EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard operating procedure

Title: Evaluation procedure for veterinary medicines initial marketing authorisation procedures and extensions		
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1. Purpose

This SOP serves to describe the procedure for the evaluation of initial marketing authorisation and extension applications (including informed consent procedures) for veterinary medicinal products.

2. Scope

This SOP applies to the appointed procedure teams for the evaluation of initial marketing authorisation and extension applications, within the Veterinary Medicines Division.

The timelines of accelerated procedures are stated in brackets after the timelines for the standard procedure, e. g. 120 (90) days.

This SOP includes also the procedure for the re-examination of CVMP opinions on initial marketing authorisation and extension applications.

3. Responsibilities

It is the responsibility of the Head of the Veterinary Medicines Department (delegated to the relevant Head of Service) to ensure that this procedure is adhered to within their own Department/Service. 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

Correction to procedural description and flow-chart.

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5. Documents needed for this SOP

- Procedure templates in SIAMED
- Procedure checklist in DREAM (EMA/161247/2017)

6. Related documents

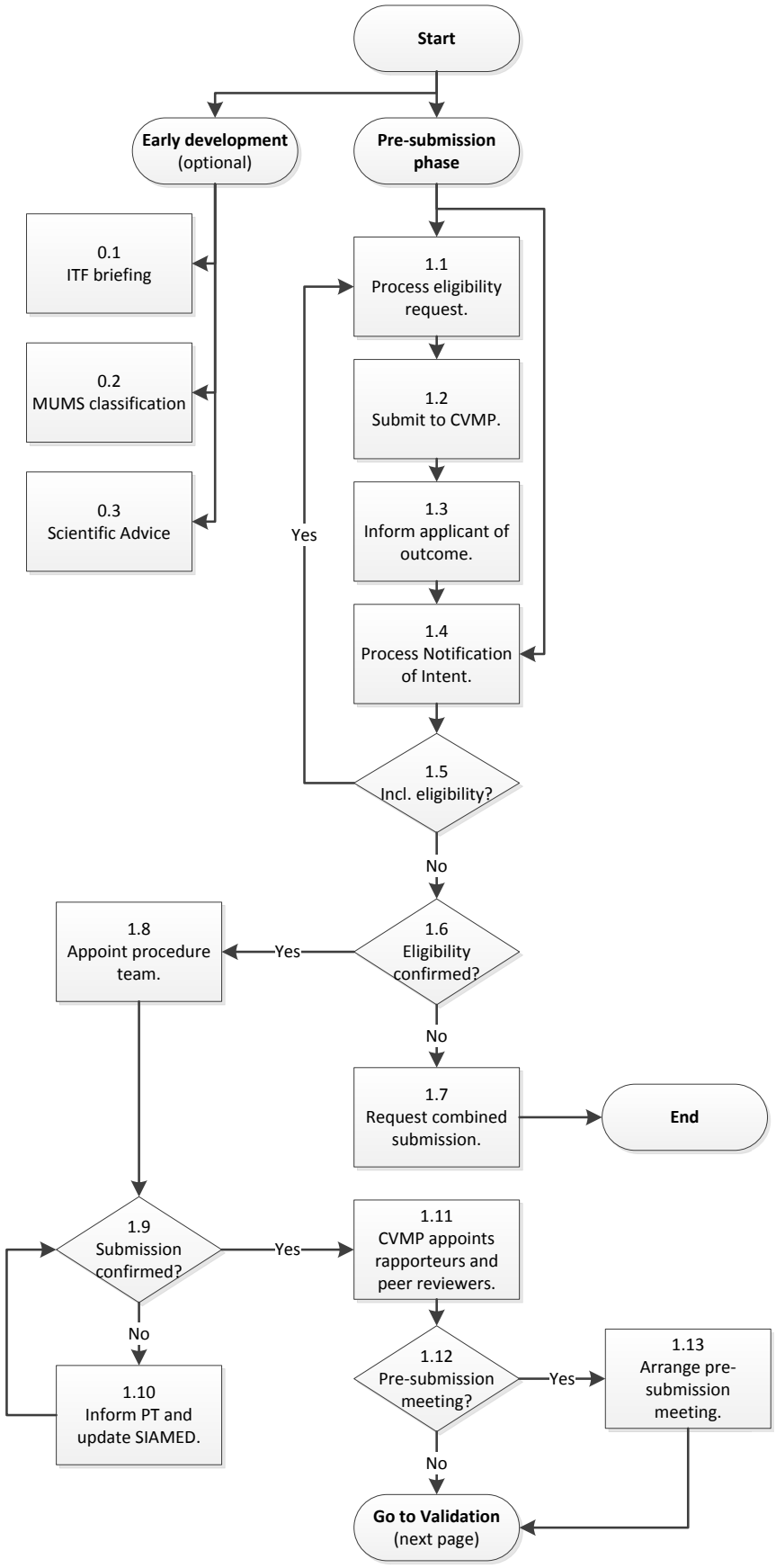
- Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2001L0082:20090807:EN:PDF
- Volume 6A – Notice to applicants and regulatory guidelines for medicinal products for veterinary use: Procedures for marketing authorisation https://ec.europa.eu/health/documents/eudralex/vol-6_en
- Guideline on the procedure for accelerated assessment pursuant to Article 39 (8) of regulation (EC) No 726/2004 (EMEA/CVMP/32995/2006)
- Pre-submission guidance for initial marketing authorisation and extension applications (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000283.jsp&mid=WC0b01ac058002da5e)
- List of recommended submission dates (published annually on the Agency website) http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000188.jsp&mid=WC0b01ac058002d9ae)
- SOP/PDM/1004 on Core Master Files of medicinal products for human and veterinary use following the centralised procedure
- SOP/H/3044 on the Organisation of Innovation Task Force briefing meetings (medicines for human/veterinary use); and
  Checklist on additional administrative actions for processing ITF queries and requests for ITF briefings for veterinary medicines (EMA/728325/2017)
- SOP/V/4111 on the Evaluation procedure for CVMP MUMS/limited markets classification requests; and
  Checklist on CVMP MUMS/limited markets classifications (EMA/728378/2017)
- SOP/V/4112 on the Evaluation procedure for CVMP Scientific Advice requests; and
  Checklist on CVMP scientific advice procedures (incl. CVMP SAWP organisation) (EMA/268710/2017)

