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Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

PROCEDURAL ADVICE ON THE RE-EXAMINATION OF CVMP OPINIONS

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Comments should be provided using this template in MS Word format (not pdf) to :

vet-guidelines@emea.europa.eu

Note on Revision 1: *This Procedural Advice (previously in the form of a Guideline) has been amended to include Referral procedures. The opportunity has also been taken to update it in line with Commission Regulation 1234/2008/EC (which comes into force on 1 January 2010).*

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1. Purpose

Re-examination procedures are designed to provide a better guarantee for Applicants/MAH's rights (Recital 25 of Regulation (EC) No 726/2004).

This document describes the procedure and gives guidance for the re-examination of the different types of CVMP opinions (applications for new marketing authorisations, extensions, renewals, annual reassessments, type II variations and referrals), on the timetable for Applicants/MAH's involvement and assessment by CVMP, rapporteurs, and Scientific Advisory Groups/Ad Hoc Expert Groups (SAG/AHEGs) if deemed necessary, and on the documentation to be supplied.

This procedural advice should be read in conjunction with the current version of the Reflection Paper on the Publication of Scientific Committee's Negative Opinion and Refusal to Recommend the Granting of a Marketing Authorisation for Veterinary Medicinal Products (EMEA/CVMP/459912/2006).

2. Legal basis for re-examinations

Centralised Procedures:

Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

- Article 34(2) of Regulation (EC) No 726/2004 states:

  "Within 15 days after receipt of the opinion referred to in paragraph 1, the Applicant may give written notice to the Agency that he wishes to request a re-examination of the opinion. In that case, the Applicant shall forward to the Agency the detailed grounds for the request within 60 days after receipt of the opinion.

  Within 60 days following receipt of the grounds for the request, the said Committee shall re-examine its opinion in accordance with the conditions laid down in Article 62(1), fourth subparagraph. The reasons for the conclusion reached shall be annexed to the final opinion."

- Article 62(1), 4th paragraph, of Regulation (EC) No 726/2004 states:

  "If there is a request for re-examination of one of its opinions, the Committee concerned shall appoint a different rapporteur and, where necessary, a different co-rapporteur from those appointed for the initial opinion. The re-examination procedure may deal only with the points of the opinion initially identified by the Applicant and may be based only on the scientific data available when the Committee adopted the initial opinion. The Applicant may request that the Committee consult a scientific advisory group in connection with the re-examination."

Variations:

Commission Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products

- Chapter III, Article 16(4) of Regulation (EC) No 1234/2008 states:
  "Article 34(1) and (2) of Regulation (EC) No 726/2004 shall apply to the opinion on the valid application……" and these articles establish the general procedure for CVMP opinions and the re-examination of CVMP opinions.

- Chapter IV, section 1, Article 19 of Commission Regulation (EC) No 1085/2003 states:
  "An application for an extension of a marketing authorisation shall be evaluated in accordance with the same procedure as for the initial marketing authorisation to which it relates." which means that a Centralised application for an extension to a Community marketing authorisation shall be evaluated in accordance with the procedures set out in Articles 28 to 32 of Regulation (EEC) No 2309/93 for veterinary medicinal products. These Articles cover the re-examination procedure.

Referral Procedures:

Directive 2001/82/EC of the European Parliament and of the Council on the Community Code relating to veterinary medicinal products, as amended

- Article 36(4) of Directive 2001/82/EC, as amended, states:

  "Within 15 days after receipt of the opinion, the Applicant or the Marketing Authorisation Holder may notify the Agency in writing of his intention to request a re-examination of the opinion. In that case, he shall forward to the Agency the detailed grounds for the request within 60 days after receipt of the opinion.

  Within 60 days following receipt of the grounds for the request, the Committee shall re-examine its opinion in accordance with the fourth subparagraph of Article 62(1) of Regulation (EC) No 726/2004. The reasons for the conclusion reached shall be annexed to the assessment report…."

Other references:

- Notice to Applicants – http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev6.htm
- CVMP Rules of Procedure (EMEA/CVMP/422/04) - http://www.emea.europa.eu/htms/general/contacts/CVMP/CVMP.html

3. Scope[1]

The re-examination procedure described in this procedural advice is applicable to:

- CVMP opinions on applications concerning veterinary medicinal products falling within the scope of Regulation (EC) No 726/2004:
  - Granting of new marketing authorisations or extensions (Article 34(2))
  - Renewal (Article 39(2))
  - Annual reassessment of marketing authorisations granted in exceptional circumstances (Article 39(7))
- CVMP opinions on type II variations and extension applications falling within the scope of Article 2 of Commission Regulation (EC) No 1234/2008
- CVMP opinions on referrals falling within the scope of Article 36(4) of Directive 2001/82/EC, as amended.

