EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Work instructions

Title: Handling of renewals for centrally authorised veterinary medicinal products		
Applies to: Veterinary Medicines Division		
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1. Changes since last revision

New WIN.

2. Records

- The electronic submission including cover letter, application form, the full variation dossier and revised submissions (where requested) are stored in the EXTEDO Universal Review System (EURS) repository.
- Amended Annexes (if applicable) are saved in DREAM in the procedure folder, in its subfolder “Translations”.
- Electronic versions of acknowledgments of receipt (where applicable) are copied to the relevant product shared mailbox. Scanned copies of all signed correspondence, relevant emails to the MAH and Rapporteur (if necessary) are saved in DREAM in the procedure folder (Cabinets/01. Evaluation of Medicines/V - C/2. Active applications/[PRODUCT]/05 Post Authorisation/Post Activities). The crucial procedure documents are to be saved in DREAM product folder and declared as records for long (30-year) preservation by adding them to the electronic cMF, in accordance with SOP/PDM/1004 and the cMF checklist applicable to the procedure.
- Paper copies of all other correspondence related to the procedure should be stored in temporary filing area by their date of submission/issue and discarded after 6 months have elapsed for the date of issue/submission.

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3. Instructions

3.1 Definitions

Renewal applications are assessed within 90 days following notification of positive outcome of validation. Validation is 10 Agency working days starting on the next working day after receipt of the application.

In the case of outstanding issues identified by day 90, the applicant can amend the application or provide supplementary information within 10 calendar days. The procedure is then extended to 120 days. Details of recommended submission dates and deadlines for the procedural steps are listed in the Recommended submissions dates document (EMA/793688/2014).

AA	Administrative Assistant in V-VM-ROS (vet.applications team member)
APH	Animal and Public Health (in V-VM)
AR	Assessment report
AST	Assistant (here: assigned product assistant for post-authorisation)
CD	Commission Decision
cMF	Core Master File
CVE	Eudranet (email) box for variations ('All veterinary CVE')
CVMP	Committee for Medicinal Products for Veterinary Use
DDPS	Detailed Description of Pharmacovigilance System
DREAM	Document Records Electronic Archive Management
EC	European Commission
EMA	European Medicines Agency
EPAR	European Public Assessment Report
Eudralink	Secure mailing system for transmission of confidential documents
EURS	EXTEDO Universal Review System
E-SR-LRS	Labelling Review and Standards Office within Human Medicines Evaluation (E) Division
HDep	Head of Department
HSer	Head of Service
LoOI	List of Outstanding Issues
MAH	Marketing authorisation holder
MS	Member States
P-CI	Compliance and Inspection Department
PI	Product Information (Summary of Product Characteristics, Labelling and Package Leaflet)
PIQ	Product Information Quality

ProcM	Procedure Manager responsible for coordinating the renewal of a given product
QRD	Working Group on the Quality Review of Documents
RSI	Request for supplementary information
SIAMED	Agency database for tracking application procedures
SOP	Standard Operating Procedure
TT	Timetable
V-VM	Veterinary Medicines Department
V-VM-ROS	Veterinary Regulatory and Organisational Support (in Veterinary Medicines Department)
VETCOM	Eudranet (e-mail) address for the Standing Committee ('All veterinary VETCOM')
WIN	Work Instruction

3.2 Related documents

- Templates and models for renewal procedures are available in SIAMED BI Templates area / Veterinary / Renewal.
- Guideline on the Processing of Renewals in the Centralised Procedure, found in the EudraLex - Volume 6 Notice to Applicants and Regulatory Guidelines for Medicinal products for Veterinary use - Volume 6C Regulatory Guidelines
- Volume 9B of The rules Governing Medicinal Products in the European Union - Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use
- EMA post-authorisation guidance on renewals (veterinary) on EMA website
- e-Submission guidance: http://esubmission.ema.europa.eu/tiges/vetesub.htm
- electronic Application Form (eAF) for renewals[1].
- Centralised procedure - Recommended submission dates (on EMA website)
- Dossier requirements for submission of marketing authorisation and maximum residue limit applications (on EMA website)
- The linguistic review process of product information in the centralised procedure - veterinary (EMA/288844/2009 Rev. 4), also referred to as "PIPIT guidance"
- The revised checking process of mock-ups and specimens of outer/immediate labelling and package leaflets in the centralised procedure for veterinary medicinal products (EMEA/14522/2007-Rev.1)
- Explanatory note on fees payable to the EMA (EMA website)
- Rules for the determination of 'strength' for the purpose of calculation of fees (Q10 of the Veterinary Pre-Submission Guidance on EMA website)
- WIN/V/4048 on the Processing of pharmacovigilance data in renewal procedures for centrally authorised medicinal products for veterinary use

