EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 July 2021
EMA/CVMP/SWP/207500/2021
Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper on the development of a guideline on determination of the need for an MRL evaluation for biological substances

Agreed by SWP-V	June 2021
Adopted by CVMP for release for consultation	15 July 2021
Start of public consultation	23 July 2021
End of consultation (deadline for comments)	30 September 2021

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

Keywords	biological substances, MRL assessment, consumer safety

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1. Introduction

This concept paper addresses the need for a guideline on determination of the need for an MRL evaluation for biological substances, when it is intended that those substances are included in products for use in food-producing species. According to Annex I Section I.7 of Commission Regulation (EU) 2018/782, the European Medicines Agency ('Agency') is requested to publish guidance in order to determine whether there is the need for an MRL evaluation for these substances. Biological substances for which it is concluded that an MRL evaluation is not required shall be published by the Agency in a list of such substances. As immunologicals are exempted from the need for MRL assessment according to Article 1 point 2 (a) of Regulation (EC) No 470/2009, this guidance concerns 'biologicals, other than immunologicals' only.

The standard assessment approaches currently used for MRL and consumer safety assessment do not always adequately match assessment requirements for biological substances and may need to be adapted. This concept paper describes and discusses the basis for new guidance in this area.

2. Problem statement

Biological substances are defined in Regulation (EU) 2019/6 as substances that are produced by or extracted from a biological source and that need for their characterisation and the determination of their quality a combination of physico-chemical-biological testing, together with knowledge of the production process and its control. They are a heterogeneous group of compounds used as active ingredients in veterinary medicinal products. Based on their specific nature, certain types of biologicals require consideration of specific assessment aspects that are not necessarily covered by conventional standard testing approaches and can often be assessed using simplified and flexible procedures.

According to Commission Regulation (EU) 2018/782 there are two groups of 'biologicals, other than immunologicals' to be distinguished: those that can be characterised as 'chemical-like' and those characterised as 'chemical-unlike'. While the first group is subject to a normal (standard) MRL procedure according to Regulation (EC) No 470/2009, the evaluation of the latter group is to be conducted on a case-by-case basis. For this purpose, a report describing the scientific basis for the request on whether a full MRL evaluation is required or not needs to be provided by the applicant. This report should be accompanied by the items listed in I.7 (a) to (e) of Annex I to Regulation (EU) 2018/782. This report shall be evaluated in accordance with the guidance published by the Agency in order to determine whether there is the need for a MRL evaluation.

Based on the criteria laid down in Commission Regulation (EU) 2018/782, the guidance to be developed concerns definitions for the groups of biologicals as well as on the criteria to evaluate the report and to identify the appropriate assessment procedure.

3. Discussion (on the problem statement)

The guidance to be developed intends to focus on the following items:

- Definitions for 'biologicals, which are not immunologicals', 'chemical-like biologicals' and 'chemical-unlike biologicals' need to be developed as each of these groups is subject to different regulatory regimens concerning MRL and consumer safety assessment based on the above-mentioned regulations. The definitions to be developed are aimed to facilitate a categorisation of the substances while at the same time retaining sufficient flexibility for dealing with borderline cases.
- Guiding questions and criteria need to be developed allowing applicants to classify their substances and collect the data required to address consumer safety, while keeping regulatory requirements to

a minimum, sufficiently flexible and tailored specifically to the information needed to reach a meaningful, scientifically justifiable conclusion in each case.

Technical guidance on the conduct of certain studies to meet the requirements of Annex I of Commission Regulation (EU) 2018/782 is not within the scope of this guideline. The need for such technical guidance may be identified based on the experience gained and lessons learnt from the implementation of this guideline and will be dealt with in follow-up guidance.

4. Recommendation

The Committee for Medicinal Products for Veterinary Use (CVMP) recommends that the Safety Working Party (SWP-V) drafts a guideline to address the problem above.

5. Proposed timetable

July 2021	Concept paper released for public consultation
September 2021	End of consultation of the concept paper (deadline for comments)
January 2022	Draft guideline adopted by CVMP and released for 3-month consultation
April 2022	End of consultation of the guideline (deadline for comments)
July 2022	Final guideline adopted by CVMP and published

6. Resource requirements for preparation

The development of the new guideline will involve the SWP-V (including a drafting group composed of 3-4 SWP-V members), the NTWP and the CVMP.

The SWP-V drafting group will meet virtually as required (e.g. 2-3 virtual meetings). Comments will be sought from NTWP. The guideline is foreseen to be discussed at 2 plenary meetings of the SWP-V.

7. Impact assessment (anticipated)

The guidance will clarify for industry and for regulators the approach to determining whether an MRL evaluation is needed for the biological substance in question and what specific data are required in order to make that determination. This approach will encourage predictable decisions.

The possibility of including certain biological active substances in a list of substances not requiring MRL evaluation was included in Commission Regulation (EU) 2018/782 specifically to allow for a streamlined and less burdensome procedure for relevant biological substances. This is expected to have a positive impact on the development of veterinary medicines containing such substances.

8. Interested parties

Veterinary pharmaceutical industry, EU competent authorities, consultants.

9. References to literature, guidelines, etc.

Commission Regulation (EU) 2018/782 of 22 May 2018 establishing the methodological principles for the risk assessment and risk management recommendations referred to in Regulation (EC) No 470/2009 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R0782&from=EN

Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R0006&from=EN

Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32009R0470