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Committee for Veterinary Medicinal Products (CVMP)

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

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1. Introduction

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

The document also gives guidance on the timetable for applicants'/MAHs' 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.

This procedural advice does not cover the re-examination procedures laid down in Article 24 of Regulation (EU) 2019/6 and Article 27 of Regulation (EU) 2019/6 for marketing authorisations for a limited market and marketing authorisations in exceptional circumstances, respectively.

2. Legal basis for re-examinations

- Article 141(4) of Regulation (EU) 2019/6 establishes that:

  "If there is a request for re-examination of an opinion where this possibility is provided for in Union law, the Committee shall appoint a different rapporteur and, where necessary, a different co-rapporteur from those appointed for the 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 opinion. The applicant may request that the Committee consult a scientific advisory group in connection with the re-examination."

Centralised procedures:

- Article 44(4) of Regulation (EU) 2019/6 establishes that:

  "The Agency shall forward the opinion to the applicant. Within 15 days of receipt of the opinion, the applicant may provide written notice to the Agency that he or she wishes to request a re-examination of the opinion. In such a case, Article 45 shall apply."

- Article 45 of Regulation (EU) 2019/6 establishes that:

  "1. Where the applicant requests a re-examination of the opinion of the Agency in accordance with Article 44(4), that applicant shall forward to the Agency detailed grounds for such request within 60 days of receipt of the opinion.

  2. Within 90 days of receipt of the detailed grounds for the request, the Agency shall re-examine its opinion. The conclusions reached and the reasons for those conclusions shall be annexed to its opinion and shall form an integral part thereof.

  3. Within 15 days of the re-examination of its opinion, the Agency shall forward its opinion to the Commission and the applicant. "

Variations requiring assessment:

- Article 66(10) and (11) of Regulation (EU) 2019/6 establishes that:

  "10. Within 15 days of receipt of the opinion […], the marketing authorisation holder may submit a written request to […] the Agency […] for a re-examination of the opinion […]. Detailed grounds for

requesting a re-examination shall be submitted to […] the Agency […] within 60 days of receipt of the opinion […].

11. Within 60 days of receipt of the grounds for the request for re-examination, […] the Agency […] shall re-examine the points of the opinion […] identified in the request for re- examination by the marketing authorisation holder and adopt a re-examined opinion […]. The reasons for the conclusions reached shall be annexed to the re-examined opinion […].”

Work-sharing procedures

- Article 65(2) of Regulation (EU) 2019/6 establishes that:

  "*Where any of the marketing authorisations referred to in paragraph 1 of this Article is a centralised marketing authorisation, the Agency shall assess the application in accordance with the procedure laid down in Article 66.*"

Union interest referral procedures:

- Article 83(6) and (7) of Regulation (EU) 2019/6 establishes that:

  "6. Within 15 days of receipt of the opinion of the Committee, the marketing authorisation holder may notify the Agency in writing of its intention to request a re-examination of that opinion. In that case, the marketing authorisation holder shall forward to the Agency the detailed reasons for the request of re-examination within 60 days of receipt of the opinion.

  7. Within 60 days of receipt of a request as referred to in paragraph 6, the Committee shall re-examine its opinion. The reasons for the conclusion reached shall be annexed to the assessment report referred to in paragraph 5."

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."

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 centralised marketing authorisation falling within the scope of Article 44 of Regulation (EU) 2019/6;
- opinions on work-sharing procedures and variations requiring assessment falling within the scope of Article 65(2) and Article 66 of Regulation (EU) 2019/6, respectively;
- opinions on referrals following the procedure described in Article 83 of Regulation (EU) 2019/6;
- opinions on applications for the establishment of maximum residue limits of pharmacologically active substances in foodstuffs of animal origin falling within the scope of Article 3 of Regulation (EC) No 470/2009.

The re-examination procedure is not applicable for CVMP opinions on procedures according to Articles 54(8), 130(4), 141(1)(c) or (e) of Regulation (EU) 2019/6 as this is not foreseen in the legislation.

A positive opinion on applications under Article 44, Article 65 and Article 66 of Regulation (EU) 2019/6 may be subject to re-examination as long as the request for re-examination relates to aspects of the opinion for which there had been objections by the CVMP, further to which the applicant opted to amend the application. In such case, the applicant, when submitting the amended documentation, (e.g. revised product information) prior to the opinion, will need to reserve the right to request re-examination in the covering letter.

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), the applicant/MAH may request a re-examination of the CVMP opinion.

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 request should clearly identify the concerned CVMP opinion and must be submitted to the European Medicines Agency (the Agency) via email to Agency's procedural contact points. In their written request 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 the CVMP to consult a SAG/AHEG in connection with the re-examination. In case the applicant/MAH requests the CVMP to consult with a SAG/AHEG, such request should be included in the written request to the Agency. The requests for consultation with a SAG/AHEG should be duly motivated.

The applicant/MAH may request to present oral explanation(s) to the SAG/AHEG and/or the CVMP.

The applicant's/MAH's written request for re-examination must be sent within the stated timeline. In case this timeline is not met, 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 applicant's/MAH's written request 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). For further details see CVMP rules on appointment and responsibilities of the CVMP rapporteur and co-rapporteur in accordance with Article 140(6) of Regulation (EU) 2019/6, and peer reviewer.

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. If these timelines are not met, 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 141(4) of Regulation (EU) 2019/6, *"[…] 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 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 request should be submitted as soon as possible (see section 4.1). 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 for re-examination of opinions for initial centralised marketing authorisation applications

In accordance with Article 45(2) of Regulation (EU) 2019/6, within 90 calendar days of receipt of the detailed grounds for the re-examination of the CVMP opinion, the Committee will re-examine its opinion. An indicative timetable is described below. This is 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 the request of re-examination of the CVMP opinion in relation to the scheduled CVMP meeting dates. In any case, the total time for assessment will never exceed 90 calendar days and there is no possibility of a clock-stop.