[1] The use of the eAF is mandatory from 1 July 2015 in the centralised procedure (Human and Veterinary), and from 1 January 2016 in all EU procedures (Human and Veterinary)

- SOP/PDM/1004 on Core Master Files of medicinal products for human and veterinary use following the centralised procedure
- SOP/EMA/0046 on PIQ/QRD review of Product Information for Renewal Procedures
- SOP/EMA/0048 on QRD Post-opinion Review of Product Information for Renewals, Referrals, Annual Reassessment and Type II Variations (60/90 Days)
- SOP/V/4038 on Updating of the European Public Assessment Report for a veterinary medicinal product

3.3 Instructions

Step	Action	Responsibility
1.0	**Pre-submission**	
1.1	*Approx. 10 months before MA expiry:* Was a pre-submission meeting requested by the MAH? If yes, go to 1.2 If no, go to 1.5	
1.2	Gather questions/areas of concern from the MAH. Check outstanding specific obligations with applicant, rapporteur/co-rapporteur. Liaise with APH (regarding pharmacovigilance data, e.g. PSURs to be included in renewal application) and Inspections (regarding Annex II Section A - GMP Inspection updates needed for some countries e.g. IE, SE, UK). *NB: Pre-submission meetings are generally not recommended for post-authorisation activities, however in exceptional circumstances MAHs may request a pre-submission meeting with EMA regarding a renewal, particularly if the product concerned has not had any post-authorisation procedures prior to the renewal. This should ideally take place at least 10 months before the anniversary of the marketing authorisation.*	AA
1.3	Schedule pre-submission meeting and invite colleagues from APH and P-CI-MCP, as applicable. Remind the MAH to submit electronic “track changes” versions of product information in English, to comply with current template. Ensure inclusion of the following documents in the meeting documentation: • Renewal guideline - Notice to applicants (Volume 6C - Guideline on the processing of renewals in the centralised procedure) (to help describe step by step the dossier requirements)	AA

Step	Action	Responsibility
	• electronic Application Form (eAF) (go through with the MAH step by step) • PIPIT guidance • Link to recommended submission dates • List of variations submitted (extractable from SIAMED BI Reports area)	
1.4	Coordinate review of meeting minutes provided by the MAH. Forward final minutes of the meeting to the MAH (in case of changes to MAH's version), the rapporteur/co-rapporteur and vet.applications team.	AA AST
1.5	*Approx. 9 months before expiry of the MA: The MAH should contact EMA on vet.applications@ema.europa.eu if any clarification is (still) required regarding the details of the renewal submission.* Review points of the query and if applicable, the appropriate recommended submission date, in liaison with HSer V-VM-ROS. If applicable, send query to pharmacovigilance colleagues in V-VM-APH service for confirmation of the PSUR requirements. *NB: An application for renewal should be submitted not less than 6 months before expiry of the MA, however we now recommend up to 9-months before for procedural reasons.*	 AA
1.6	Send response to MAH contact point via Eudralink, cc: Rapporteur and co-rapporteur. Proceed to 2.0	AA
2.0	**Submission and technical check**	
2.1	Day 0-1: Following receipt, process application according to WIN/V/4062[2], including technical validity check. If requested by MAH, send a confirmation of receipt of the application to MAH electronically. *NB: Receipt of a renewal application (must be at least 6 months prior to the actual expiry date of the MA as stated in the Commission Decision granting or renewing the marketing authorisation).*	AA
2.2	Check the presence of the formatted table template to be inserted in application submission cover letters for veterinary procedures.	ProcM

[2] The application is initially handled by AA appointed to monitor the mailbox.