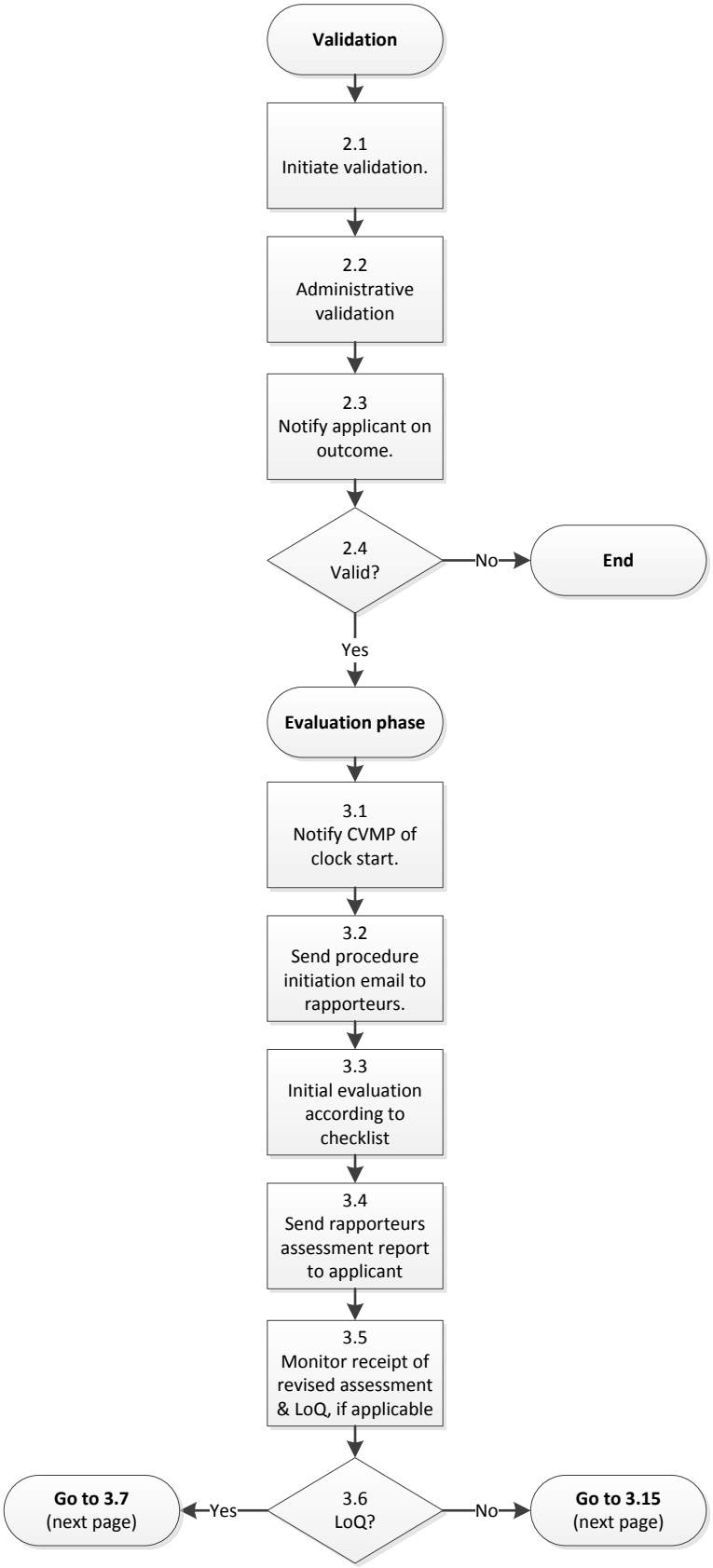
7. Definitions

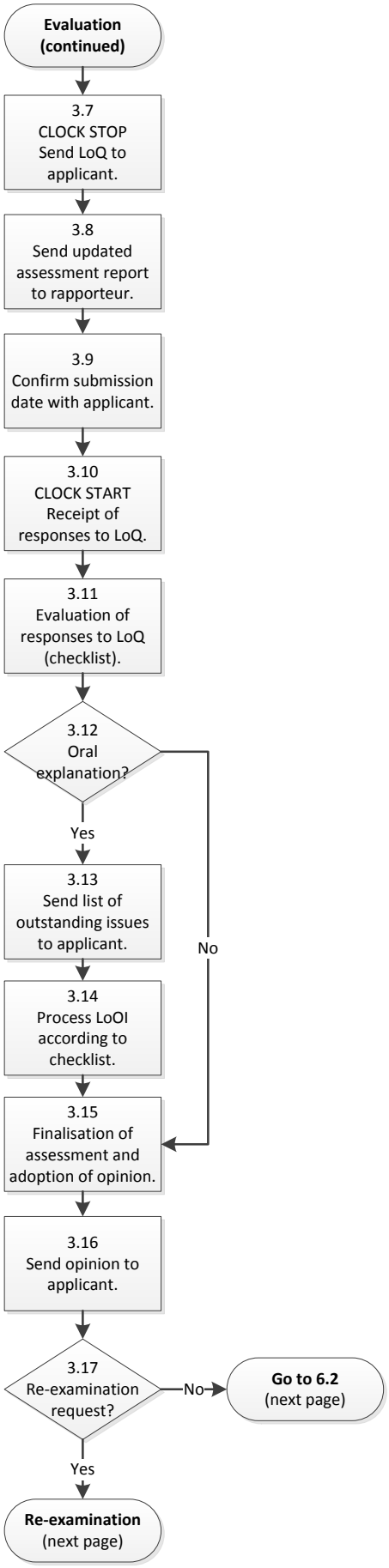
AA	Administrative Assistant responsible for processing submissions received in vet.applications mailbox (here: Administrative Assistant in VROS)
Checklist	Agency-internal document describing all administrative steps involved in a specific procedure. In this case refers to checklist on initial and extension marketing authorisation procedures, unless otherwise specified.
cMF	Core Master File
CVMP	Committee for Medicinal Products for Veterinary Use

