CMDv

**Reference:** *Article 33(3) of Directive 2004/28/EC of the European Parliament and of the Council amending Directive 2001/82/EC on the Community code and relating to veterinary medicinal products.*

#### 1. Background

When one or more of the Member States involved in a particular Decentralised Procedure (DCP), Mutual Recognition Procedure (MRP), type II variation or worksharing procedure cannot approve the (draft) assessment report, FVAR, SPC, labelling or PL within the period allowed in article 28(4), (90 days), from receipt of the relevant documents according to Article 32(4) of the above mentioned Directive, the points of disagreement shall be referred to the CMDv. Within this procedure Member States shall use their best endeavours to reach agreement and in doing so, shall allow the applicant to make his point of view known orally or in writing.

This guidance should contribute to effective and efficient running of the oral explanations given by the applicants to the CMDv.

#### 2. Advice on an oral explanation

In the case of disagreement in a particular procedure, the list of concerns is agreed and the areas of concern clarified in the first scheduled CMDv meeting of the referral. CMDv members may also take a preliminary common position whether an oral explanation by the applicant might be useful for all specific questions. On the first working day after the first CMDv meeting, the CMDv secretariat sends to the applicant the following:

- List of questions;
- Request to send a written response document which addresses each question from the list, including the description of impact on the SPC and PL (if relevant) within 15 days after the first CMDv meeting;
- Recommendation to discuss with the RMS whether an oral explanation in addition to a written response document would be useful, specifying questions which should be addressed (if applicable);
- Request to inform the CMDv secretariat and the RMS contact, within two weeks following the receipt of the List of concerns, about the applicant's wish to present its point of view orally at the following CMDv meeting.

#### 3. Preparation for an oral explanation

If an oral explanation is agreed, the CMDv secretariat will send to the applicant confirmation of the assigned time slot one week prior to the meeting. This will be with prior agreement with the RMS.

The applicant should not be represented by more than five persons in total; a list of the names of proposed attendees representing the applicant, as well as details of their affiliation and their role in the oral explanation should be sent to the RMS and the CMDv secretariat by Monday before the CMDv meeting at which the oral explanation will be heard. The applicant should indicate the technical support required for their presentation during the oral explanation (e.g. overhead projector, own computer, slide projector). It is recommended, whenever possible, to make a computer assisted presentation.

|   |              |
|---|--------------|
| <b>STANDARD OPERATING PROCEDURE</b><br><br><b>For</b><br><br><b>Disagreement in procedures – Referral to CMDv</b> | CMDv/SOP/001 |
|   | Ed: 03       |
|   | Page 10/10   |

At the request of the applicant and upon agreement of the CMDv a teleconference may be arranged by the CMDv secretariat.

The applicant should provide the RMS, CMDv members and CMDv secretariat with the final electronic version of the presentation in electronic version by Tuesday before the oral explanation (not later than 3 p.m. GMT)

The applicant should arrive at the EMEA premises no earlier than one hour before the time of the oral explanation, checking in at the reception on the 4th floor. The applicant should check out at the EMEA reception before leaving the premises.

#### **4. Oral explanation**

Oral explanation takes place in the scheduled CMDv meeting according to the timetable.

Before the arrival of the applicant the RMS should summarise:

- RMS's assessment of the response document submitted by the applicant;
- Comments on the new SPC, labelling and PL or commitments proposed by the applicant, if relevant;
- Remaining issues of concern;
- The RMS should ask the MSs which have raised a potential serious risk to human health, animal health or to the environment, if their concerns have been addressed. An agreed approach to the questioning of the applicant should be defined by the CMDv members before inviting the applicant to participate.

The oral explanation should be prepared by the applicant taking into account that the actual presentation should:

- Be maximum 20 minutes;
- Focus on responses to the most relevant questions from the List of concerns followed by a conclusive statement;
- If appropriate, describe the impact on the SPC and PL and/or commitments proposed by the applicant.

The actual presentation may be followed by a questions and answers session. The overall duration of an oral explanation including the questions and answers session should be maximum 40 minutes, taking into account the number of questions and the nature of the concerns.

After the applicant has left the room, the CMDv members should continue their discussions on the outstanding issues, with the objective to reach agreement on the action to be taken. In principle, final agreement on the outcome of the procedure is aimed to be reached within the CMDv meeting. In the case that no agreement can be reached at the CMDv meeting, the full 60 days as foreseen in the legislation should be used to resolve any outstanding issues between RMS, CMSs and the applicant if at all possible.

After the oral explanation and subsequent discussion, the RMS informs the applicant about the outcome of the discussion and of any remaining issues.