Title: **Submission and evaluation procedure for an application for the establishment of Maximum Residue Limits (MRLs)**		
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1. Purpose

The purpose of this document is to define a transparent procedure for the submission of an application for the establishment of Maximum Residue Limits.

2. Scope

This Standard Operating Procedure (SOP) applies to procedures in accordance with Article 6 of Council Regulation (EEC) No 2377/90, as amended. It addresses Applicants, CVMP Members and the EMEA Secretariat.

3. Responsibilities

The responsibility for the execution of a particular part of this procedure is identified in the right-hand column of the procedure as defined under point 7 of this document.

4. Changes since last revision

SOP revised to take into account revision of fee regulation.

5. Documents needed for this SOP

- Application form as published on pages 36 and 37 of Volume 8 – Notice to Applicants and note for Guidance

6. Related documents

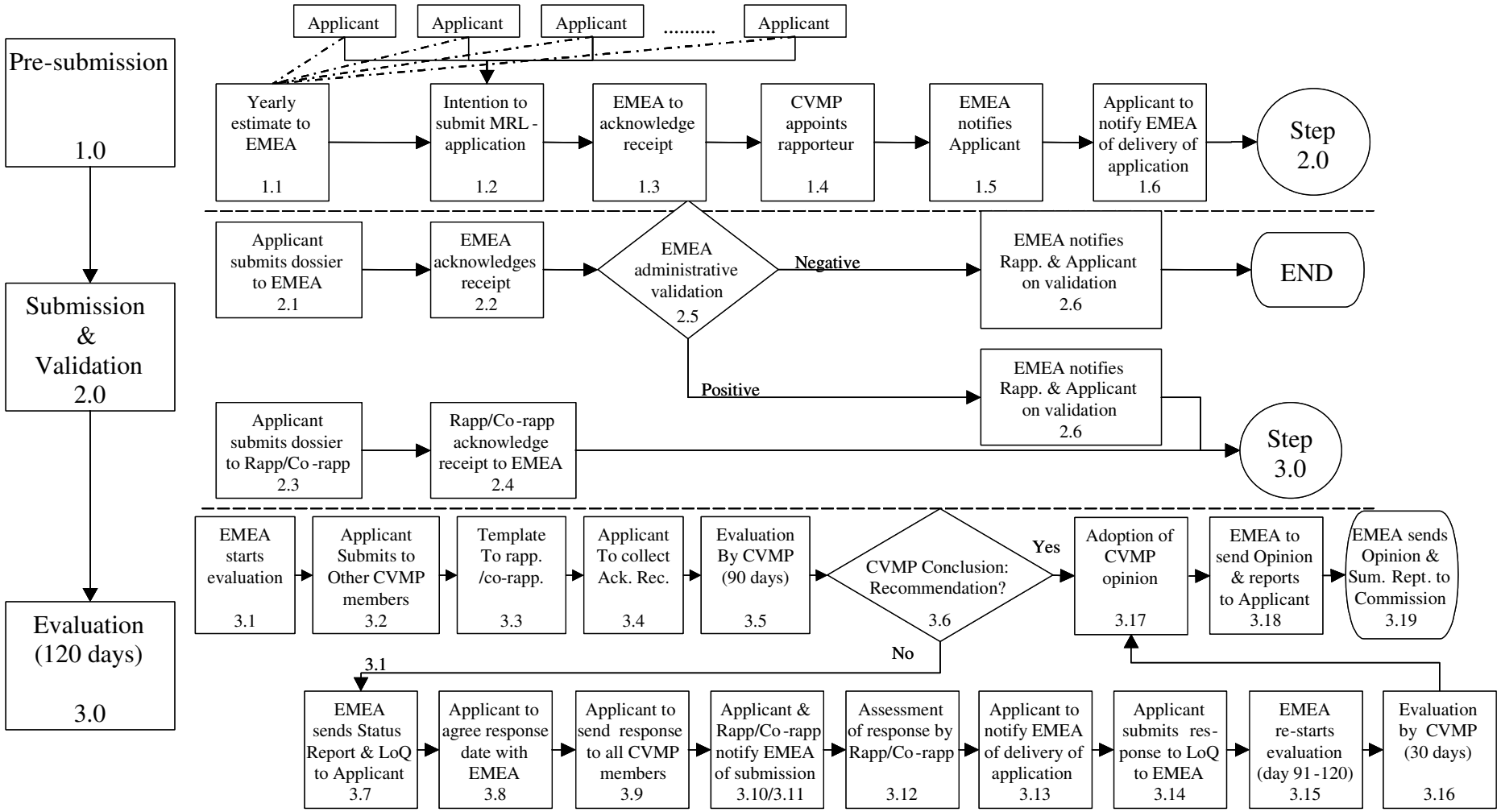
- Council Regulation (EEC) No 2377/90 of 26.6.1990, OJ L 224 of 18.8.1990, laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin, and amending legislation:
- Commission Regulation (EEC) No 762/92 of 27.3.1992, OJ L 84 of 28.3.1992,
- Council Regulation (EC) No 434/97 of 3.3.1997, OJ 76 of 7.3.1997,
- Council Regulation (EC) No 1308/99 of 15.6.1999, OJ 156 of 23.6.1999.
- Council Regulation (EC) No 297/95, of 10.2.1995, OJ L 35 of 15.2.1995, on fees payable to the European Agency for the Evaluation of Medicinal Products, and amending legislation:
- Council Regulation (EC) No 2743/98 of 14.12.1998, OJ L 345 of 19.12.1998;
- Commission Regulation (EC) No 494/2003 of 18.03.2003, OJ L 73 of 19.03.2003;
- Council Regulation (EC) No 1905/2005 of 14.11.2005, OJ L 304/1 of 23.11.2005.
- Volume 8 Notice to Applicants and Note for Guidance Establishment of maximum residue limits (MRLs) for residues of veterinary medicinal products in foodstuffs of animal origin – September 2001