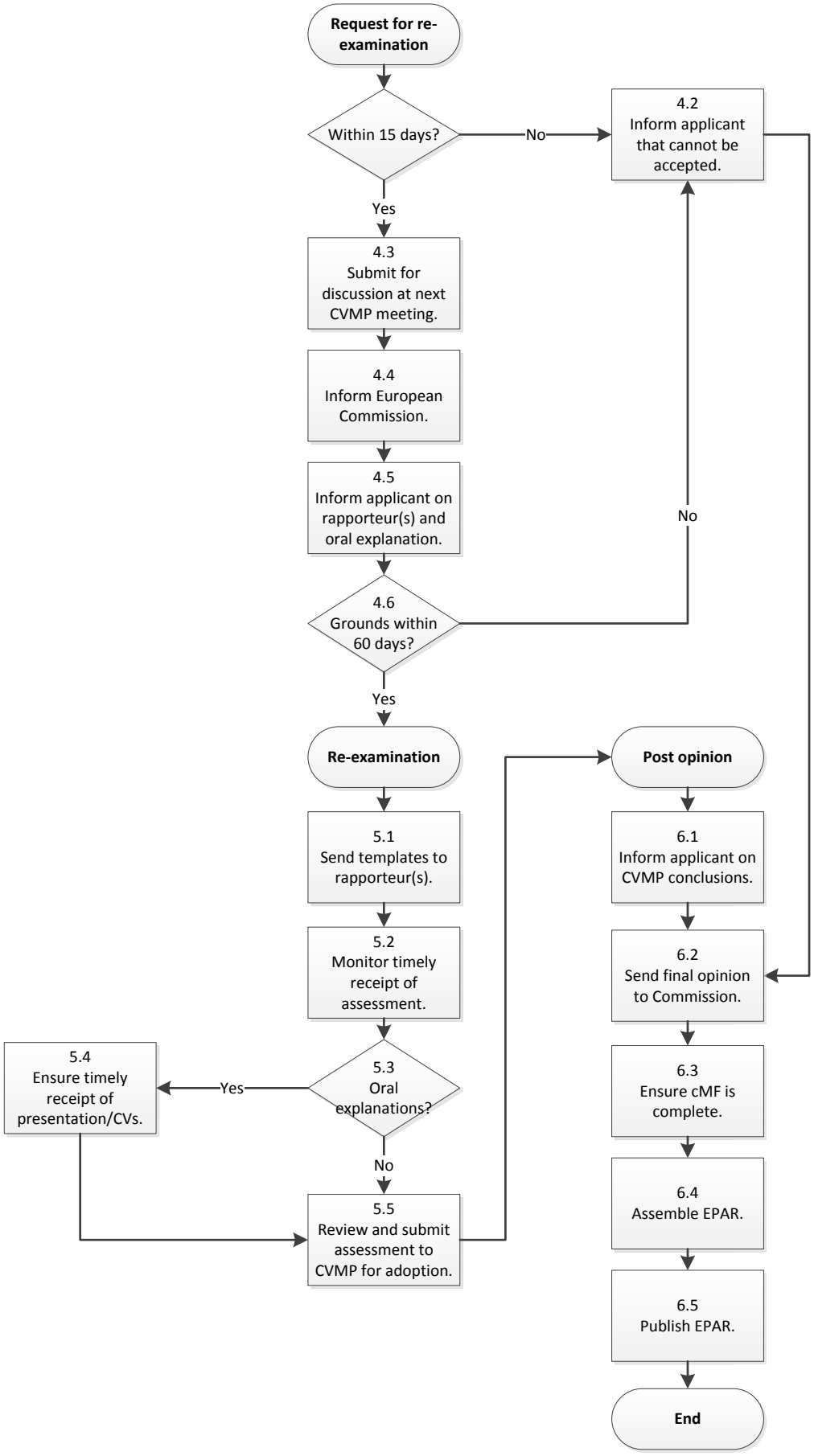
EPAR	European Public Assessment Report
DREAM	Document Records Electronic Archive Management
EPAR PC	Procedure Coordinator, typically an Assistant, assigned to the management of the EPAR preparation and publication procedure
ER/NOI PC	Procedure Coordinator, typically an Assistant, assigned to the management of the eligibility request and notification of intent procedures
HSer	Head of Service
ITF PC	Procedure Coordinator, typically an Assistant, assigned to the management of ITF briefing procedures
LoOI	List of outstanding issues
LoQ	List of questions
MUMS	Minor use minor species/limited markets
MUMS PC	Procedure Coordinator, typically an Assistant, assigned to the management of MUMS/limited markets classification procedures
PC	Procedure Coordinator, typically an Assistant, assigned to the management of the procedure
Peer reviewer	CVMP member and/or alternate (who is not acting as rapporteur or co-rapporteur in the procedure) tasked with quality assurance of CVMP documents (in this case related to the establishment of maximum residue limits)
(Co-)Rapporteur	CVMP member and/or alternate appointed for the assessment of the application
SIAMED	Product information and application tracking system of the Agency
S/CL	Scientific administrator assigned as the scientific/content lead for the procedure
SA	Scientific advice
SA PC	Procedure Coordinator, typically an Assistant, assigned to the management of Scientific Advice procedures
SOP	Standard operating procedure; Agency document describing steps involved in a specific procedure
VO	Validating Officer, responsible for the validation of the application dossier (here: Administrative Assistant in VROS)
VROS	Veterinary Regulatory and Organisational Support service (in the Veterinary Medicines department)

