



Standard operating procedure

Title: Procedures in accordance with Article 78 of Directive 2001/82/EC, related to pharmacovigilance measures for veterinary medicinal products authorised in the European Union		
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1. Purpose

To describe the procedure following notification from a Member State in accordance with Article 78 (1) of Directive 2001/82/EC where it considers that a marketing authorisation should be suspended, withdrawn or varied to restrict the indications or availability, amend the posology, add a contraindication or add a new precautionary measure as a result of evaluation of pharmacovigilance data, where after the CVMP is to give its opinion on the matter in accordance with Article 78 (3) of Directive 2001/82/EC. The procedure is to ensure an effective, transparent and harmonised procedure.

The procedure does not describe steps to be taken by the Member States prior to notification, or steps taken by the European Commission post opinion.

2. Scope

This standard operating procedure (SOP) applies to the European Medicines Agency (EMA) staff of the Veterinary Medicines Division. Article 78 of Directive 2001/82/EC is as follows:

- **Article 78(1) of Directive 2001/82/EC:** *“Where, as a result of the evaluation of veterinary pharmacovigilance data, a Member State considers that a marketing authorisation should be suspended, withdrawn or varied to restrict the indications or availability, amend the posology, add a contraindication or add a new precautionary measure, it shall forthwith inform the Agency, the other Member States and the marketing authorization holder.”*
- **Article 78(2) of Directive 2001/82/EC:** *“If urgent action is necessary for protecting human or animal health, the Member State concerned may suspend the marketing authorisation of a veterinary medicinal product, provided that the Agency, the Commission and the other Member States are informed on the following working day at the latest.”*



- **Article 78(3) of Directive 2001/82/EC:** *"When the Agency is informed in accordance with paragraphs 1 or 2, it shall give its opinion as soon as possible, according to the urgency of the matter. On the basis of this opinion, the Commission may request all Member States in which the veterinary medicinal is marketed to take temporary measures immediately..."*

3. Responsibilities

It is the responsibility of the Head of the Veterinary Medicines Department (delegated to the APH Service Head) to ensure that this SOP is adhered to. The responsibility for the execution of a particular part of this procedure is identified in the right-hand column of section 9 in this SOP.

4. Changes since last revision

Update to reflect new Agency structure and contact details. Update of internal EMA working document to support SOP (checklist to replace former working instruction).