- EMEA/CVMP/931/00-Rev.2: SOP on Appeal against CVMP Opinions on the establishment of MRLs and Provision of Detailed Grounds for Appeal

7. Definitions

CVMP:	Committee for Medicinal Products for Veterinary Use
MRL:	Maximum Residue Limit
MRL-application:	Application for the establishment of maximum residue limits
EMEA PM:	EMEA scientific administrator appointed as Project Manager to follow the procedure for the evaluation of the application

8. Process Map(s)/ Flow Chart(s)



9. Procedure

Step	Action	Responsibility
1.0	**Pre-submission Phase**	
1.1	Forward a yearly estimate of intentions to submit MRL-applications to the EMEA.	Applicants
1.2	Notify EMEA of intention to submit an MRL-application (letter of intent indicating substance, intended use, target species and intended date of submission to the EMEA no later than **3 months** before the intended MRL-submission. Note: If applicants also intend to submit an application for a Community Marketing Authorisation under the centralised procedure for the same substance, the MRL application should be made at least **6 months** before the application for the centralised procedure.	Applicant
1.3	Send acknowledgement of receipt to the applicant.	EMEA Secretariat
1.4	Appointment of rapporteur (and co-rapporteur, if appropriate). Note: If applicants intend to submit an application for a Community Marketing Authorisation under the centralised procedure, the rapporteur will usually be the same as for the MRL procedure. For applications for extension or modification of MRLs usually no co-rapporteur is appointed.	CVMP
1.5	Notify the applicant of the appointed rapporteur and co-rapporteur and of the ideal submission date (closest to the submission date identified by the applicant). Note: Each year the EMEA identifies a series of ideal submission dates in order to allow synchronisation of the assessment of an application with CVMP meeting dates.	EMEA PM
1.6	Notify EMEA of delivery of application, 3 days before submission.[1]	Applicant
2.0	**Submission and validation of the MRL-application**	
2.1	Submit the application to the EMEA. Note: The EMEA requires a full dossier according to Annex V of Regulation (EEC) No 2377/90 as amended (application form[2], Safety file incl. Expert report[2] and Residue file incl. Expert report[2]) plus an extra copy of each expert report. Applicants are also requested to provide an electronic copy of the routine analytical method for the detection of residues (Item B.3 of the dossier).[3]	Applicant
2.2	Send acknowledgement of receipt of application to the applicant.	EMEA PM
2.3	Submit the application dossier to rapporteur and co-rapporteur. Note: The EMEA suggests submission of the dossier to rapporteur and co-rapporteur at the same time as the submission is made to the EMEA. This is to ensure best coordination with the CVMP meeting schedule as ideal submission dates take account of time needed for validation.	Applicant

[1] Such notification is requested for security reasons.
[2] Containing the original signatures
[3] The request for an electronic copy of the routine analytical method is an outcome agreed by all parties involved of the EMEA Workshop on the Requirements and Provision of Analytical Methods for Drug Residue Control in Animal Products on 24-25 January 2000. Further information on the outcome of this Workshop is available on the EMEA WebSite at http:/www.emea.eu.int

