EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard operating procedure

Title: Annual reassessment of centrally authorised veterinary medicinal products under exceptional circumstances		
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Lead author	Approver	Effective date: 12-MAY-16
Name: Faye Ioannou	Name: Fia Westerholm	Review date: 12-MAY-19
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1. Purpose

The purpose of this SOP is to provide staff in the Veterinary Medicines Division with guidance on the procedure to be followed for dealing with annual reassessments for centrally authorised medicinal products for veterinary use authorised under exceptional circumstances.

2. Scope

This standard operating procedure (SOP) applies to the Veterinary Medicines Division.

3. Responsibilities

It is the responsibility of the Head of Veterinary Medicines department (delegated to the Service Head for Development and Evaluation of Veterinary Medicines) to ensure that this procedure is adhered to within their department. The responsibility for the execution of a particular part of this procedure is identified in the right-hand column of section 9.

4. Changes since last revision

Main changes relate to updated VROS procedures on submission and validation tasks.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

5. Documents needed for this SOP

- (Draft) CVMP opinion in accordance with the latest agreed QRD template; available on the EMA external website and in SIAMED
- Recommended submission dates (EMA/793688/2015); *submission dates for Type II (60 day) procedures apply*
- Models/templates for all correspondence; available in SIAMED

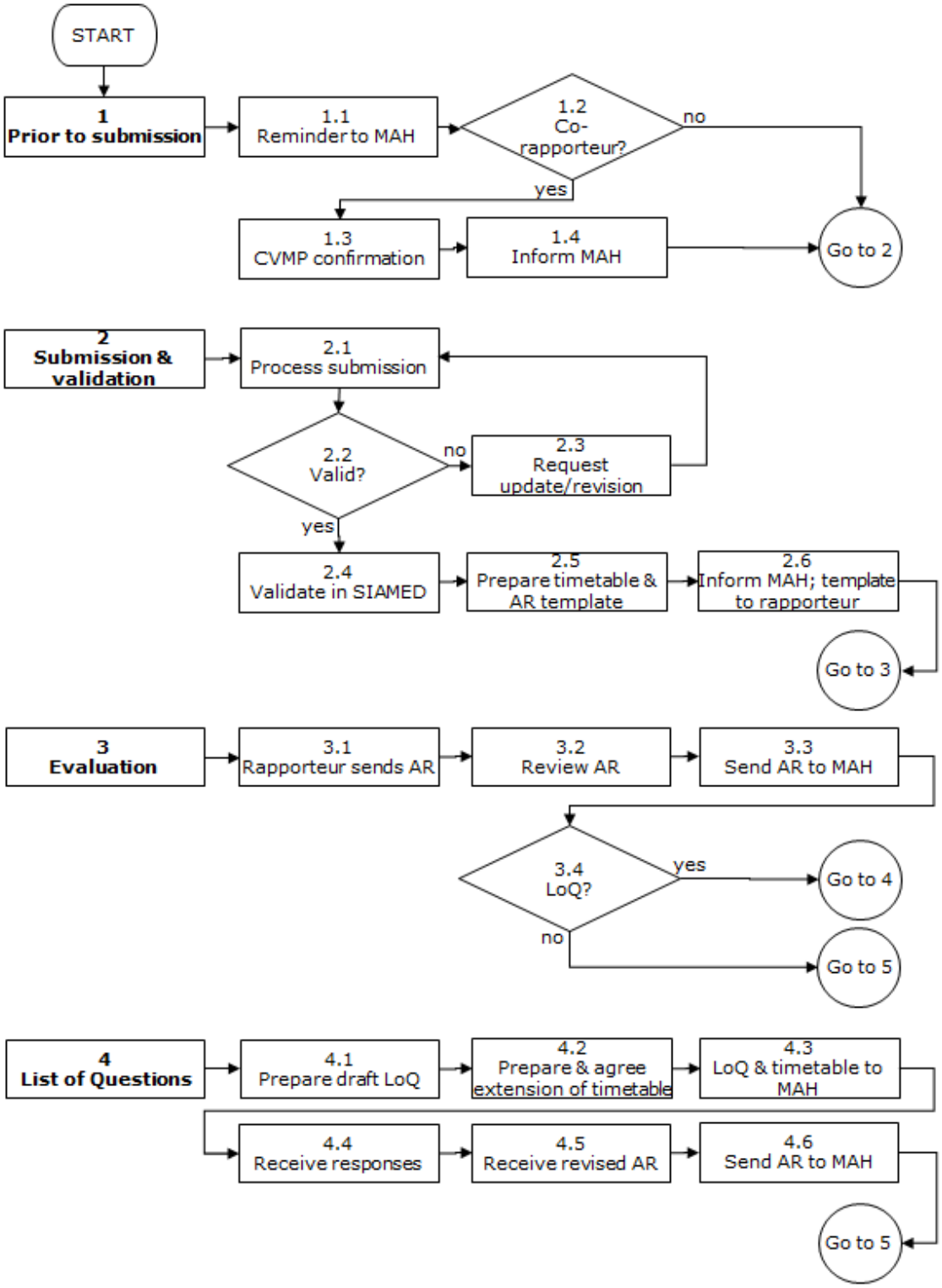
6. Related documents

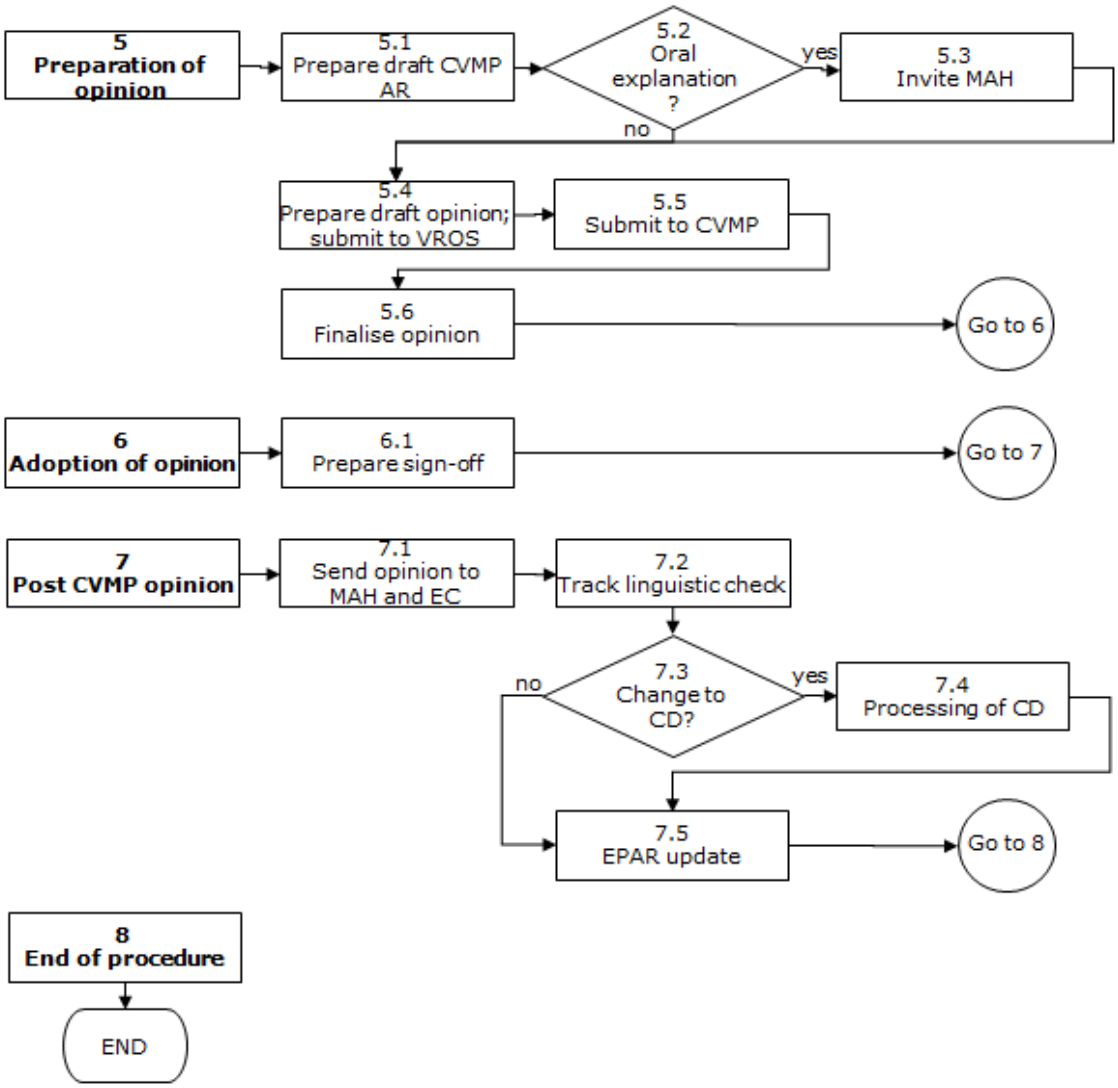
- Article 39(7) of Regulation (EC) No 726/2004 of 31 March 2004
- Directive 2009/9/EC, Title III(6)
- Article 26(3) of Directive 2001/82/EC, as amended
- EMA post-authorisation guidance: available on the EMA external website under: Regulatory – Veterinary Medicines – Post authorisation
- The new Linguistic Review Process of Product Information in the Centralised Procedure (EMA/288844/2009).
- SOP/V/4004 on processing of Type II variations for medicinal products for veterinary use
- SOP/V/4038 on the Updating of the European Public Assessment Report for a veterinary medicinal product

