EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard operating procedure

Title: Involvement of the CVMP Antimicrobials Working Party in the evaluation of applications for centralised marketing authorisations for veterinary medicinal products containing antimicrobial substances		
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1. Purpose

According to the CVMP rules of procedure, the Committee may consult its working parties on any scientific issue related to their specific fields of expertise. The CVMP Antimicrobials Working Party was established to provide advice, on a consultative basis, to specific questions raised by the Committee on all matters regarding authorisation and use of veterinary medicines containing antimicrobial substances. The CVMP Antimicrobials Working Party (AWP) carries forward the work initiated by the former CVMP Scientific Advisory Group on Antimicrobials (SAGAM).

This document lays out the criteria and procedure to involve AWP in the evaluation of applications for centralised marketing authorisations containing antimicrobials and possible involvement of the group on assessment of MRL applications. Involvement of AWP in referrals is outside of the scope of this SOP and will be addressed on a case by case basis, although the procedure described here below can be used as a basis for such involvement.

2. Scope

This SOP applies to staff in the Veterinary Medicines Division, AWP members and CVMP members and alternates.

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2.1. Participation of (co-)rapporteurs or other members of committees or working parties at AWP discussions

Concerned (co-)rapporteurs might participate as observers, usually via Adobe, in the product related discussions of the AWP. Members of EMA committees and working parties, assessors from NCAs, experts and regulators from non-EEA countries under confidentiality agreement with the Agency may also participate as observers, following agreement from the AWP coordinator and Chair for the procedure, and their presence should be notified to the AWP and CVMP.

Under exceptional circumstances, the applicant might be invited to provide an oral explanation to the AWP meetings.

2.2. Marketing authorisation applications routinely involving AWP

Any new centralised marketing authorisation application for a veterinary medicinal product containing (an) antimicrobial substance(s) not assessed by the CVMP before, and intended for food-producing species will be forwarded to AWP for comments. The CVMP is routinely asked to confirm the involvement of the AWP.

2.3. Marketing authorisation applications to be forwarded to AWP after CVMP consideration

For the following products the CVMP will, on a case-by-case basis, decide on the need for AWP to be involved in the assessment:

For food producing species:

- Any application for a major change or extension to an existing centralised marketing authorisation for a veterinary medicinal product containing (an) antimicrobial substance(s) for food producing species that may vary substantially the exposure of the animals to the product.

For non-food producing species:

- Centralised marketing authorisation applications (initial and major post authorisation changes) concerning antimicrobial substances that are of special relevance for human or animal health; this would include at least third generation fluoroquinolones and third and fourth generation cephalosporins.
- Any centralised marketing authorisation application for long acting or other sustained release antimicrobial products.
- Any other centralised marketing authorisation application for antimicrobials claiming new antimicrobial properties.

2.4. Points to be addressed by AWP

The AWP should focus in particular on Part 3 of the dossier, sections 4.2 (*microbiological properties of residues*), and 4.4 (*development of resistance*) and on Part 4.A sections 1 *(Pharmacodynamics),* 2 *(Development of resistance),* and 3 *(Pharmacokinetics)* including the PK/PD-relationship, and on the relevant parts of the proposed SPC.

A pre-defined list of points to be addressed will include the following standard questions, which will be sent to AWP for all applications:

- Does AWP have comments on the conclusions drawn on microbiological safety?
- Does AWP have comments on the conclusions drawn on the PK/PD relationship?
- Does AWP have comments on the proposed dose, dosing frequency and duration of treatment from a microbiological safety perspective?
- Does AWP have comments on the indications of use proposed from a microbiological safety perspective?
- Does AWP have comments on the adequacy of the prudent use warnings and precautions proposed in the SPC?
- Are there any questions AWP would like to add to the draft CVMP list of questions/list of outstanding issues to be presented to the applicant?
- Are there any questions/outstanding issues on the draft CVMP list of questions/list of outstanding issues that AWP considers superfluous?

The final AWP report to the CVMP will be forwarded to the applicant for information.

The AWP may also provide comments on specific issues directly to the (co-)rapporteur, if requested by the (co-)rapporteur. In this case, the CVMP should be informed on such request and the respective AWP comments.

The application is discussed at the next AWP physical meeting. When no scheduled physical meeting fits with the time table for the application, the application is discussed in a virtual meeting. The responses to the CVMP questions should be agreed at that meeting.