Step	Action	Responsibility
2.3	Check entry in SIAMED against the dossier. Make sure the correct timetable is chosen (as per recommended submission dates). Liaise with AST or vet.applications team in case corrections are required.	ProcM
2.4	Prepare and save as soon as possible the renewal validation checklist in the renewal procedure folder (include the final minutes from the renewal pre-submission meeting, if applicable). Check the information on the template for fee initiation email to Financial Workflow (template in DREAM: EMA/461339/2014) to see whether the email is still required. If so, inform AST.	ProcM ProcM
2.5	Prepare validation correspondence and renewal assessment report (AR) template in accordance with list of templates relevant for renewal applications: Run templates from SIAMED BI area; save in procedure folder in DREAM and send links to ProcM for review.	AST
2.6	Complete renewal AR template and: • Send to P-CI-MCP (gxp.validation2@ema.europa.eu), informing of the receipt of application and location of electronic files (email template available in SIAMED BI area), for validation of manufacturers' information and completion of relevant section of AR (including Sampling and Testing). • Send to Pharmacovigilance team in APH, informing of receipt of application and location of electronic files (email template available in SIAMED BI area), for validation of pharmacovigilance data. • If the renewal application includes an update of the Risk Management Plan liaise with Pharmacovigilance team in APH. • Send copy of application to Legal Service, if legal issues arise during validation (consult HSer in case of doubt). Proceed to 3.0	ProcM
3.0	**Validation (working day 0-10)**	
3.1	Check the submission contents against requirements. *NB: For details of checks to be performed on the dossier, refer to the renewal validation checklist. The checklist is available in SIAMED BI templates area and should be run for each renewal procedure, saved in DREAM procedure folder and duly completed.*	ProcM
3.2	Can the renewal be validated? If yes, go to 3.8 If no, go to 3.3	
3.3	Request corrections/outstanding information from applicant by	ProcM

Step	Action	Responsibility
	working day 4.	
3.4	Has the outstanding information been submitted within the agreed deadline? If yes, go to 3.6 If no, go to 3.5	ProcM
3.5	Suspend validation and inform MAH or prepare negative validation correspondence (liaise with HSer V-VM-ROS). Update SIAMED. If validation suspended, instruct the MAH of the deadline for provision of amended dossier (usually next recommended submission date). Return to 3.4 If validation negative, inform MAH, rapporteur and co-rapporteur and update SIAMED. Proceed to 6.0	ProcM
3.6	Save the (re)submitted electronic dossier in EURS. Check that all validation issues have been addressed. Forward relevant responses to Inspections/ Pharmacovigilance team in APH, as appropriate, for final confirmation.	ProcM
3.7	Can the renewal be validated? If yes, go to 3.8 If no, go to 3.5	
3.8	Finalise renewal AR template to reflect the latest information received during validation. Update SIAMED where relevant (e.g. manufacturing sites, contact persons, presentations that are being renewed and those which are not, customer reference numbers for fee purposes, etc.) *Note: If certain presentations are not to be renewed, ensure that these presentations will be "surrendered" in SIAMED so that they will not appear in Annex A of subsequent procedures. Liaise with AST or vet.applications if corrections are needed.*	ProcM
3.9	Prepare validation correspondence and submit for review and sign-off. Review RSI correspondence and submit for sign-off to HSer. Check if rapporteur and co-rapporteur have received the application and documentation (written confirmation of receipt of application and date).	AST ProcM AST
3.10	Send renewal AR template completed with administrative data to the rapporteur.	AST

Step	Action	Responsibility
	Send validation letter to applicant including reference to recommended submission dates document (email with copy to APH service). Send validation e-mail to CVMP including timetable. If applicable, send fee workflow email to Financial Workflow (*email template for fee initiation* EMA/461339/2014).	
3.11	Validate the procedure in Siamed. Liaise with E-SR-LRS for review of English product information (SIAMED template). If changes introduced to PI, they should be made visible in tracked changes mode. Provide deadline (approx. day 35) for comments, to be forwarded to rapporteur/co-rapporteur/MAH, if appropriate[3]. Proceed to 4.0	ProcM
4.0	**Evaluation (day 1 to day 90)**	
4.1	Day 35 Check whether QRD provided comments on the EN PI and forward to rapporteur/co-rapporteur.	ProcM
4.2	Day 45 Monitor submission of the rapporteur's renewal assessment report to All Veterinary CVE, co-rapporteur and Agency.	ProcM
4.3	Day 55 Monitor submission of joint rapporteur's/co-rapporteur's renewal assessment report to All Veterinary CVE and Agency. In case of missing information or contradictions with QRD templates/guidance, liaise with rapporteur.	ProcM
4.4	Send joint rapporteur's/co-rapporteur's renewal assessment report to MAH together with the QRD comments on PI (SIAMED template).	AST
4.5	Update SIAMED as soon as possible with the outcome type and date and with other changes arising from the assessment (e.g. if PI will be affected by the renewal despite intention of the MAH). Forward joint rapporteur's/co-rapporteur's renewal AR to Vet Pharmacovigilance colleagues in V-VM-APH for review of PhV section of assessment report. Comments to be received ideally by day 66 (same as CVMP comments). *NB: APH comments would need to be reflected in the CVMP*	ProcM

