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Committee for Medicinal Products for Veterinary Use

Procedural advice to applicants/marketing authorisation holders on re-examination of CVMP opinions

1. Introduction

Re-examination procedures are designed to guarantee applicant's/marketing authorisation holder's (MAH) rights. This document describes the procedure and gives guidance for the re-examination of different types of opinions of the Committee for Medicinal Products for Veterinary Use (CVMP).

The document also gives guidance on the timetable for applicant's/MAH's involvement and for the assessment by CVMP, rapporteurs, and Scientific Advisory Group/Ad Hoc Expert Group (SAG/AHEG) if deemed necessary, and on the documentation to be supplied.

2. Legal basis for re-examinations

Centralised procedures:

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

  "Within 15 days after receipt of the opinion referred to in paragraph 1, the applicant may provide 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 after 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) 5th subparagraph of Regulation (EC) No 726/2004 establishes that:

  "If there is a request for re-examination of one of its opinions where this possibility is provided for in Union law, 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."

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Type II variation procedures:

- Article 16(4) of Commission Regulation (EC) No 1234/2008 establishes that:

  "[…] Article 34(1) and (2) of Regulation (EC) No 726/2004 shall apply to the opinion on the valid application.

  Within 15 days from the adoption of the final opinion on the valid application, the measures provided for in Article 17 shall be taken."

Extensions of marketing authorisation

- Article 19(1) of Commission Regulation (EC) No 1234/2008 establishes that:

  "*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.*"

Worksharing procedures

- Article 20(7) of Commission Regulation (EC) No 1234/2008 establishes that:

  "*Where the reference authority is the Agency, […] Article 34(1) and (2) of Regulation (EC) No 726/2004 shall apply to the opinion […].*"

Maximum Residue Limit procedures:

- Article 8(3) of Regulation (EC) No 470/2009 establishes that:

  "*[…] Within 15 days of receipt of the opinion, the applicant may provide written notice to the Agency that he wishes to request a re-examination of the opinion. In that case the applicant shall submit the detailed grounds for his request to the Agency within 60 days of receipt of the opinion.*

  Within 60 days of receipt of the applicant's grounds for a re-examination request, the Committee shall consider whether its opinion should be revised and adopt the final opinion. The reasons for the conclusion reached on the request shall be annexed to the final opinion."

Referral procedures:

- Article 36(4) of Directive 2001/82/EC establishes that:

  "[…]

  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[…]."

3. Scope

The re-examination procedure described in this procedural advice is applicable to the opinions adopted by CVMP as follows:

- opinions on applications for granting of new marketing authorisations, renewals and annual reassessment of marketing authorisations granted under exceptional circumstances concerning

veterinary medicinal products falling within the scope of Regulation (EC) No 726/2004 (Article 34(2), Article 39(2) and Article 39(7) respectively);

- opinions on type II variations, extensions of marketing authorisations and worksharing procedures falling within the scope of Commission Regulation (EC) No 1234/2008 (Article 16(4), Article 19(1) and Article 20(7) respectively);
- opinions on applications for the establishment of maximum residue limits of pharmacologically active substances in foodstuffs of animal origin falling within the scope of Regulation (EC) No 470/2009 (Article 3 thereof);
- opinions on referrals subject to the procedure laid down in Article 36 of Directive 2001/82/EC (i.e. referral procedures according to Article 33(4), Article 34 and Article 35 of Directive 2001/82/EC; Article 13 of Commission Regulation (EC) No 1234/2008).

The re-examination procedure is not applicable for CVMP opinions on procedures according to Article 45 of Regulation (EC) No 726/2004 or Article 78 of Directive 2001/82/EC as this is not foreseen in the legislation.

4. Steps and timing of re-examination procedure

4.1. Applicant's/marketing authorisation holder's request for re-examination

Within 15 calendar days of receipt of the CVMP opinion (date of receipt by applicant/MAH as documented by Eudralink/registered mail), the applicant/MAH may request a re-examination of the CVMP opinion. The request should clearly identify the concerned CVMP opinion and must be submitted in writing to the European Medicines Agency (the Agency) via email to vet.applications@ema.europa.eu. In their written notice to the Agency, the applicant/MAH is advised to specify the area(s) to which the re-examination would relate.