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




Validation
2.1
Initiate validation.
2.2
Administrative validation
2.3
Notify applicant on outcome.
2.4
Valid?
No
End
Yes
Evaluation phase
3.1
Notify CVMP of clock start.
3.2
Send procedure initiation email to rapporteurs.
3.3
Initial evaluation according to checklist
3.4
Send rapporteurs assessment report to applicant
3.5
Monitor receipt of revised assessment & LoQ, if applicable
3.6
LoQ?
Yes
Go to 3.7
(next page)
No
Go to 3.15
(next page)


Evaluation (continued)
3.7 CLOCK STOP Send LoQ to applicant.
3.8 Send updated assessment report to rapporteur.
3.9 Confirm submission date with applicant.
3.10 CLOCK START Receipt of responses to LoQ.
3.11 Evaluation of responses to LoQ (checklist).
3.12 Oral explanation?
Yes
No
3.13 Send list of outstanding issues to applicant.
3.14 Process LoOI according to checklist.
3.15 Finalisation of assessment and adoption of opinion.
3.16 Send opinion to applicant.
3.17 Re-examination request?
No
Go to 6.2 (next page)
Yes
Re-examination (next page)


Request for re-examination
Within 15 days?
No
4.2
Inform applicant that cannot be accepted.
Yes
4.3
Submit for discussion at next CVMP meeting.
4.4
Inform European Commission.
4.5
Inform applicant on rapporteur(s) and oral explanation.
No
4.6
Grounds within 60 days?
Yes
Re-examination
5.1
Send templates to rapporteur(s).
5.2
Monitor timely receipt of assessment.
5.4
Ensure timely receipt of presentation/CVs.
Yes
5.3
Oral explanations?
No
5.5
Review and submit assessment to CVMP for adoption.
Post opinion
6.1
Inform applicant on CVMP conclusions.
6.2
Send final opinion to Commission.
6.3
Ensure cMF is complete.
6.4
Assemble EPAR.
6.5
Publish EPAR.
End

9. Procedure

Step	Action	Responsibility
0.0	**(Early) Development phase (optional steps)**	
0.1	Receipt of form requesting an **ITF briefing** meeting • Follow instructions in SOP/H/3044 on the organisation of Innovation Task Force briefing meetings (medicines for human / veterinary use); and, in parallel, • Follow additional instructions in checklist on additional administrative actions for processing ITF queries and requests for ITF briefings for veterinary medicines.	ITF PC
0.2	Receipt of request for **MUMS/limited market** classification • Follow the SOP on CVMP MUMS classification procedure; and, in parallel, • Follow additional instructions in checklist on MUMS classification procedures.	MUMS PC
0.3	Receipt of **scientific advice** request if applicable • Follow instructions in SOP on CVMP scientific advice procedure; and, in parallel, • Follow additional instructions in checklist on CVMP scientific advice procedures.	SA PC
1.0	**Pre-submission phase**	
1.1	*Eligibility request received at any time up to 7 months before intended submission* Upon receipt eligibility request is processed following the procedural steps described in the checklist (pre-submission tab). *NB: If eligibility request is submitted at same time as notification of intent (steps 1.4 ff.); both submissions are processed in parallel.*	ER/NOI PC
1.2	Submit eligibility request to CVMP for consideration.	ER/NOI PC
1.3	Inform applicant on outcome of CVMP discussion.	ER/NOI PC
1.4	*Notification of intention to submit initial (or extension) marketing authorisation application is usually received **7 months** before the intended submission* Upon receipt of letter of intent the notification is processed following the procedural steps described in the checklist (pre-submission tab).	ER/NOI PC
1.5	Was an eligibility request submitted at the same time? If **yes**, go to 1.1 If **no**, go to 1.6	
1.6	Has eligibility for the proposed product been confirmed at an earlier stage? If **yes**, go to 1.8 If **no**, go to 1.7	
1.7	Send request to applicant to (re-)submit a combined eligibility request and notification of intent. Proceed to 7.0 (end of procedure)	ER/NOI PC
1.8	Appoint procedure team.	HSer