[3] Refer to SOP/EMEA/3046 on PIQ/QRD review of product information for renewal procedure

Step	Action	Responsibility
	assessment report, and would only be sent to the Rapporteur for review in case of substantial issues (APH to advise depending on the case). Ensure any relevant procedures awaiting transmission to EC are marked in the renewal outcome as to be handled at the same time as the renewal. If so, a line listing of the relevant procedures will need to be sent to EC with the renewal Opinion.	
4.6	Day 66 Ensure comments of CVMP members are sent to rapporteur/co-rapporteur and Agency (All Vet CVE mailbox to be CCed). Agency comments (if any) to be sent to rapporteur/co-rapporteur.	ProcM
4.7	Day 70 Monitor submission of rapporteur's revised assessment report to CVMP (All Veterinary CVE) and Agency.	ProcM
4.8	Is an opinion anticipated at day 90? If yes, go to 4.14 If no (list of outstanding issues), go to 4.9	
4.9	Prepare draft CVMP LoOI, send to HSer for review, and if applicable, Pharmacovigilance team in APH with regard to PhV recommendations (before the first CVMP mailing). Circulate the documents and the joint rapporteurs' AR for adoption in the first mailing.	ProcM
4.10	If any new comments received after mailing, inform the rapporteur and co-rapporteur and include in the revised draft CVMP AR in the second mailing, and again in the third mailing where applicable. Prepare and review the renewal opinion/LoOI correspondence, in accordance with the list of templates relevant for renewal applications.	ProcM
4.11	Day 90: Adoption of LoOI Submit correspondence together with adopted LoOI for sign-off to Hser. Send LoOI to MAH, together with cover letter including deadline for responses (10-11 days after the opinion) and a reference to recommended submission dates document. Ensure final documents as adopted by the CVMP are included in the final CVMP mailing (by Tuesday following CVMP week). Update procedure outcome in SIAMED (set as final) and the Table of Actions for CVMP.	ProcM AST ProcM ProcM

Step	Action	Responsibility
4.12	Day 100	
	Monitor timely receipt of responses by the recommended date. Check if rapporteur/co-rapporteur have received documentation (CVMP members should indicate if they did NOT receive documentation).	ProcM
	Save the responses submission in EURS (liaise with vet.applications if needed). The responses dossier should follow the same vNeeS structure as the initial submission and vNeeS report should be provided (unless it is a single document submission).	ProcM
4.13	Day 110	
	Monitor timely receipt of revised joint rapporteur's/co-rapporteur's renewal assessment report by CVMP and Agency.	ProcM
	Send revised joint rapporteur's/co-rapporteur's renewal assessment report to MAH for information. Obtain agreement from the MAH with the proposed changes by 3rd mailing.	ProcM
4.14	Draft/revise CVMP renewal opinion and CVMP renewal AR taking into account the list of outstanding issues, the responses and the rapporteur/co-rapporteur assessment report on MAH's responses, as applicable. Send the renewal opinion for a legal scrutiny check. Send to HSer for review and to Pharmacovigilance team in APH for review with regard to PhV recommendations. *NB: On the CVMP AR any comments from QRD or CVMP members should be deleted, unless they have not been implemented by MAH. If not implemented, MAH should justify and the rapporteur should confirm if this is acceptable. The SPC in the CVMP AR put into mailing should only have the changes to text in track changes, but no pure comments. The separate PI document put in the mailing with the opinion for adoption should have all those changes accepted, i.e. should be a clean version.* *The CVMP AR should not have section on outstanding issues or assessment of responses but these should be reported in the main body of the report under the relevant topic section – section headings should be kept exactly like in the template.*	ProcM
4.15	Inform MAH of the documents put forward for CVMP adoption – in case additional corrections were made to PI, inform the MAH immediately. MAH should indicate if they disagree with any of the changes before the 3rd mailing. *NB: All product information annexes are part of the opinion, however they form a separate electronic document. They should be included in the CVMP mailing, with all comments received*	ProcM

