

CMDv/GUI/009

GUIDANCE

for

Actions after an opinion from an article 33

CVMP referral

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1. INTRODUCTION

Where one or more of the Concerned Member States (CMSs) cannot approve the assessment report and product information on grounds of a potential serious risk to human or animal health or to the environment during a Mutual Recognition (MRP) or Decentralised procedure (DCP), the matter is referred to the Coordination group under the 60 day referral procedure. If after that the RMS and CMSs are still unable to reach agreement, an arbitration mechanism is invoked. A scientific evaluation of the areas of divergent opinion is undertaken by the European Medicines Agency's (EMA) scientific committee, CVMP.

After the opinion has been given by the CVMP, the Commission decision making process will follow. If the Commission decision is positive, a Marketing Authorisation (MA) will be issued. In case of a negative decision the granting of an authorisation will be refused in all Member States involved and existing Marketing Authorisations will be revoked or suspended.

2. AIM AND SCOPE

The aim of this guidance document is to describe the actions that will follow the opinion of the CVMP in both cases, a negative and positive opinion.

3. REFERENCES AND RELATED DOCUMENTS

Directive 2001/82/EC as amended by Directive 2004/28/EC.
 Notice to Applicants, Volume 6A, Chapter 3 Community Referral.
 CMDv documents.
 The new Linguistic Review Process of Product Information in the Centralised Procedure, EMEA/5542/02.

4. DESCRIPTION OF THE PROCEDURE

4.1 Procedure after a positive CVMP opinion

4.1.1. The opinion and final SPC

The positive CVMP opinion will include two or more annexes and also one appendix; the last containing the initial referral notification. Annex I includes the name, pharmaceutical form, strength of the medicinal product, animal species, routes of administration, and marketing authorisation holder. Annex II indicates the scientific conclusions.

Annex I will be translated to all EU official languages (Icelandic and Norwegian, only if these countries were involved in MRP/DCP) by the applicant, while annex II will be translated by the EMA.

Also annexed to the opinion is normally the English version of the texts for the Summary of Product Characteristics (SPC), labelling and package leaflet (annex III).

In cases where the CVMP only discussed and agreed on certain part(s) of the SPC (e.g. the indications), it will be possible in the annex III to note only the opinion relating to those parts

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which were subject to amendments during the referral. A statement will also be included. This will state that for the remaining parts the SPC, labelling and PL, the final versions are the ones achieved during the MRP respective DCP and subsequent 60-day referral procedure in the coordination group.

The applicant will update the texts of the SPC, labelling and package leaflet with the text agreed by the CVMP, and send it to the RMS who will check it and send it to the EMA. This will be the final agreed version of the product information.

It is the duty of the applicant to translate relevant parts of the SPC, labelling and PL into all EU official languages (Icelandic and Norwegian, only if these countries were involved in MRP/DCP). The relevant parts of the product information are the parts which the CVMP has agreed upon.

4.1.2. Translation check

For the translation check the EMA linguistic review procedure should be followed, see annex 1.

Five days after the opinion has been issued, the applicant will have to provide electronically the translations of annex I and annex III to all Member States QRD Contact Points for a linguistic check, http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC5_00004437.pdf, and a copy to the EMA secretariat <PM for the procedure>. A normal 14 days time frame will be applied for Member States to complete the translation check; the applicant/MAH does inform the MSs of the deadline.

In order to facilitate the issuing of a MA within 30 days after the Commission decision (see also 4.1.4.) it is recommended that the applicant will send the complete translation of the product information texts to concerned Member States and that these Member States will check the entire text during the linguistic review procedure.

To the Member States that are not involved in the procedure, the applicant will send only the translation of the relevant parts of the agreed text.

When conducting the translations the applicant should take into consideration the national requirements as presented in the Notice to Applicants, Volume 6, Chapter 7, with regard to the labelling and package leaflet.

The Member States will send the corrected translations to the applicant's contact point(s) and a copy to the EMA secretariat <PM for the procedure>. The applicant will have 3 days to make the necessary corrections and will then forward the corrected versions of product information to the EMA (vet.translations@ema.europa.eu).

EMA will compile the English opinion and the Annexes in all EU official languages, (Icelandic and Norwegian, only if these countries were involved in MRP/DCP), and send final copies to the Commission, Members of the Standing Committee and the MAH within 5 working days.

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4.1.3. The Commission decision making procedure

After the linguistic review procedure has been finalised, the EMA will send the opinion together with the annexes and product information to the Commission to initiate the decision making procedure, see annex 2. This will include the Standing Committee phase in a written procedure (22 days) and the decision making phase immediately after this if there are no objections from the members of the Standing Committee.

4.1.4. The National Marketing Authorisations

Once the Commission decision has been issued, it is the duty of the concerned Member States to issue the MA within 30 days in accordance with Article 38 of the amended Directive. The Member States will inform the Commission about the decision. The Member States, who are not involved in the procedure, are not required to take any action.