2.5. Involvement of AWP in MRL applications

MRL applications for antimicrobials will not be forwarded to AWP routinely but on a case-by-case basis at CVMP request.

The AWP might be required to be involved in the assessment of MRLs in case there are issues related to antimicrobial resistance to be addressed when establishing a microbiological ADI. Considering the very low number of MRL applications in which the AWP support might be required, there is no need to establish a standard procedure for AWP involvement in the evaluation of MRL applications. In the case of a request to AWP, the procedure should be agreed with the (co-)rapporteur. The final AWP report to the CVMP will be forwarded to the applicant for information.

3. Responsibilities

It is the responsibility of the Head of Veterinary Medicines Department to ensure that this procedure 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.

4. Changes since last revision

The procedure has been updated to recognise the establishment of the AWP, replacing SAGAM. In addition, structural changes at the EMA are reflected in the revised SOP.

5. Documents needed for this SOP

Model letters and templates (in SIAMED):

- Letter to applicant to confirm rapporteurs and involvement of AWP [MAA-EXT – 01 – validation to applicant (letter)]
- Letter to AWP with list of questions for consideration [MAA-EXT – 01 – validation letter to AWP]
- Timetable (identifying the appointed AWP Coordinator) [MAA-EXT – 01 - timetable]

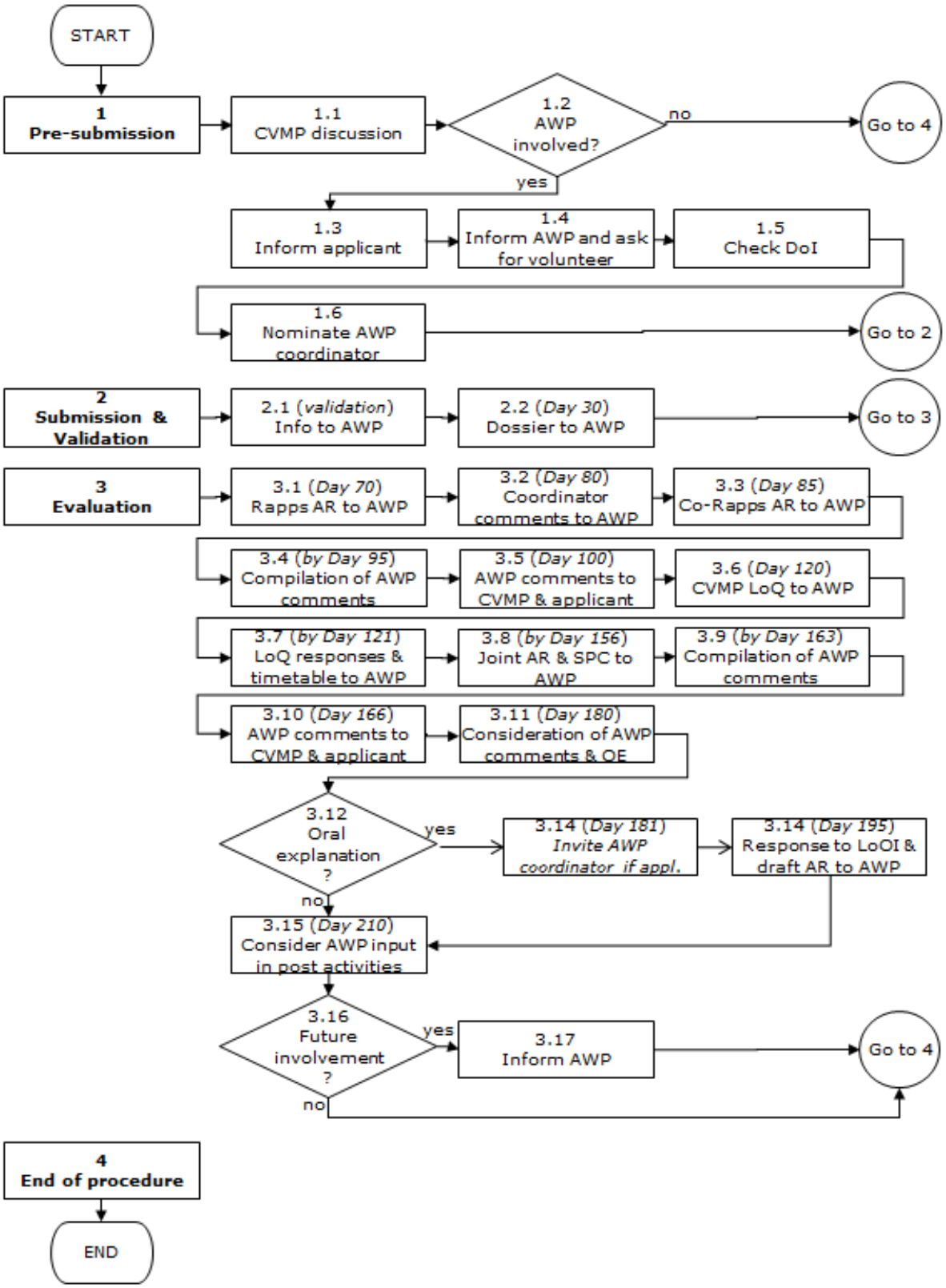
6. Related documents

- Mandate, objectives and rules of procedure for the CVMP Working Party on Antimicrobials (AWP) EMA/CVMP/749774/2012
- SOP/EMA/0040 on Evaluation of conflicts of interest of experts
- SOP/V/4013 on the Submission of an application for the granting of a community marketing authorisation
- SOP/V/4004 on Type II variations
- SOP/V/4051 on the Evaluation procedure for applications and requests for the establishment of maximum residue limits

7. Definitions

ADI	Acceptable daily intake
AR	Assessment report
AWP	Antimicrobials Working Party
CVMP	Committee for Medicinal Products for Veterinary Use
(Co-)Rapporteur	Member of the CVMP appointed to lead the evaluation for the product concerned (assisted by the co-rapporteur, a second Member of the CVMP)
V-DEM	Development and Evaluation of Medicines service in V-VM
DoI	Declaration of interest
EEA	European Economic Area
LoOI	List of outstanding issues
LoQ	List of questions
MA	Marketing authorisation
NCA	National competent authority
OE	Oral explanation