4. Timing of re-examination procedure

4.1. Timetable for the Applicant/MAH

Within 15 calendar days (= date sent by Applicant/MAH as documented by fax/EudraLink/registered mail) after receipt of the opinion (= date of receipt by Applicant/MAH as documented by fax/EudraLink/registered mail), the Applicant/MAH may give written notice to the Agency that he wishes to request a re-examination of the opinion, and also if he wishes that a Scientific Advisory Group (SAG) or Ad Hoc Expert Group (AHEG) be consulted. If the Applicant/MAH wishes to have an oral explanation before the CVMP and/or SAG/AHEG, this should be requested as early as possible.

Within 60 calendar days after receipt of the opinion the Applicant/MAH forwards to the Agency detailed grounds for requesting a re-examination.

[1] Maximum Residue Limits – an SOP for 'Appeal against CVMP Opinions on the establishment of MRLs and Provision of Detailed Grounds for Appeal' (EMEA/CVMP/931/00) is available.

4.2. Timetable for the assessment

General principles:

Within 60 calendar days following receipt of the grounds for the request, the CVMP shall re-examine its opinion. The detailed timetable presented below (as guidance) will depend on, amongst other factors, the date of receipt of the detailed grounds for the request of re-examination in relation to the CVMP meeting dates. However, it will never exceed 60 calendar days (there is no clock stop).

During the CVMP meeting following receipt of the Applicant/MAH's written notice to the Agency that he wishes to request a re-examination of the opinion, the CVMP appoints a different rapporteur, and, for opinions where a co-rapporteur was involved in the initial evaluation, a different co-rapporteur from that appointed for the initial opinion. (These new rapporteurs will coordinate the evaluation for the duration of the re-examination procedure only.) At this CVMP meeting, the Committee may have preliminary discussions on the need for consultation by, and the composition of, a SAG/AHEG. If possible, the CVMP will adopt a draft List of Questions (LoQ) to the SAG/AHEG, and, if applicable, additional questions to the Rapporteurs (for example, relating to the overall benefit-risk) at this same meeting.

Timetable:

- Day 0: Receipt by EMEA of Applicant/MAH's detailed grounds for the request of re-examination
- Day 1: Next calendar day
- At first CVMP meeting: CVMP appoints new Rapporteur and, if applicable, a Co-Rapporteur; and decides on the need to consult a SAG/AHEG. If an AHEG is to be consulted its composition is agreed. A draft LoQ to the SAG/AHEG is then adopted;
- Approx. Day 30: Circulation of (co)rapporteur(s) assessment report(s) to CVMP (including, if applicable, a draft revised LoQ to the SAG/AHEG)
- Approx. Day 40: CVMP comments
- Approx. Day 45: Joint assessment report (including, if applicable, revised LoQ to the SAG/AHEG)
- SAG/AHEG meeting (or written procedure) including, if agreed by the CVMP, an oral explanation by the Applicant/MAH to the SAG/AHEG
- Approx. Day 50: If applicable, SAG/AHEG recommendation to CVMP (via a SAG/AHEG meeting, or via a written procedure)
- At the latest on Day 60: If requested, the Applicant/MAH has an oral explanation with the CVMP. CVMP then adopts the final opinion.

5. Information to be supplied

5.1 The Applicant/MAH shall forward to the Agency the detailed grounds for the request for re-examination of the opinion. As stated in Article 62(1) paragraph 4 of Regulation 726/2004:

"*If there is a request for re-examination of one of its opinions, the Committee…….. The re-examination procedure may deal only with the points of the opinion initially identified by the Applicant and may be based only on the scientific data available when the Committee adopted the initial opinion. The Applicant may request that the Committee consult a Scientific Advisory Group in connection with the re-examination.*"

5.2 Thus the rule for re-examinations is that only scientific data available when the Committee adopted the initial opinion is admissible at the re-examination stage. No new data may be submitted.

5.3 If the Applicant/MAH wishes the Committee to consult a SAG/AHEG in connection with the re-examination, the Applicant/MAH should inform the CVMP as soon as possible of this request, and include it in the notification letter, and also in the cover letter submitted with the grounds for the request for re-examination.

6. CVMP assessment and final opinion

The general principles of coordination of the evaluation (that is, the roles and interactions of rapporteur, co-rapporteur, CVMP, EMEA, SAG/AHEG) will not be further detailed in this document. Please refer to the guidance and procedures detailed in the Notice to Applicants (NTA) Volume 6A and in the CVMP Rules of Procedure. However, in view of the particularly strict timetable of re-examination procedures (as outlined above), this section provides additional detail on the involvement of SAGs/AHEGs in re-examination procedures.