5. Documents needed for this SOP

Models available under X:\Templates\Others\Vet\Article 78 procedure

6. Related documents

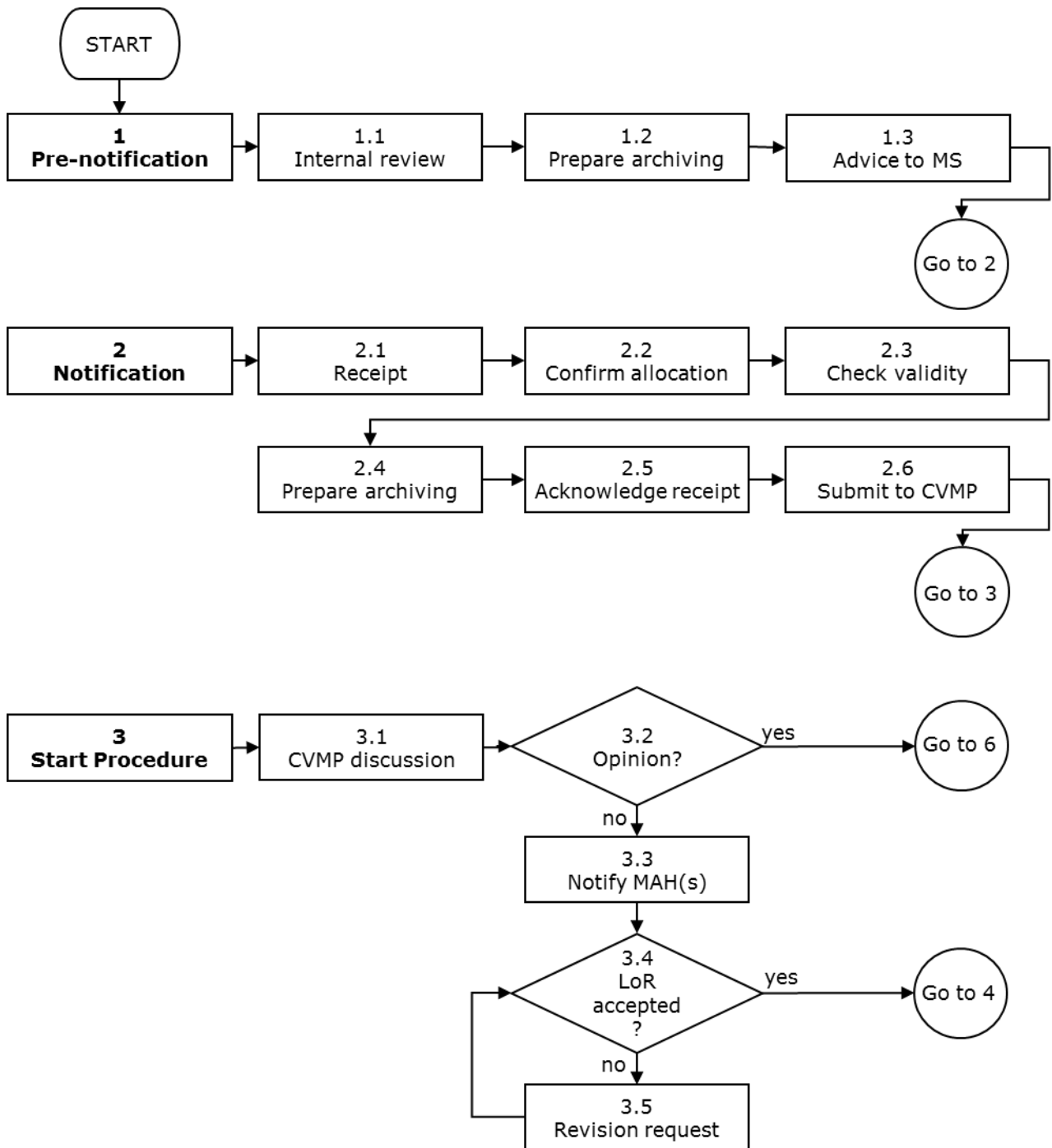
- Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products;
- Volume 9B of the Rules Governing Medicinal Products in the European Union Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use;
- Reflection paper on "Pharmacovigilance urgent measures" procedure under Article 78 of Directive 2001/82/EC (EMA/CVMP/356746/2005);
- SOP/V/4041 on Management of pharmacovigilance rapid alerts (RAs) and non urgent information (NUI) for medicinal products for veterinary use;
- Incident management plan for medicines for veterinary use (EMA/711053/2010);
- SOP/V/4003 on Procedure to be followed when the incident management plan for medicines for veterinary use is triggered;
- Checklist on post opinion phase following CVMP opinions on procedures under Articles 33(4), 34, 35 and 78 of Directive 2001/82/EC, as well as Article 13 of Commission Regulation (EC) No 1234/2008 (EMA/412328/2015);
- Checklist on the management of procedures in accordance with Articles 78 of Directive 2001/82/EC related to pharmacovigilance measures for veterinary medicinal products authorised in the European Union (EMA/392666/2015);
- Appointment and responsibilities of rapporteur and co-rapporteur for procedures regarding veterinary medicinal products (EMA/CVMP/468877/2009-Rev.1);
- The linguistic review process of product information in the centralised procedure – veterinary (EMA/420004/2015-Rev.5);