PM	Project manager: responsible for procedural support to the rapporteur and co-rapporteur and to act as a liaison point between the applicant for marketing authorisation and the agency for the relevant application
PK/PD	Pharmacokinetics/pharmacodynamics
SAGAM	Scientific Advisory Group on Antimicrobials (former group)
SIAMED	The European Medicines Agency's product information and application tracking system
SPC	Summary of product characteristics
V-VM	Veterinary Medicines Department
V-ROS	Veterinary Regulatory and Organisational Support service in V-VM

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



9. Procedure

Please note that this procedure details **only the additional steps** to be taken for the evaluation of products containing antimicrobial substances and **has to be read in conjunction** with the relevant SOP for handling the specific procedure:

- SOP/V/4013 on the Submission of an application for the granting of a community marketing authorisation
- SOP/V/4004 on Type II variations
- SOP/V/4051 on the Evaluation procedure for applications and requests for the establishment of maximum residue limits

The timetable can differ for Type II, MRLs and referrals procedures. For these procedures a case by case timetable will be prepared by the AWP secretariat in coordination with the PM of the procedure.

Step	Action	Responsibility
1.0	**Pre-submission**	
1.1	Upon receipt of the letter of intent, the CVMP is requested to appoint the (co-) rapporteur and confirm the involvement of AWP in the evaluation of a MA, or decides on AWP involvement as per criteria under heading *2. Scope*.	DEM
1.2	Will AWP be involved in the evaluation? If yes, go to 1.3 If no, go to 4.0	
1.3	Inform applicant on the involvement of AWP in the evaluation procedure with the letter of appointment of (co-)rapporteur and the need to provide extra electronic versions of the dossier also to AWP, copy AWP secretariat.	V-DEM/V-ROS
1.4	Inform AWP on its involvement following the CVMP decision, AWP members are invited to volunteer to act as coordinator for the comments to be prepared for CVMP consideration.	AWP secretariat
1.5	Ensure that the Declaration of Interest of the volunteering AWP member is up to date; following *SOP/EMA/0040 on Evaluation of conflicts of interests of experts for involvement in Agency activities*.	AWP secretariat
1.6	Nomination of AWP coordinator. Proceed to 2.0	AWP chair
2.0	**Submission and validation of application**	
2.1	*At validation* Send the following information to AWP: - Pre-defined list of points to be considered - Evaluation timetable as received (i. e. timetable for the relevant evaluation, including AWP steps)	AWP secretariat