4.1.5. Variations to Marketing Authorisations issued before the Commission decision

Some Member States might have issued a MA at the request of the applicant after the coordination group phase. In cases where there have been changes to the SPC during the CVMP arbitration, these will have to be implemented to the product information texts already approved in Member States.

The same 30 day time frame also applies to those Member States who have already issued a MA. National rules apply in these situations (see Notice to Applicants Volume 6A Chapter 7). It is the duty of the applicant to take the necessary actions to comply with the Commission decision.

The same procedure also will be followed if a repeat use procedure ends up at arbitration and the SPC is changed. The changes to the SPC should be implemented to the product information texts already approved in the concerned Member States involved in the first round.

4.2 Procedure after a negative CVMP opinion

4.2.1 The negative opinion

If the application does not satisfy the criteria for authorisation, the CVMP will give a negative opinion.

The negative opinion will include two or three annexes. Annex I includes the name, pharmaceutical form, strength of the medicinal product, animal species, routes of administration, and MAH. Annex II indicates the scientific conclusions.

In some cases an Annex III will be added which includes the condition for the lifting of the suspension of the National MA(s).

The Annex I will be translated by the applicant to all EU official languages (Icelandic and Norwegian, only if these countries were involved in MRP/DCP), while Annex II and Annex III will be translated by the EMA.

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4.2.2. The Commission decision making procedure

The EMA will send the opinion together with the annexes to the Commission to initiate the decision making procedure. This will include the Standing Committee phase in a written procedure (22 days) and the decision making phase immediately after this if there are no objections from the Members of the Standing Committee.

4.2.3. The national actions after the Commission decision

Once the national agencies have received the Commission decision, they will have to take action within 30 days.

Member States which have agreed to issue a MA should have to suspend or revoke the authorisation in accordance with the Commission Decision. In all other CMSs the granting of an authorisation should be refused.

The actions to be taken will follow national rules and the Member States will inform the Commission thereof afterwards.

4.2.4. Suspension of Marketing Authorisations issued before the Commission decision and its lifting

According to Article 33(6), *“Member States that have approved the assessment report, summary of product characteristics, labelling and package leaflet of the reference Member State may, on request by the applicant, grant a marketing authorisation for the veterinary medicinal product without waiting for the outcome of the procedure laid down in Article 36. In that case, the authorisation granted shall be without prejudice to the outcome of that procedure.”*, the situation may occur that some Member States have authorised the product while the final decision of the Commission is negative afterwards.

To illustrate, a number of scenarios can be considered:

- DCP – decision to refuse the granting of the authorisation and to suspend the MA where appropriate. In case the RMS has not issued a MA, the RMS has to refuse the granting of the authorisation. Only the Member States which have authorised the product can suspend the authorisation and only in these Member States the suspension could be lifted by the submission of additional data. In such cases a new RMS has to be appointed, who has the competence to assess the additional data (submitted as a variation), which could finally lead to the lifting of the suspension. If the applicant would like to market their product in the Member States involved originally, a repeat use procedure would then be required, using the newly appointed RMS.
- MRP – decision to refuse the granting of the authorisation and to suspend the MA where appropriate. It concerns a mutual recognition procedure and therefore the RMS does have an authorisation, which has to be suspended. The situation is the same for CMSs which have already granted an authorisation; they have to suspend

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the authorisation. A variation is required to provide the information that would lift the suspension in the RMS and CMSs. Those CMSs who did not issue a MA would not longer be involved and the MAH would need to follow a repeat use procedure in those CMSs. If none of the CMSs have issued an authorisation, with the exception of the RMS, a repeat use procedure is not possible: a new MRP should be started.

- Repeat use procedure – decision to refuse the granting of the authorisation and to suspend the MA where appropriate. Besides the RMS and the CMSs which have issued a MA in the repeat use procedure, all CMSs in the first MRP/DCP round would need to suspend the product. A variation would be required in the RMS and authorising CMSs to lift the suspension.

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ANNEX 1

Timetable for the finalisation of the CVMP opinion and the annexes in all EU languages (*linguistic review procedure*)

Day 0	Positive opinion from the CVMP
Day 5	for the applicant to submit translations of product information (as applicable) and Annex I in all EU official languages (Icelandic and Norwegian, only if these countries were involved in MRP/DCP) to Member States and EMA. The applicant will inform the MSs of the deadline for the check.
Day 19	for the Member States QRDs to check the translations and send comments to the applicant (with a copy to EMA)
Day 22	for the applicant to implement the corrections to product information and to send the corrected versions to the EMA
Day 27	for the EMA to do final PIQ check and to compile the English opinion and the Annexes in all languages and send final copies to the Commission, Members of the Standing Committee and the MAH

ANNEX 2

Timetable for Commission decision making procedure after referral

Day 29	for the Commission to prepare the draft decision and start the Standing Committee phase
Day 51	End Standing Committee phase
Day 67	for the Commission to make the final Commission decision