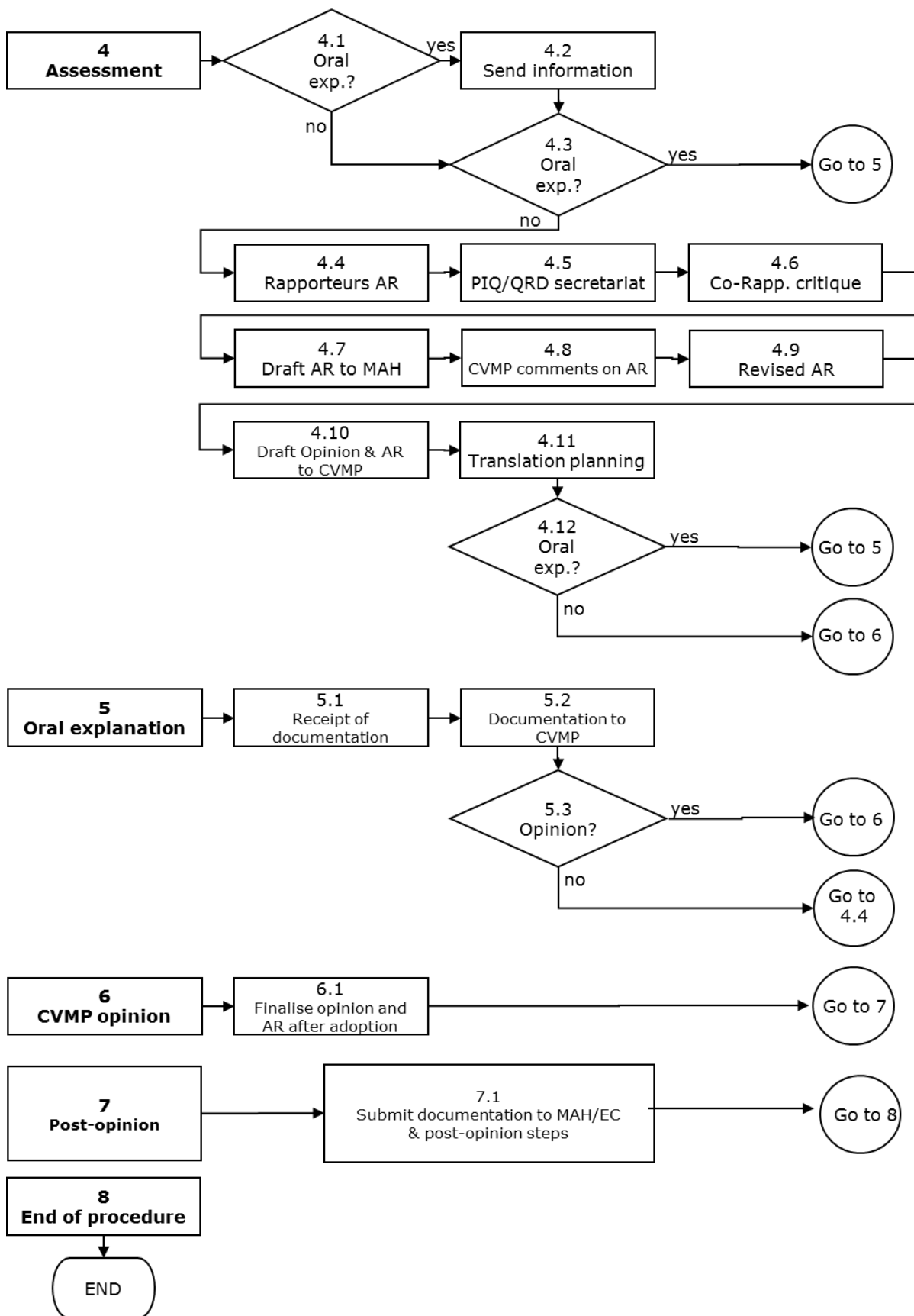
- SOP/EMA/0073 on PIQ/QRD pre-opinion review of product information for referral procedures;
- SOP/PDM/1004 on core master files of medicinal products for human and veterinary use following the centralised and referrals procedures.