7. Definitions

AA	Administrative assistant
APH	Animal and Public Health service in the V-VM department
AR	Assessment report
AST	Assistant
CD	Commission Decision
CVMP	Committee for Medicinal Products for Veterinary Use
DEM	Development and Evaluation of Veterinary Medicines service in the V-VM department)
EC	European Commission
EPAR	European Public Assessment Report
LoQ	List of questions
MA	Marketing authorisation
MAH	Marketing authorisation holder
OE	Oral explanation
PM	Project manager (responsible scientific administrator in DEM appointed for the product/procedure)
PSUR	Periodic safety update report
SOs	Specific obligations
SPC	Summary of Product Characteristics
ToA	Table of actions
V-VM	Veterinary Medicines department
VROS	Veterinary Regulatory and Organisational Support service in the V-VM department)

8. Process map(s)/ flow chart(s)




5
Preparation of opinion
5.1
Prepare draft CVMP AR
5.2
Oral explanation ?
yes
5.3
Invite MAH
no
5.4
Prepare draft opinion; submit to VROS
5.5
Submit to CVMP
5.6
Finalise opinion
Go to 6
6
Adoption of opinion
6.1
Prepare sign-off
Go to 7
7
Post CVMP opinion
7.1
Send opinion to MAH and EC
7.2
Track linguistic check
7.3
Change to CD?
no
yes
7.4
Processing of CD
7.5
EPAR update
Go to 8
8
End of procedure
END

9. Procedure

Step	Action	Responsibility
1.0	**Prior to submission**	
1.1	*3-4 months prior to annual anniversary*[1]: Contact MAH to remind submission of documentation which should be at the product's annual anniversary (-/+2month), in line with recommended submission dates[2].	PM
1.2	Consider involvement of co-rapporteur (if applicable). *N.B: Normally, the co-rapporteur is not involved unless it is deemed necessary, i.e potential revocation of authorisation. In the latter case, contact rapporteur to discuss if the involvement of the co-rapporteur is needed.* Is the involvement of the co-rapporteur recommended? If yes, go to 1.3 If no, go to 2.0	PM
1.3	Include proposal for involvement of co-rapporteur in CVMP mailing and request confirmation by CVMP.	PM
1.4	Once co-rapporteur involvement has been confirmed by CVMP, inform the MAH accordingly. Proceed to 2.0	PM
2.0	**Submission & validation**	
2.1	<u>Receipt of annual reassessment application (day 0)</u> Upload the application to EURS. Create a subfolder in the product folder in DREAM (*Evaluation of Medicines/V-C/<medicinal product>/Post-authorisation/Annual reassessment*). Send link to the annual reassessment documentation to the PM.	 AA AA AA
2.2	<u>Validation</u> Check the application documentation. Identify any remaining SOs that are applicable to this procedure (either from the opinion of the initial authorisation of the product or previous annual re-assessment opinion(s)). Is the application valid? If yes, go to 2.4 If no, go to 2.3	 PM