Step	Action	Responsibility
1.9	*Approx. 3 months before intended submission* Confirm submission date with applicant. Has the intended submission date been confirmed? If **yes**, go to 1.11 If **no**, go to 1.10	ER/NOI PC
1.10	Notify PT and update SIAMED. Proceed to 1.9	ER/NOI PC
1.11	*Appointment of rapporteur and co-rapporteur, as well as peer reviewers by CVMP* Notify the applicant of the appointed rapporteur and co-rapporteur, and of the recommended submission date(s).	ER/NOI PC
1.12	Has applicant requested a pre-submission meeting? If **yes**, go to 1.13 If **no**, go to 2.0	
1.13	Arrange pre-submission meeting following procedural steps described in the checklist (pre-submission tab). Proceed to 2.0	PC
2.0	**Submission and validation**	
2.1	Upon receipt the initial or extension marketing authorisation application is processed following the procedural steps described in the checklist.	AA
2.2	*Within 13 working days*: Carry out administrative validation.	VO
2.3	Notify applicant, PT, rapporteur and co-rapporteur of the outcome of the validation of the application.	VO
2.4	Was the validation positive? If **yes**, go to 3.0 If **no**, proceed to 7.0 (end of procedure)	
3.0	**210 (120)[1] day Evaluation Phase**	
3.1	Notify CVMP of clock start: day 1.	PC
3.2	Send the procedure initiation emails to rapporteur, co-rapporteur and peer reviewers.	PC
3.3	Initial evaluation within 120 (90) days following procedural steps described in checklist. Monitor timely receipt of: • draft assessment report and scientific overview including list of questions, if applicable, from rapporteur • critique of rapporteur's assessment report from the co-rapporteur, if applicable • comments on assessment report from the peer reviewers, CVMP members and any others, as applicable.	PC
3.4	Send rapporteur's assessment report (incl. co-rapporteur's critique, if applicable) to applicant.	PC
3.5	Monitor receipt of revised scientific overview including list of questions, if applicable, from the rapporteur.	PC

[1] The number of days in brackets refers to the timeline for an accelerated procedure in accordance with Art. 15 of Regulation (EC) 470/2009

Step	Action	Responsibility
3.6	*Conclusion on initial evaluation and adoption of the scientific overview, if applicable, by CVMP (Day 120 (90)).* Did CVMP adopt a list of questions? If **yes**, go to 3.7 If **no**, go to 3.15	
3.7	***Clock Stop*** Send scientific overview with LoQ to applicant[2].	PC
3.8	Confirm the exact submission date for responses to the LoQ with the applicant 2 months prior to the deadline.	PC
3.9	Once the response[3] has been received on the agreed date according to submission dates, ***restart clock*** of the remaining evaluation period for days 121-180.	PC
3.10	*Evaluation of responses to list of questions within the next 60 days following procedural steps described in checklist*. Monitor timely receipt of: • updated assessment report and scientific overview with assessment of responses to LoQ, and proposed LoOI from rapporteur • comments on updated assessment report from the peer reviewers, CVMP members and any others, as applicable.	PC
3.11	Send updated joint assessment report to applicant.	PC
3.12	Has CVMP agreed to request or grant an oral explanation (and when to hear it) (Day 180)? If **yes**, go to 3.13 If **no**, go to 3.15	
3.13	***Clock stop*** Send list of outstanding issues to applicant, if applicable. Arrange oral explanations according to steps described in checklist.	PC
3.14	***Clock start (Day 181-210)*** Monitor timely receipt of revised rapporteurs' assessment report following oral explanation from the rapporteur.	PC
3.15	Monitor finalisation of assessment report and adoption of opinion for recommendation at day 210.	PC
3.16	Send opinion including CVMP assessment report to applicant and European Commission according to procedural steps described in the checklist.	PC
3.17	Did the applicant request a re-examination[4]? If **yes**, go to 4.0 If **no**, go to 6.2	
4.0	**Receipt of a notification to request re-examination of CVMP opinion by the applicant**	
4.1	Was the notification received within the 15 day deadline? If **yes**, go to 4.3 If **no**, go to 4.2	