7. Definitions

AA	Administrative assistant
AR	Assessment report
AST	Assistant allocated to support the procedure
c-MF	Core Master File
CV	Curriculum Vitae
CVMP	Committee for Medicinal Products for Veterinary Use
EC	European Commission
EMA	European Medicines Agency
HDep	Head of Department (here: Veterinary Medicines)
HSer	Head of Service
LoQ	List of questions
LoR	Letter of representation
MAH	Marketing authorisation holder(s)
MS	Member State(s)
PIQ	Product information quality
PM	Project manager
PhV	Pharmacovigilance
QRD	Quality review of documents
SA	Scientific administrator
SOP	Standard operating procedure
VROS	Veterinary Regulatory and Organisational Support

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





9. Procedure

Step	Action	Responsibility
1.0	Pre-notification	
1.1	Upon receipt of draft notification (pre-notification), notify HDep and convene meeting to discuss the matter to be notified, especially the legal basis and adequacy of the pre-notification, with appropriate SnH(s), SA(s), legal sector and, if necessary, compliance and inspection sector representative. Inform VROS AA of potential procedure. Allocate the procedure to the appropriate section and appoint project team.	PhV SA PhV SA HDep
1.2	Create standard electronic folder structure in DREAM; c-MF and a procedure shared mail box.	AA
1.3	Advise MS on the adequacy of the pre-notification ¹ , including legal basis, in accordance with internal EMA discussions.	HDep
1.4	Inform all MSs of pending procedure and request identification of MAH(s) and products concerned for the procedure using model letter.	PM
2.0	Receipt of formal notification & initiation of procedure	
2.1	Receive rapid alert from MS notifying a procedure under Article 78 with AR attached. Forward to PM responsible for Article 78 procedure, as applicable. Follow ' <i>SOP/V/4003 on Procedure to be followed when the incident management plan for medicines for veterinary use is triggered</i> '.	PhV SA responsible for RA/NUIS
2.2	Confirm allocation of the procedure to the appropriate section and project team composition including PM, as necessary.	HDep/HSer
2.3	Check validity of formal notification in consultation with legal sector, HSer and HDep in preparation of CVMP discussion. Inform AA of start of procedure.	PM
2.4	Allocate procedure number and ensure electronic folder structure in DREAM, c-MF and procedure shared mail box have been set up.	AA
2.5	Acknowledge receipt of the notification using model letter to be signed by HDep. Inform all MSs of the receipt of the notification ensuring information on the national marketing authorisations and contact details for the	PM

¹ NB. the notification itself should be accompanied by an assessment report and circulated via the pharmacovigilance rapid alert system

Step	Action	Responsibility
	MAH(s) has been requested. Ensure timely receipt of information and send reminder(s), as necessary.	
2.6	Include the notification on the agenda of the next CVMP meeting for confirmation of start of Art. 78 procedure.	PM
3.0	Start of Procedure	
3.1	<i>CVMP meeting</i> Ensure CVMP: <ul style="list-style-type: none"> starts the Art.78 procedure. appoints rapporteur, co-rapporteur and peer reviewers. determines the urgency for consideration of the issue and endorses timetable for the procedure (to be decided on a case-by-case basis), or adopts opinion, as applicable. adopts list of questions for the MAH(s), if applicable. 	PM
3.2	Did CVMP adopt an opinion at the initial meeting at the start of the procedure? If yes, go to 6.0 If no, go to 3.3	
3.3	Send letter with the procedure notification, adopted list of questions, timetable, list of products involved in procedure and, if appropriate, models for letter(s) of representation to the MAH(s). <i>N.B.: where possible, MAH(s) are invited to provide oral explanation to the CVMP.</i>	PM
3.4	Confirm receipt and adequacy of the letters of representation received in consultation with the legal department, if necessary. Are letters of representation acceptable? If yes, go to 4.0 If no, go to 3.5	PM
3.5	Request revised letters of representation. Once received and adequate, proceed to 4.0	AST
4.0	Scientific assessment	
4.1	Is an oral explanation scheduled for the next CVMP meeting (in case of a short timetable)? If yes, go to 4.2 If no, go to 4.3	