[1] NB: 5th annual re-assessment will be incorporated into the renewal procedure.
[2] Submission dates for Type II (60 day) procedures apply

Step	Action	Responsibility
2.3	If the application is not correct or complete (i.e. no updated benefit/risk assessment, not all SOs addressed or some pages not legible), contact the MAH in writing (copy to the (Co-) Rapporteur, if applicable) listing the outstanding issues along with comments and clarifications or additional information requested. The MAH would be requested to reply within a timeframe allowing the start of the annual reassessment application as per the recommended start dates for Type II variations (60 days). Go to 2.2	PM
2.4	Validate procedure in SIAMED.	PM
2.5	Prepare a draft 60-day timetable for the annual reassessment and annual AR report template.	AST
2.6	Send email confirming the start of the procedure incl. timetable to the MAH by email. Send validation correspondence to (co)rapporteur, together with annual re-assessment template and timetable. Send validation confirmation and timetable to CVMP members. Proceed to 3.0	AST
3.0	**Evaluation (day 1 - day 60)**	
3.1	Ensure that the rapporteur circulates the annual reassessment AR to all CVMP members for comments (All CVE mailbox) and to the Agency on time, in accordance with the adopted timetable.	PM
3.2	Review the AR. If necessary, ensure that the AR includes an evaluation of and conclusion on any pharmacovigilance requirements (e.g. consideration of the PSUR cycle) specified as a condition of the authorisation under exceptional circumstances based on pharmacovigilance data assessed to date (liaise with APH). If the rapporteur recommends the conversion of the authorisation to normal, check if there are any pharmacovigilance or other requirements to be specified as a condition of the marketing authorisation, including whether the PSUR cycle should be re-set and if the relevant sentence is present in the AR.	PM
3.3	Send the Rapporteurs' AR to the MAH for information.	PM

Step	Action	Responsibility
3.4	Identify if there are significant issues preventing the adoption of the opinion (i.e. especially when there may be a conversion of the authorisation to normal or unresolved points of critical importance). Is a request for supplementary information (LoQ) foreseen at day 60? If yes, go to step 4.0 If no, go to step 5.0	PM
4.0	**Request for supplementary information (LoQ) (day 60)**	
4.1	Prepare the draft LoQ based on Rapporteur's AR and CVMP members' comments.	PM
	Include the draft LoQ in the CVMP mailing.	AST
4.2	Prepare a draft 30 day extension of the timetable including a 30 or 60 day clock stop and agree with (co)rapporteur.	PM
4.3	Following adoption of the LoQ by CVMP, send the CVMP LoQ and revised timetable to the MAH.	PM
4.4	Receive MAH responses to LoQ, upload to EURS and send link to PM.	AA
	Store the electronic documentation in the product folder in DREAM.	AST
4.5	Ensure that the rapporteur circulates the assessment of the responses to the LoQ to all CVMP members for comments and to the Agency on time, in accordance with the extended timetable.	PM
4.6	Forward the revised rapporteurs' AR to the MAH. Proceed to 5.0	PM
5.0	**Preparation of the opinion**	
5.1	Prepare the draft CVMP AR, based on the rapporteur's AR (of the response to the LoQ, if applicable) and CVMP members' comments.	PM
	Send the draft CVMP AR to the rapporteur for consideration/ comments.	PM
5.2	In case there are substantial discussion/controversial issues foreseen during the CVMP meeting related to the annual reassessment (e.g. on the proposed SPC wording, potential for revocation of the authorisation), liaise with the rapporteur and the MAH to explore the need to have the MAH present at the Agency during the CVMP week (for possible oral clarifications). Are oral explanations required? If yes, go to step 5.3 If no, go to step 5.4	
5.3	Invite MAH for oral explanations at the relevant CVMP meeting.	PM

