EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Work instructions

Title: Checking of MRL status of constituents of veterinary medicinal products subject to a marketing authorisation application to the EMA		
Applies to: Veterinary Medicines		
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1. Changes since last revision

Review of legal basis and other relevant documents, list of abbreviations and minor editorial changes in process.

2. Records

Electronic copies are saved in the relevant product folder in DREAM (*Cabinets\01. Evaluation of Medicine\V - C\Active applications\XX-YY\PRODUCT NAME\01 Pre Authorisation\02 Validation*).

3. Instructions and background information

3.1. Documents needed for this WIN

3.1.1. Legal basis

- Directive 2001/82/EC, as amended, of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products (*http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2001L0082:20090807:EN:PDF*)
- Regulation (EC) No 470/2009 of the European Parliament and of the Council laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin (*http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:152:0011:0022:en:PDF*)
- Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin (*http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:015:0001:0072:EN:PDF*)

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3.1.2. Other documents of relevance

- Latest revision of the substances considered as not falling within the scope of Regulation (EC) 470/2009 (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000165.jsp)[1]
- MRL status of excipients in centralised MA (*Cabinets/01. Evaluation of Medicines /V- Maximum Residue Limits/V- MRL General/Excipients – Adjuvants*)[2]
- Approaches on how to consider excipients in the context of Regulation 2377/90 (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000384.jsp&mid=WC0b01ac058002dd37#EstablishmentofMRLs)
- Guideline on data to be provided in support of a request to include a substance in the list of substances considered as not falling within the scope of regulation (EC) No 470/2009 (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000384.jsp&mid=WC0b01ac058002dd37#EstablishmentofMRLs)
- List of approved **food additives** (http://ec.europa.eu/food/food/fAEF/additives/lists_authorised_fA_en.htm)
- Regulation (EC) No 1331/2008 establishing a common authorisation procedure for **food additives, food enzymes and food flavourings** (*http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32008R1331:EN:NOT*)
- Regulation (EC) No 1332/2008 on **food enzymes** and amending Council Directive 83/417/EEC, Council Regulation (EC) No 1493/1999, Directive 2000/13/EC, Council Directive 2001/112/EC and Regulation (EC) No 258/97 (*http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32008R1332:EN:NOT*)
- Regulation (EC) No 1333/2008 on **food additives** (*http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32008R1333:EN:NOT*)
- Regulation (EC) No 1334/2008 on **flavouring and certain food ingredients with flavouring properties** amending Council Regulation (EEC) no 1601/91, Regulations (EC) No 2232/96 and (EC) No 110/2008 and Directive 2000/13/EC (*http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32008R1334:EN:NOT*)
- Checklist for centralised applications for veterinary medicinal products (validation phase) (*Cabinets/Template Management/Draft/Vet - review of product checklist*)

3.1.3. Templates

- Model for response (*Cabinets\Template Management\Published\For Databases\Siamed-BI\Veterinary\Initial MAA - Extension\MAA-EXT – 01 Response re MRL status*)

3.2. Definitions

APH	Animal and Public Health (Service in V-VM department)
CVMP	Committee for Medicinal Products for Veterinary Use
DEM	Development and Evaluation of Veterinary Medicines (Service in V-VM department)
DREAM	Document Records Electronic Archive Management (electronic filing system at EMA)
MA	Marketing authorisation
MRL	Maximum residue limit(s)
PM	Project manager (in DEM)
SA	Scientific Administrator (in APH)
HSer	Service Head
V-VM	Veterinary Medicines department
WIN	Work Instruction

[1] Most recent version of this document is linked at the bottom of this website.
[2] This is an unofficial working document, to be used for reference only.

3.3. Instructions

This WIN describes how to handle a request originating from the Development and Evaluation of Veterinary Medicines service (DEM) of the Veterinary Medicines department for assessment of the MRL status of the constituents of an intended veterinary medicinal product during the validation process of an application for a centralised marketing authorisation. It addresses specifically the allocation of responsibilities in the Animal and Public Health service (APH) in order to respond to the request of the MRL status of the constituents of such a product, and the way of obtaining the information on the MRL status.

Step	Action	Responsibility
1.0	**Receipt of request from DEM**	
1.1	Was a project team member from APH appointed for the evaluation procedure and entered in SIAMED? (*NB: In this case the request is sent directly to the SA allocated for this procedure. If not, the request is sent to the APH HSer.)* If yes, go to 2.0 If no, go to 1.2	
1.2	Allocate task to APH SA and pass request on accordingly. Proceed to 2.0	HSer
2.0	**MRL status assessment** *(to be provided within deadline specified in request)*	
2.1	Is/are the **active substance**(s) listed in Table 1 of the Annex of Commission Regulation (EU) No 37/2010 for the species concerned and condition of use?	SA

	Is/are the **non-active constituent**(s), i. e. excipient(s), adjuvant(s), preservative(s) and/or others, listed in the above mentioned Annex for the species concerned and condition of use *or* included in the list of substances not within the scope of Regulation (EC) No 470/2009 for the dose/concentration and condition of use as in intended product?
	If (both) yes, go to 2.3
	If (one or both) no, go to 2.2
		SA

2.2	Prepare memo informing of outcome using model "*MAA – EXT -01 Response re MRL status*". Describe the reasons and suggest solutions[3], if possible. If in doubt, discuss with HSer. Go to 2.4	SA
2.3	Prepare memo informing of outcome using Model "*MAA – EXT -01Response re MRL status*". If in doubt, discuss with HSer.	SA
2.4	Submit memo to PM in DEM[4] who requested the information (and any additional staff in CC of memo model, as applicable).	SA
	Update internal list on MRL status of excipients in centralised MA.	SA
	Proceed to 3.0	
3.0	**End of procedure**	

[3] Example: Could the substance(s) not covered in any of the lists fall under an entry in Annex II or be added to the list of substances not within the scope of Regulation 470/2009?

[4] In case of outstanding issues, the DEM PM might request further clarification from the applicant in the validation letter, and initiate discussion at next possible CVMP, if not successfully sorted out.