[2] The Agency identifies an approximate submission date in the cover letter to the status report and LoQ; in general 6 months are granted to respond to the LoQ. This timeframe may be extended only exceptionally upon request and if duly justified.

[3] One consolidated response to all questions should be submitted

[4] Within 15 days of receipt of the opinion, the applicant may provide written notice to the Agency secretariat of his intention to request re-examination of the recommendation (see *Annex IV*)

Step	Action	Responsibility
4.2	Inform applicant that re-examination request cannot be accepted as deadline has passed. Go to 6.2	PC
4.3	Inform applicant of submission of notification to CVMP, including notification of deadline for submission of detailed grounds for re-examination (see *Annex IV*). Submit notification for discussion (and decision on oral explanation, if requested by applicant) and appointment of rapporteur (and co-rapporteur, if appropriate) at next CVMP meeting.	PC PC
4.4	Inform European Commission of receipt of notification to request re-examination.	PC
4.5	*Within 5 days after CVMP meeting:* Inform applicant on rapporteur(s) for the re-examination and of decision on oral explanations, if applicable.	PC
4.6	Were the detailed grounds received within the 60 day deadline? If **yes**, go to 5.0 If **no**, go to 4.2	
5.0	**Re-examination of CVMP opinion**	
5.1	Send the template for the assessment of the grounds for re-examination and CVMP assessment report (previously adopted) in electronic format to the rapporteur for the assessment of the re-examination, to facilitate the inclusion of changes to the assessment. Submit detailed grounds for discussion at next CVMP meeting (first meeting after receipt of detailed grounds).	PC
5.2	Monitor timely receipt of report on assessment of detailed grounds for re-examination as well as revised version of assessment report from rapporteur.	PC
5.3	*Following initial discussion at CVMP meeting:* Has CVMP agreed to grant an oral explanation (and when to hear it)? If **yes**, go to 5.4 If **no**, go to 5.5	
5.4	If not already done earlier in the procedure, inform applicant of date and timing of oral explanation. At least 1 week before the CVMP meeting: Monitor timely receipt of presentation and CVs of applicant representatives.	PC
5.5	At least 6 working days before the CVMP: review draft revised assessment report, draft final opinion for adoption by CVMP. Proceed to 6.0	S/CL
6.0	**Post Opinion**	
6.1	*On the last day of CVMP meeting:* finalise letter to applicant informing on the CVMP conclusions. Finalise CVMP opinion and CVMP assessment report. Send letter with opinion and assessment report to applicant via Eudralink.	PC
6.2	On the following day after the end of the CVMP meeting (usually Friday) send final opinion including assessment report to the European Commission, following the steps in checklist.	PC
6.3	*Following end of Standing Committee phase* Assemble EPAR.	EPAR PC

Step	Action	Responsibility
6.4	*Following receipt of Commission Decision* Arrange for publication of EPAR on Agency website. Proceed to 7.0	EPAR PC
6.5	Check the completeness of the electronic cMF. Declare documents as a record in DREAM for the electronic cMF, if not done previously.	PC
7.0	**End of procedure**	

10. Records

Electronic copies are saved in the appropriately labelled folder in DREAM.

Annex I

Submission of marketing authorisation application dossiers to CVMP (published as a separate document) (http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/11/WC500014483.pdf)

As of 1 January 2016 it is mandatory for applicants to use the electronic Application Forms (eAF) for all application procedures (authorisations, variations and renewals).

As of 1 January 2017 it is mandatory for applicants to use the eSubmission Gateway/Web Client for all veterinary procedural submissions to the Agency. For more information, including links to guidance on registration with the system, refer to the Veterinary e-submission website: http://esubmission.ema.europa.eu/tiges/vetesub.htm.