6.1 Consultation of a SAG/AHEG

Article 62(1), 4th paragraph, of Regulation (EC) No 726/2004 states that "*The Applicant may request that the Committee consult a Scientific Advisory Group in connection with the re-examination.*"

The decision on consultation of a SAG/AHEG for a re-examination procedure will depend, amongst other factors, on the Applicant/MAH's request for the CVMP to consult a SAG/AHEG. The Applicant/MAH will preferably inform the CVMP of this request as early as possible. If there is no such request from the Applicant/MAH, the CVMP will decide whether there is a need for additional expertise.

If no established SAG has the required competence, the advice of additional available expertise will be sought in the form of an AHEG meeting.

During the CVMP meeting following receipt of the Applicant/MAH's written notice to the Agency and/or detailed grounds for requesting a re-examination of the opinion, the CVMP makes the decision regarding consultation of a SAG/AHEG and its composition. The CVMP also adopts a List of Questions to the SAG/AHEG at this meeting.

If the timing is such that a LOQ to the SAG/AHEG cannot be adopted during a CVMP meeting, it will be adopted by a written procedure.

The EMEA will provide all the SAG/AHEG Members with a copy of the List of Questions to the SAG/AHEG. The CVMP/rapporteurs and the SAG/AHEG secretary will decide whether any on the additional documents should given to the SAG/AHEG/ad hoc experts, such as, for example, the Applicant/MAH's detailed grounds, the rapporteur(s)' draft assessment report on the re-examination, the CVMP's initial opinion, etc.

The rapporteur's assessment report on the re-examination and the List of Questions for the SAG/AHEG is also sent for information to the Applicant/MAH. The CVMP will decide whether the Applicant/MAH will be invited for an oral presentation to the SAG/AHEG.

The SAG/AHEG recommendation will be reflected in the CVMP assessment report.

6.2 CVMP final opinion on re-examination

Within 15 calendar days after its adoption, the Agency shall send the final CVMP opinion to the Commission, to the Member States and to the Applicant/MAH.

If the final opinion on the granting/maintaining of a Community MA/variation is favourable, the following documents shall be annexed to the opinion:

- Annex A (as per the Veterinary QRD template and listing all the presentations)

- Draft SPC, labelling and package leaflet (i.e., Annexes I, IIIA & IIIB), if applicable[1]
- Details of conditions affecting the authorisation (supply) (i.e., Annex II), if applicable[2]
- Details of recommended conditions or restrictions with regard to the safe and effective use of the veterinary medicinal product (i.e., Annex II), if applicable[3]

The CVMP assessment report will be appended to the opinion.

If the final opinion on the granting/maintaining of a Community MA/variation is not favourable, the following documents shall be annexed to the opinion:

- Annex A
- Scientific conclusions and grounds for the refusal of the granting of the Marketing authorisation. (This must be called simply "Annex".) Initially this is sent to the Commission in English only, but then needs to be translated and sent to the Commission, as they will publish on their website a Decision and Annex in each official EU language.

The CVMP assessment report will be appended to the CVMP opinion.

For a referral procedure, the following documents shall be annexed to the final opinion:

- Annex I - listing all the veterinary medicinal products and Applicants/MAHs concerned
- Annex II - reflecting the scientific conclusions and grounds for the granting, or refusal of the granting, of a Marketing Authorisation, a variation to the terms of the Marketing Authorisation, the suspension, or the withdrawal of a Marketing Authorisation
- Annex III - containing the SPC, labelling and package leaflet, in English only, if applicable
- Annex IV - containing details of conditions affecting the authorisation (supply), if applicable.

The CVMP assessment report will be appended to the CVMP opinion.

6.3 Special situations

In case of procedures involving several Applicants/MAHs, a request for re-examination of an opinion by one of the parties involved, the final CVMP opinion will be delayed for all the parties involved.

In case of a withdrawal (by the Applicant/MAH) of their request for a re-examination, the initial CVMP opinion will immediately become the final CVMP opinion.

7. Transparency/communication

The start of the re-examination procedure and the adoption of the final CVMP opinion are reported in the CVMP press release and CVMP monthly report, both of which are published on the EMEA website. If the EMEA considers that a specific Public Statement is necessary, one might be published at the opinion stage.

For details on what is to be published, and the relevant timeframes with regard to centralised procedures/variations, details can be found in the current versions of the Reflection Paper on the Publication of Scientific Committee's Negative Opinion and Refusal to Recommend the Granting of a Marketing Authorisation for Veterinary Medicinal Products (EMEA/CVMP/459912/2006), and the

[1] For example, these would not be necessary for a Type II variation application which did not result in any changes to the Annexes.
[2] As above.
[3] As above.

Reflection Paper on the Publication of Withdrawals of Marketing Authorisation Applications for Veterinary Medicinal Products (EMEA/CVMP/425558/2006).

With regard to referrals, once the European Commission has issued a Commission Decision, the EMEA will publish a document giving background information on the referral, the scientific conclusions reached, the list of products included in the referral, the Product Information, and any conditions to the Marketing Authorisations as adopted by the CVMP, if relevant.