The applicant/MAH may request a consultation with a SAG/AHEG and/or to present oral explanation(s) to the SAG/AHEG and/or the CVMP, in which case this should ideally be included in the written notice.

Where the last day of the 15-day period is a public holiday/Saturday/Sunday, the period will end on the following working day.

The applicant's/MAH's written notice for re-examination must be sent within the stated timeline. In case this deadline is not respected, the request for re-examination is considered inadmissible and the CVMP opinion becomes final.

4.2. Appointment of CVMP rapporteur(s) for re-examination

During the CVMP meeting following receipt of the written notice for re-examination, the CVMP will appoint a different rapporteur and, for opinions where a co-rapporteur was involved in the initial evaluation, a different co-rapporteur from those appointed for the initial opinion (these rapporteurs are to be appointed for the duration of the re-examination procedure only).

4.3. Applicant's/marketing authorisation holder's detailed grounds for re-examination of the CVMP opinion

Within 60 calendar days of receipt of the CVMP opinion the applicant/MAH must submit to the Agency a cover letter and the detailed grounds for the re-examination of the CVMP opinion.

Where the last day of the 60-day period is a public holiday/Saturday/Sunday, the period will end on the following working day.

The detailed grounds for re-examination of the CVMP opinion must be sent within the stated timelines. In case these deadlines are not respected, the request for re-examination is considered inadmissible and the CVMP opinion becomes final.

The detailed grounds submitted will determine the scope of the re-examination procedure and may encompass all aspects set out in the CVMP opinion or only certain aspects of it.

In the detailed grounds for re-examination of the CVMP opinion the applicant/MAH should provide their justification for disagreement(s) with the specific points of the CVMP opinion that are being challenged. As stated in Article 62(1) 5th subparagraph of Regulation (EC) No 726/2004, *"*[t]*he 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.[…]"*

Thus, for re-examination procedures, only scientific data available at the time when the CVMP adopted the initial opinion are admissible at the re-examination stage. No new data can be submitted nor considered. It is not acceptable to include, for example, results from new studies not previously submitted or results from ongoing-studies with a later data cut-off than the data provided to the CVMP by the time of the initial CVMP opinion. On the other hand, new presentation, elaboration or clarification of previously-provided data can be acceptable, provided that it is not based on new underlying factual information.

In case the applicant/MAH requests the CVMP to consult a SAG/AHEG in connection with the re-examination, such a request should be submitted as soon as possible (see section 4.1) and within 60 days of receipt of CVMP opinion. The request should be duly motivated.

Due to the very tight legal timeframe, the applicant/MAH is strongly advised to contact the Agency procedure coordinator as early as possible to discuss the most appropriate dates for submission of the detailed grounds for re-examination of the CVMP opinion, within the legal timeframe, to accommodate, as far as possible, the scheduled CVMP meeting dates.

4.4. Assessment of the applicant's/marketing authorisation holder's detailed grounds for re-examination of the CVMP opinion

4.4.1. Timetable

Within 60 calendar days of receipt of the detailed grounds for the re-examination of the CVMP opinion, the CVMP will re-examine its opinion. The timelines described below are presented for guidance only and may be modified on a case-by-case basis, depending on, amongst other factors, the date of receipt of the detailed grounds for re-examination of the CVMP opinion in relation to the scheduled CVMP meeting dates. In any case, the total time for assessment can never exceed 60 calendar days (i.e. there is no possibility of a clock-stop).

Where the last day of the 60-day period is a public holiday/Saturday/Sunday, the period will end the following working day.

The timetable below includes the steps of consultation with a SAG/AHEG. In case the SAG/AHEG consultation is not required, the respective steps for the SAG/AHEG do not apply.