Step	Action	Responsibility
2.4	Send acknowledgement of receipts of full dossier (including amendments during validation) to EMEA.	Rapporteur (and co-rapporteur)
2.5	Administrative validation within 10 working days. - If **positive**, go to Step 2.6 followed by Step 3.0. - If **negative**, go to Step 2.6 and end procedure.	EMEA PM
2.6	Notify applicant, rapporteur and co-rapporteur of the outcome of the validation of the application.	EMEA PM
3.0	**120-day-Evaluation Phase**	
3.1	Start of evaluation when EMEA, rapporteur and co-rapporteur have received the dossier as validated. Notify Applicant and CVMP Members of clock start.	EMEA PM
3.2	Submit the required documentation to the other CVMP Members and alternates according to the requirements specified in Annex I Note: The members that request in general a reduced dossier (application form, expert reports incl. the required annexes, in particular tabulated study reports) are, however, entitled to the full documentation, which should be provided upon request.	Applicant
3.3	Send the assessment report template to the rapporteur in electronic format.	EMEA PM
3.4	Collect acknowledgements of receipt from CVMP members and alternates which should be kept as reference and made available to the EMEA, if required.	Applicant
3.5	Perform initial evaluation within 90 days • Prepare assessment report • Critique on assessment report[4] • Comments on assessment report • Send rapporteur's assessment report and co-Rapporteur's critique[4] to applicant • Revise assessment report	Rapporteur Co-rapporteur CVMP members EMEA PM Rapporteur
3.6	Conclusion on initial evaluation and adoption of the summary/status report. Can the CVMP make a recommendation for inclusion in one of the Annexes of Council Regulation No 2377/90? - If **Yes** go to 3.18 - If **No** go to 3.6	CVMP
3.7	Send Status report with List of Questions (LoQ) to Applicant. Note: In general 6 months are granted to respond to the LoQ[5]. This time frame may be extended only exceptionally upon request and if duly justified.	EMEA Secretariat
3.8	Contact EMEA 1 month prior to the deadline for responding to the LoQ for exact submission dates.	Applicant
3.9	Submit response[6] to rapporteur, co-rapporteur and CVMP members and alternates on the date agreed with the EMEA[7] under 3.7. Note: One consolidated response to all questions should be submitted.	Applicant

[4] If a Co-Rapporteur has been appointed
[5] The EMEA identifies an only approximate submission date in the cover letter to the Status report and LOQ.

Step	Action	Responsibility
3.10	Notify EMEA of submission to CVMP members and alternates.	Applicant
3.11	Notify EMEA of receipt of response.	Rapporteur (and co-rapporteur)
3.12	Evaluate the response to the LoQ.	Rapporteur (and co-rapporteur)
3.13	Notify EMEA of delivery 3 days prior to submission to EMEA[8].	Applicant
3.14	Submit response to the EMEA 30 days after submission to CVMP.	Applicant
3.15	Restart clock of the remaining evaluation period (days 91-120).	EMEA PM
3.16	Perform evaluation of responses to list of questions within the remaining 30 days • Prepare assessment report • Critique on assessment report[9] • Comments on assessment report • Send rapporteur's assessment report and co-Rapporteur's critique[9] to applicant • Revise assessment	Rapporteur Co-rapporteur CVMP members EMEA PM Rapporteur
3.17	Finalise assessment and adopt Opinion and Summary Report for recommendation of MRL(s) by day 120.	CVMP
3.18	Send Opinion, CVMP assessment report and Summary Report to applicant. Note: Within 15 days of receipt of the opinion, the Applicant may provide written notice to the EMEA Secretariat that he wishes to appeal[10].	EMEA Secretariat
3.19	Within 30 days after adoption by CVMP send Opinion and Summary Report to the European Commission.	EMEA PM

[6] If the response consists of data or reasoning only, the complete data should be sent to all CVMP members and the EMEA. If accompanied by addenda to or updates of relevant expert reports, Rapporteur, Co-rapporteur and EMEA receive the full response, while the other CVMP members only receive the updates or addenda.
[7] The amendment of Regulation (EEC) No 2377/90 no longer includes the 90 days originally allowed for the evaluation of additional data, where these were requested by the CVMP (list of questions). The CVMP therefore must accommodate the evaluation of the original submission and of a consolidated response, where appropriate, within 120 days. Therefore, the total 120-day evaluation period had to be divided into 90 days for the assessment of the original submission and 30 days for the assessment of additional data, if a list of questions is adopted. It is, however, not possible to carry out the necessary steps involved in the evaluation of additional data and CVMP reaching an opinion within 30 days. Therefore Applicants are strongly encouraged to submit the response to the CVMP-members 30 days prior to a submission to the EMEA. This period will be used for the evaluation of the data by the rapporteur. The clock will only be restarted once the EMEA, too, has received the response. In the remaining 30 days of the 120 day-evaluation period the remaining CVMP-members are consulted.
[8] Such notification is requested for security reasons.
[9] When a Co-Rapporteur has been appointed
[10] Further guidance on Appeals against Opinions on the establishment of MRLs and Provision of Detailed Grounds for Appeal is given in the EMEA Standard Operating Procedure on this subject, document EMEA/CVMP/931/00/Final.

10. Records

When completed, approved and numbered, the retention of the hard copy of the CVMP Opinions, assessment reports and Summary Reports will be the responsibility of the EMEA.

The EMEA will also keep an archive of all routine analytical methods for the detection of residues of substances for which MRLs have been established.

Annex

Addresses of CVMP Members, to whom MRL-applications shall be submitted