Annex II
Standard timetable for evaluation of initial and extension marketing authorisation applications

Pre-submission phase

Day	Step
- 7 months	Notification of intent to submit an application (incl. eligibility request if not confirmed before)
- 3 months	CVMP plenary meeting Appointment of rapporteur(s) and peer reviewer; notification of recommended submission dates to applicant
-14	Submission of application dossier
0	Validation

Evaluation

Day	Step
+1	Start of assessment procedure
+70	Rapporteur's assessment report
+85	Co-rapporteur's critique
+120	CVMP decision on the need for further information with the adoption of a scientific overview including a list of questions
	Clock stop
	- 6 months timeline for submission of responses –
+121	Submission of written responses by the applicant (*clock re-start*)
+150	Outcome of QRD check of the product literature
+160	Rapporteurs' updated assessment report with assessment of responses to the list of questions including rapporteurs' views on need for oral or written explanations; applicant may (also) request to provide oral explanations to CVMP
+180	CVMP discussion of draft opinion *or* CVMP request for oral or written explanations on outstanding issues[5] CVMP may agree a 1-2 month clock stop to allow for preparation of oral or written explanations, if justified.
	Clock stop
	Oral explanation (as appropriate)
	Clock re-start
+210	CVMP opinion

[5] Oral explanations can also be granted at the request of the applicant

Annex III
Timetable for accelerated evaluation of initial and extension marketing authorisation applications

Pre-submission phase

- as for standard timetable –

Initial evaluation

Day	Step
+1	Start of assessment procedure
+45	Rapporteurs' assessment report
+90	CVMP opinion *or* CVMP expresses the need for further information (list of questions); in the latter case:
	Clock stop
	- 6 months timeline for submission of responses[6] –
+91	Submission of written responses by the applicant (*clock re-start*)
+115	Rapporteurs' joint assessment report including rapporteurs' views on need for oral or written explanations; applicant may request to provide oral explanations to CVMP
+119	CVMP discussion of draft opinion *or* CVMP request for oral or written explanations CVMP may agree a 1-2 month clock stop to allow for preparation of oral or written explanations, if justified.
+120	Oral explanation (as appropriate)
+150	CVMP opinion

[6] Depending on the extent of the list of questions and the amount of data expected the CVMP might decide to revert the assessment to a standard timetable, i. e. evaluation of the responses to the list of questions in 90 days instead of 30 days.

Annex IV
Presentation of detailed grounds for request for re-examination

Requests for re-examination and supporting grounds shall contain argumentation and clarification of data previously submitted in the original application. It is not considered the purpose of a re-examination to provide an opportunity for the submission of new data.

The detailed grounds for re-examination shall be presented in one of the following ways:

a. Attached to the written notice by the applicant to the Agency secretariat of his intention to request the re-examination of the CVMP opinion (send within 15 days after receipt of the CVMP opinion).

b. Submitted separately from the written notice within 60 days of receipt of the CVMP opinion to the Agency secretariat and to CVMP members and alternates taking into account the dossier submission requirements in Annex I (addresses as per CVMP member list: http://www.ema.europa.eu/htms/general/contacts/CVMP/CVMP_members.html).

The day of the receipt is the day when the applicant receives the opinion by Eudralink. Days are counted as calendar days. The period starts at the day following the receipt of the opinion. Where the last day in a specific period falls on a Saturday, Sunday or Public Holiday the following working day will be considered as the final day.

Applicants are advised to contact the Agency secretariat before submitting the grounds for re-examination to discuss submission date and to clarify the most suitable option.

Timeline for re-examination procedure

Day 0 – 15 after receipt of CVMP opinion by Eudralink:	Applicant sends notification of request for re-examination
Next CVMP meeting:	Appointment of (co-) rapporteur for re-examination procedure
Day 0 – 60 after receipt of CVMP opinion by Eudralink:	Applicant sends detailed grounds for re-examination of CVMP opinion
First CVMP meeting after receipt of grounds:	Initial discussion at CVMP, agreement on need/granting of oral explanations
Second CVMP meeting after receipt of grounds:	Oral explanations (if applicable) Adoption of final (revised or unchanged) CVMP opinion