The indicative 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	The applicant needs to notify the Agency via email to Agency's procedural contact

Time point	Step
of receipt of CVMP opinion	points of their intention to request a re-examination of the CVMP opinion. In case the applicant requests the CVMP to consult a SAG/AHEG in connection with the re-examination, such request should be submitted as soon as possible (see section 4.1). The applicant 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 number of participants) of the group and the data to be provided to the experts. The date of submission of the detailed grounds for the re-examination is agreed with the applicant (within 60 days of the receipt of the CVMP opinion).
Within 60 days of receipt of CVMP opinion Day 0	The applicant 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 30	Rapporteur's assessment report and draft list of questions to the SAG/AHEG, if applicable.
Day 45	Critique from co-rapporteur on assessment report.
Day 50	Comments from CVMP members.
Day 60	CVMP discussion on the assessment report, and adoption of a list of questions for the applicant, if applicable. If applicable, CVMP endorsement of SAG/AHEG's members and adoption of list of questions to be addressed by the group.
Approximately Day 75	If applicable, SAG/AHEG meeting. If applicable, an oral explanation by applicant to the SAG/AHEG.
Approximately Day 80	Revised rapporteur's assessment report.
Day 90	Adoption of final CVMP opinion and assessment report (following an oral explanation by applicant to the CVMP, if applicable).

4.4.2. Timetable for re-examination of opinions for work-sharing procedures, variations requiring assessment, referrals and establishment of maximum residue limits

In accordance with Article 65(2), Article 66(11), Article 83(7) of Regulation (EU) 2019/6 and Article 8(3) second subparagraph of Regulation (EC) No 470/2009, within 60 calendar days of receipt of the detailed grounds for the re-examination of the CVMP opinion for the respective procedure, the CVMP will re-examine its opinion. An indicative timetable is described below. This is 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 will never exceed 60 calendar days and there is no possibility of a clock-stop.

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 needs to notify the Agency via email to Agency's procedural contact points 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 request should be submitted as soon as possible (see section 4.1). 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 number of participants) of the group and the data to be provided to the experts. The date of submission of the detailed grounds for the re-examination is agreed with the applicant/MAH (within 60 days of the receipt of the CVMP opinion).
Within 60 days of receipt of CVMP opinion Day 0	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, and adoption of a list of questions for the applicant/MAH, if applicable.

Time point	Step
	If applicable, CVMP endorsement of SAG/AHEG's members and adoption of list of questions to be addressed by the group.
Approximately Day 44	If applicable, SAG/AHEG meeting. If applicable, an oral explanation by applicant/MAH to the SAG/AHEG.
Approximately Day 50	Revised rapporteur's assessment report.
Day 60	Adoption of final CVMP opinion and assessment report (following an oral explanation by applicant/MAH to the CVMP, if applicable).

4.4.3. 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 CVMP rules of procedure[1] and the Agency's pre-submission[2] and post-authorisation[3] guidance documents for the respective assessment procedures.

As outlined above in section 4.3, Article 141(4) of Regulation (EU) 2019/6 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.

4.4.4. Consultation of a SAG/AHEG

A SAG 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. In an area where no SAG is established, the advice of additional available expertise will be requested in the form of consultation of an AHEG.

If a consultation with SAG/AHEG has been requested or is felt necessary, the CVMP will consider the mandate, composition, data to be provided by the Agency to the SAG/AHEG as well as adopt a list of questions to the SAG/AHEG. The key steps of consultation with a SAG/AHEG are outlined above in section 4.4.1 and 4.4.2 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 for 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.

4.4.5. 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.

[1] https://www.ema.europa.eu/en/committees/committee-medicinal-products-veterinary-use-cvmp
[2] https://www.ema.europa.eu/en/veterinary-regulatory/marketing-authorisation
[3] https://www.ema.europa.eu/en/veterinary-regulatory/post-authorisation

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 which is sent to the European Commission, in line with the legislative requirements and the practice for the particular procedure.

Detailed information on the decision-making process can be found on the European Commission website.

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. For centrally authorised products, the Agency will publish the EPAR based on the assessment report adopted by CVMP at the time of adoption of the 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.

4.8. Information to be made available to the public

The start of a re-examination procedure will be mentioned in the CVMP meeting highlights. The outcome of the re-examination will be published on the Agency's website. Depending on the procedure, different types of documents will be publish by EMA (e.g. summary of opinion, EPAR, refusal EPAR, questions and answers on referrals, all annexes of the CVMP opinion, etc.). The re-examination will be clearly identified.

In line with the legislative requirements and the practice for the particular procedure, the European Commission would also publish the outcome of the procedure in the Union Register of medicinal products[4]. For example:

[4] https://ec.europa.eu/health/documents/community-register/html/index_en.htm

- If the re-examination for an initial marketing authorisation application is followed by a positive CVMP opinion, the European Commission will publish the Commission Decision with Annexes in all EU languages.
- If the re-examination for an initial marketing authorisation application is followed by a negative CVMP opinion, the European Commission will publish the Commission Decision and grounds for refusal in all EU languages.
- For variations requiring an assessment concerning centrally authorised veterinary medicinal products, the European Commission will publish the Commission Decision amending the marketing authorisation.
- For referral procedures, irrespective of the outcome of the re-examination, the European Commission will publish the Commission Decision with Annexes in all EU languages.