Step	Action	Responsibility
5.4	Prepare draft CVMP opinion including the latest annex(es), and the draft CVMP annual reassessment AR (incl. Letter of Undertaking for the applicant to confirm the undertaking of the specific obligations, if applicable). Submit the draft opinion to VROS for checking. *If the authorisation is to convert to normal status*: Update opinion accordingly (i.e. use standard heading, include justification for conversion [e.g. all SOs have been fulfilled], delete specific obligations and, if necessary, include pharmacovigilance requirements, e.g. reset of PSUR cycle in Annex II). Ensure the correct opinion template is used if the MA is to be suspended or withdrawn.	PM
5.5	Include the draft CVMP opinion (with annexes and appendices) in the CVMP mailing.	PM
5.6	Taking into account any comments from the rapporteur and comments that may have emerged during the CVMP discussion, finalise the CVMP opinion. Proceed to 6.0	PM
6.0	**Adoption of CVMP Opinion (day 60/90 or at the end of the extension of the timeframe)**	
6.1	Prepare the sign-off folder for CVMP chair signature of the CVMP opinion according to one of the following options: ***CVMP positive opinion recommending the update of the MA and to keep the product under exceptional circumstances:*** Adopted CVMP opinion includes • Revised full set of annexes; • CVMP AR (as an appendix to the opinion); • A revised list of SOs (and information on PSUR cycle) set out in Annex II.D of the opinion (and CD); • A revised original, signed Letter of Undertaking from the MAH (if applicable) agreed by the CVMP (covering all remaining recommendations/SOs and changes to PSUR cycle etc); • Divergent position(s) (as an appendix to the opinion), if applicable; • Translation timetable for the finalisation of the procedure, if appropriate (PIPIT).	PM

Step	Action	Responsibility

CVMP positive opinion recommending the update of the MA and that the product is no longer under exceptional circumstances (all SOs have been fulfilled):

Adopted CVMP opinion includes

- Revised full set of annexes;
- CVMP AR (as an appendix to the opinion);
- All specific obligations are deleted as they are considered fulfilled;
- Divergent position(s) (as an appendix to the opinion), if applicable;
- Translation timetable for the finalisation of the procedure, if appropriate (PIPIT);
- A revised agreement from the MAH on remaining recommendations (if applicable) agreed by the CVMP.

CVMP positive opinion recommending NO update of the MA:

Adopted CVMP opinion includes

- CVMP AR (as an appendix to the opinion);
- A revised list of specific obligations, if applicable;
- Divergent position(s) (as an appendix to the opinion), if applicable;
- A revised agreement to remaining recommendations from the MAH (if applicable) as agreed by the CVMP.

CVMP recommending the revocation of the MA:

Adopted CVMP opinion includes

- Annex I: scientific conclusions and grounds for the revocation of the MA;
- CVMP AR (as an appendix to the opinion);
- Divergent position(s) (as an appendix to the opinion), if applicable;

Liaise with the Media and Public Relations Service (S-CO-MPR) regarding publication of the revocation of the MA.

Step	Action	Responsibility
	CVMP recommending the suspension of the MA:	
	Adopted CVMP opinion includes: • Annex I: scientific conclusions and grounds for the suspension of the MA; • CVMP AR (as an appendix to the opinion); • Divergent position(s) (as an appendix to the opinion), if applicable.	
	Liaise with the Media and Public Relations Service (S-CO-MPR) regarding publication of the suspension of the MA.	
	Proceed to 7.0	
7.0	**Post CVMP Opinion**	
7.1	Send the adopted opinion to the MAH and EC. Check the content of the CVMP ToA related to the outcome of the annual reassessment application. Update SIAMED accordingly to generate the EPAR (Module 8).	PM
7.2	Track the linguistic post-opinion check.	AST
7.3	Is the outcome of the annual reassessment leading to amendments to the previous CD? If yes, go to 7.4 If no, go to 7.5[3]	PM
7.4	CD phase is the same as for a full opinion. Send final translations of revised Annexes to EC.	AST
7.5	Update of the EPAR as a consequence of the outcome of the annual reassessment application, as appropriate, following procedural steps in SOP/V/4038 on EPAR updates Proceed to 8.0	PM
8.0	**End of procedure**	

10. Records

An electronic copy of all the correspondence related to the procedure is stored in the specific product folder in DREAM (Evaluation of Medicine/V-C/<medicinal product>/Post-authorisation/Annual Re-Assessment). A database and application tracking system is provided by SIAMED.

[3] No amendment of previous Commission Decision results when no update of the marketing authorisation is recommended.