Step	Action	Responsibility
	(including QRD) in track changes as background information. The AR usually only contains the SPC. *If there is agreement on the changes to PI between all involved parties, inform the MAH of the proposed changes and ask them to provide final EN PI version with all proposed changes incorporated, by second mailing at the latest. Include this version in the opinion as final (with all track changes accepted).*	
4.16	Circulate draft CVMP renewal AR and opinion for adoption in the 2nd mailing (based on the revised joint rapporteur's/co-rapporteur's renewal AR). *NB: Where there is an opinion and the CVMP and rapporteurs are in full agreement, the renewal should be included under 'silent adoption'. This is not the case for list of outstanding issues or negative opinion.*	ProcM
	Prepare the renewal opinion correspondence, in accordance with the list of templates relevant for renewal applications.	AST
4.17	Are oral explanations requested? If yes, go to 4.18 If no, go to 5.0	
4.18	Oral explanation at day 120 Liaise with CVMP secretariat to arrange oral explanation at day 120 (submission of CVs, presentation requirements, invitation etc.). *NB: In general, if an oral explanation takes place, the opinion should be adopted at the following CVMP plenary.* Proceed to 4.20	ProcM
4.20	<u>Day 120: Adoption of Opinion</u> Submit correspondence together with adopted opinion for sign-off to Hser. Ensure final documents as adopted by the CVMP are included in the final CVMP mailing (by Tuesday following CVMP week). Update procedure outcome in SIAMED (set as final) and the Table of Actions for CVMP. Proceed to 5.0	ProcM ProcM ProcM
5.0	**Post opinion**	
5.1	Distribute renewal documentation as follows: • to Commission: o adopted English CVMP opinion and if applicable adopted	AST

Step	Action	Responsibility
	revised PI (electronically) o adopted CVMP renewal assessment report (electronically) • to MAH: o adopted EN CVMP opinion and if applicable adopted revised PI o adopted CVMP renewal assessment report (electronically) o post-opinion linguistic review timetable (PIPIT) – *only if PI has been revised during the renewal* • to CVMP members (All Veterinary CVE): o adopted EN CVMP opinion and if applicable adopted revised PI (electronically) o adopted CVMP renewal assessment report (electronically)	
5.2	Was re-examination requested by MAH? If yes, go to 5.3 If no, go to 5.4	
5.3	Process the re-examination request according to steps 6.1 - 6.10 of SOP/V/4004 on Type II variations. Proceed to 5.4	ProcM
5.4	Was a positive renewal opinion adopted? If yes, go to 5.5 If no, go to 5.7	
5.5	Was the PI amended during the renewal? If yes, go to 5.6 If no, go to 5.7	
5.6	Translations check: Refer to SOP/EMA/0048. Compile the EN opinion and annexes in all languages and send final copies in an email to Commission, Standing Committee Members, Norway, Iceland and CVMP (i.e. All-Veterinary VETCOM mailbox, All CVE mailbox) as follows: • Opinion (EN) • Translations in all languages in Word format (zip-file) and PDF format (zip-file) • CVMP renewal assessment report • Line listing of swept procedures (if applicable)	AST

Step	Action	Responsibility
5.7	Upon receipt of the Commission Decision Update SIAMED with date of Commission Decision, check correctness of information, especially the procedure dates, deletion of presentations and affected annexes (liaise with vet.applications for SIAMED update, if necessary). If certain presentations have not been renewed, ensure that these presentations are “surrendered” in SIAMED so that they will not appear in Annex A in subsequent procedures.	ProcM
5.8	Process EPAR update in accordance with SOP/V/4038.	AST
5.9	Save latest version of product information in DREAM under Renewal Folder/Translations. Once finalised for publication, paste link to product folder under 11. EPAR, subfolder PI.	AST
5.10	Once published, record EPAR revision in SIAMED, including all relevant previous procedures. The procedure status should now be changed to “Closed”. Rename folder in DREAM with the date of CD and to reflect which annexes have been amended by the renewal.	AST
5.11	Mark all relevant documents as “Potential” to be added to the Core Master File in DREAM, as per the cMF checklist for renewals. If appropriate, check mock-ups, in accordance with The revised checking process of mock-ups and specimens of outer/immediate labelling and package leaflets in the centralised procedure for veterinary medicinal products.	ProcM
5.12	Add all relevant documents to the Core Master File in DREAM, as per the cMF checklist for renewals. Proceed to 6.0	AST
6.0	**End of procedure**	