Step		Action	Responsibility
		Send list of contact details for AWP members to applicant for submission of additional electronic copies.	
	2.2	*By day 30*	Ensure that AWP coordinator and members have received the dossier from the applicant.	AWP secretariat
			Circulate to AWP additional/specific points to be addressed as proposed by the (co-)rapporteur or AWP chair (if any).	AWP secretariat
		Proceed to 3.0	
3.0		**Evaluation**	
	3.1	*Day 70*	Send rapporteur's assessment report to AWP secretariat, who will forward it to the AWP.	PM
			Highlight any other additional point to be addressed by AWP, if specifically requested by rapporteur or co-rapporteur.	AWP secretariat
	3.2	*Day 80*	Send initial comments from AWP coordinator to AWP members.	AWP secretariat
	3.3	*Day 85*	Send co-rapporteur's critique of the rapporteur's assessment report to AWP secretariat, who will forward it to the AWP.	PM
	3.4	*By day 95*	Send comments to AWP coordinator with copy to AWP secretariat.	AWP members
			Compile all AWP comments and discuss any inconsistencies electronically with the AWP group. Send resulting AWP comments to the AWP secretariat.	AWP coordinator
	3.5	*Day 100*	Forward AWP comments to all CVMP and AWP members (using the CNA mailbox for initial applications and CVE mailbox for other applications), with copy to and product specific mailbox and PM. Comments from AWP to be tabled for information at CVMP.	AWP secretariat PM
			Send AWP comments to the applicant.	
			AWP coordinator might attend the Adobe rapporteurs meeting	
	3.6	*Day 120*	Circulate the LoQ adopted by CVMP to AWP secretariat, who will forward it to the AWP.	PM

Step	Action		Responsibility
3.7	*By day 121*	Ensure that AWP coordinator and members have received the answers to the LoQ and revised timetable.	AWP secretariat
3.8	*By day 156*	Circulate joint rapporteur and co-rapporteur assessment report on responses to LoQ and revised draft SPC to AWP secretariat.	PM
		Forward joint rapporteur and co-rapporteur assessment report on responses to LoQ and revised draft SPC, together with the revised timetable to AWP.	AWP secretariat
3.9	*By day 163*	Send comments on the relevant parts of the rapporteur and co-rapporteur assessment to AWP coordinator with copy to AWP secretariat.	AWP members
		Compile the AWP comments and to discuss any inconsistencies electronically with the AWP group. Send resulting AWP comments to the AWP secretariat.	AWP coordinator
3.10	*Day 166*	Forward AWP comments to all CVMP and AWP members (CNA / CVE mailbox), with copy to DEM/V-ROS-PM and product specific mailbox.	AWP secretariat
		Send AWP comments to the applicant.	PM
3.11	*By day 180*	Ensure CVMP take into account comments from AWP when discussing the need for a list of outstanding issues and an oral explanation. Send list of outstanding issues, if applicable, to AWP secretariat.	PM
		Ensure CVMP considers the need for involvement of AWP in case of oral explanation. Inform AWP secretariat of CVMP outcome.	PM AWP secretariat
3.12	AWP involvement in oral explanation? If yes, go to 3.13 If no, go to 3.15		
3.13	*Day 181*	*If applicable, invite the AWP coordinator to the Oral explanation.*	AWP secretariat
3.14	*Day 195*	Ensure that the AWP have received LoOI.	AWP secretariat
		Forward the draft CVMP assessment report to AWP secretariat, who will forward it to the AWP.	PM
3.15	*Day 210*	Ensure CVMP considers the need for AWP or AWP coordinator to be involved in antimicrobial resistance surveillance as post-marketing authorisation	PM

Step	Action	Responsibility
	obligation, if applicable and inform AWP secretariat of outcome.	
3.16	AWP involvement post-marketing authorisation obligations? If yes, go to 3.17 If no, go to 4.0	
3.17	Inform AWP on its involvement following the CVMP decision. Proceed to 4.0	AWP secretariat
4.0	**End of procedure**	

10. Records

When completed and approved, originals are filed in the Master File. Electronic copies are saved in the appropriately labelled folder in DREAM and labelled as Core Master File, as appropriate.