Time point	Step
Within 15 days of receipt of CVMP opinion	The applicant/MAH may notify the Agency in writing of their intention to request a re-examination of the CVMP opinion. In case the applicant/MAH requests the CVMP to consult a SAG/AHEG in connection with the re-examination, such a request should be submitted as soon as possible (see section 4.1) and within 60 days of receipt of CVMP opinion. The applicant/MAH may also request to present oral explanation(s) to the SAG/AHEG and/or the CVMP.
After receipt of request for re-examination	CVMP appointment of rapporteur(s) for re-examination. CVMP decision on consultation with a SAG/AHEG. In case of consultation with a SAG/AHEG, the CVMP considers the mandate and composition (the field of expertise required and approximate numbers of participation) of the group and the data to be provided to the experts.
Within 60 days of receipt of CVMP opinion	The applicant/MAH submits to the Agency the detailed grounds for the re-examination of the CVMP opinion.
Day 1	Re-examination procedure starts the next calendar day following receipt of detailed grounds.
Day 14	Rapporteur's assessment report and draft list of questions to the SAG/AHEG, if applicable
Day 21	Critique from co-rapporteur on assessment report.
Day 25	Comments from CVMP members.
Day 30	CVMP discussion on the assessment report. If applicable, CVMP endorsement of SAG/AHEG's members and adoption of list of questions to be addressed by the group.
Day 44	If applicable, SAG/AHEG meeting. If applicable, an oral explanation by applicant/MAH to the SAG/AHEG.
Day 50	Revised rapporteur's assessment report.
Day 60	Adoption of final CVMP opinion and assessment report (if applicable, following an oral explanation by applicant/MAH to the CVMP).

4.4.2. CVMP assessment procedure

The general principles of coordination of the evaluation (i.e. role and interactions of rapporteur, co-rapporteur, CVMP, the Agency) apply to the re-examination procedure; please refer to the guidance and procedures detailed in Notice to Applicants Volume 6A, CVMP rules of procedure and the Agency's pre-submission and post-authorisation guidance documents for the respective assessment procedures.

As outlined above in section 4.3, Article 62(1) 5th subparagraph of Regulation 726/2004 states that *"the re-examination procedure may deal only with the points of the opinion initially identified by the applicant […]".* The scope of the re-examination procedure is therefore limited to those elements of the initial opinion that have been contested by the applicant/MAH in their detailed grounds for re-examination.

4.4.3. Consultation of a SAG/AHEG

A SAG/AHEG will be consulted if requested by the applicant/MAH or in cases where the CVMP itself considers that there is a need for additional expertise.

If a consultation with SAG/AHEG has been requested or felt necessary, the CVMP will consider the mandate, composition and data to be provided by the Agency to the SAG/AHEG. The key steps of consultation with a SAG/AHEG are outlined above in section 4.4.1 and they can be altered in order to reflect the particularities of the re-examination procedure.

The Agency will forward to the applicant/MAH, the rapporteur's assessment report on the re-examination and the CVMP list of questions to the SAG/AHEG, for information.

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

Further details about CVMP consultation with SAG/AHEG are available on the Agency's website.

4.4.4. Oral explanation at CVMP meeting

The applicant/MAH has the right to be heard by the CVMP in an oral explanation. In light of the short timelines of the re-examination procedure, any request for an oral explanation should be submitted as early as possible in the procedure.

The applicants/MAHs are reminded that they are only allowed to provide clarification of the aspects relating to the scope of the re-examination (those elements of the initial opinion that have been contested by the applicant/MAH in their detailed grounds for re-examination) and that no new information (as compared to the information available to the CVMP at the time of initial opinion) can be included in the context of the oral explanation in the re-examination procedure.

Practical guidance to applicants/MAHs on oral explanations to the CVMP is available on the Agency's website.

4.5. CVMP final opinion on re-examination

The procedure for adoption of the final CVMP opinion at the CVMP meeting follows the principles described in the CVMP rules of procedure.

The CVMP assessment report and other support documents (as applicable) are appended to the final CVMP opinion, in line with the legislative requirements and the practice for the particular procedure.

4.6. Withdrawal of request for re-examination

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

4.7. Procedures involving multiple parties

In case of a referral procedure involving several applicants/MAHs, all parties involved in the procedure may request a re-examination and can do so independently. However, all grounds and arguments will be considered within a single re-examination procedure. In case of re-examination request by one of several parties, all parties involved in the referral procedure will be notified about the re-examination and that the final CVMP opinion will be delayed for all parties involved in the referral.