Step	Action	Responsibility
4.2	Send details for oral explanation to MAH(s), also requesting presentation materials and CVs of representatives in time for 2nd mailing of the CVMP meeting when the explanation will be held.	PM
4.3	Ensure response(s) to the LoQ are received by EMA and circulated to CVMP by timetable deadline. Is an oral explanation scheduled for the next CVMP meeting after the start of the procedure? If yes, go to 5.0 If no, go to 4.4	PM
4.4	<i>Rapporteur's assessment</i> Ensure rapporteur's assessment report is circulated to CVMP members and EMA via Eudranet to <i>All Veterinary CVMP</i> by timetable deadline and send reminders if necessary.	PM
4.5	If applicable, send proposed amendments to product information to PIQ/QRD secretariat for review and comment.	PM
4.6	<i>Co-rapporteur's critique on rapporteurs assessment report</i> Ensure co-rapporteur's critique is circulated to CVMP and EMA via Eudranet to <i>All Veterinary CVMP</i> by timetable deadline and send reminders if necessary.	PM
4.7	Send rapporteur's assessment report incl. co-rapporteurs critique to MAH(s) including information on arrangements for oral explanations ² , if applicable, and any potential need for translations.	PM
4.8	<i>Comments from peer reviewers and CVMP members on rapporteur's assessment report</i> Ensure comments on rapporteur's assessment report are circulated to CVMP and EMA via Eudranet to <i>All Veterinary CVMP</i> . If required, send any comments received from PIQ/QRD secretariat on the proposed product information to rapporteur.	PM
4.9	<i>Revised assessment</i> Ensure rapporteur's revised assessment report is circulated to CVMP and EMA via Eudranet to <i>All Veterinary CVMP</i> and send reminders if necessary.	PM
4.10	Prepare draft opinion and draft CVMP assessment report and circulate to CVMP for the next meeting. Send draft CVMP opinion for legal scrutiny.	PM

² Details for scheduling of oral explanation, also requesting presentation materials and CVs of representatives in time for 2nd mailing of the CVMP meeting when the explanation will be held.

Step	Action	Responsibility
4.11	Send Annex II of the draft opinion to Translations team for planning of translations to be coordinated after adoption of opinion.	PM
4.12	Is an oral explanation scheduled for CVMP meeting at which the draft opinion and draft CVMP assessment report will be discussed? If yes, go to 5.0 If no, go to 6.0	
5.0	Oral explanation	
5.1	Ensure receipt of presentation materials and CVs from MAH(s) and send reminder(s), if necessary.	PM
5.2	Circulate presentation(s) from the MAH(s) and CVs of MAH representatives to CVMP.	PM
5.3	<i>Oral explanation</i> Is CVMP finalising the opinion at the same meeting? If yes, go to 6.0 If no, go to 4.4	
6.0	CVMP opinion	
6.1	Finalise opinion and CVMP assessment report following CVMP discussion/adoption.	PM
7.0	Post-opinion	
7.1	Follow ' <i>Checklist on post opinion phase following CVMP opinions on procedures under Articles 33(4), 34, 35 and 78 of Directive 2001/82/EC, as well as Article 13 of Commission Regulation (EC) No 1234/2008</i> ' for submission of CVMP opinion to the MAH(s) and to the EC for adoption by Standing Committee and subsequent post-opinion steps.	PM
8.0	End of procedure	

10. Records

Electronic copies of all correspondence and documents related to the procedure are saved in the appropriately labelled folder in DREAM and c-MF, as necessary.