EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Veterinary Medicinal Products (CVMP)

Concept paper on the revision of the guideline on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.1)

Agreed by CVMP Safety Working Party	April 2024
Adopted by CVMP for release for consultation	18 July 2024
Start of public consultation	26 July 2024
End of consultation (deadline for comments)	31 October 2024

The proposed guideline will replace the guideline on user safety for pharmaceutical veterinary medicinal products' (EMEA/CVMP/543/03-Rev.1).

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

Keywords	user safety, veterinary medicinal products

1. Introduction

In 2005 the Guideline on user safety for pharmaceutical veterinary medicinal products was introduced (EMEA/CVMP/543/03-FINAL). The last revision of the Guideline on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.1) came into effect in 2010. Since that time, legislation has changed and regulatory experience with the guideline has proceeded. Also, the Guideline on user safety of topically administered veterinary medicinal products (EMA/CVMP/SWP/721059/2014) and the reflection paper providing an overview of the current regulatory testing requirements for veterinary medicinal products and opportunities for implementation of the 3Rs" (EMA/CHMP/CVMP/3Rs/164002/2016) were published. This has prompted a review of the current guideline. The objective of the guideline is to provide guidance and advice on user safety risk assessments for all applications for Marketing Authorisations for pharmaceutical veterinary medicinal products. The guideline is to be used in conjunction with the 'Guideline on user safety of topically administered veterinary medicinal products' (EMA/CVMP/SWP/721059/2014).

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2. Problem statement

The guideline is to be revised to reference current legislation (i.e. Regulation (EU) 2019/6 and its Annex II, as amended by Commission Delegated Regulation (EU) 2021/805) and to take into account updated definitions. The revision also aims to align more closely with the associated 'Guideline on user safety of topically administered veterinary medicinal products'. Regulatory experience gained through use of the guideline will assist in reflecting on the adequacy of the currently applied user risk assessment, including user risk mitigation measures. In accordance with paragraph I.1.7[1] of Annex II of Regulation (EU) 2019/6 opportunities for implementation of the 3Rs and alternative testing approaches as part of the user risk assessment should also be included.

3. Discussion (on the problem statement)

The Guideline on user safety for veterinary medicinal products is planned to be revised in relation to:

- reference to current legislation (i.e. Regulation (EU) 2019/6 and its Annex II as amended by Commission Delegated Regulation (EU) 2021/805) and amend definitions where necessary.
- reference to the "Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches" (EMA/CHMP/CVMP/JEG-3Rs/450091/2012) and the "Reflection paper providing an overview of the current regulatory testing requirements for veterinary medicinal products and opportunities for implementation of the 3Rs" (EMA/CHMP/CVMP/3Rs/164002/2016) including general statements and reference to in vitro tests when considering local tolerance.
- providing clarification on the wording from Annex II to Regulation (EU) 2019/6 on the 'significant user exposure' as stated in the sentence 'For the evaluation of user safety, standard developmental toxicity testing […] shall be performed in all cases where significant user exposure may be expected'.
- provide more guidance on adequate risk mitigation measures, taking into account changes to the QRD-template.
- the harmonisation of common approaches with the 'Guideline on user safety of topically administered veterinary medicinal products' (EMA/CVMP/SWP/721059/2014) where necessary.
- provide more guidance on the uncertainty factors that can be applied when evaluating the acceptability of the margin of exposure.

4. Recommendation

The Committee for Medicinal Products for Veterinary Use (CVMP) recommends that the Safety Working Party (SWP-V) in collaboration with the 3Rs Working Party (3RsWP) revises the 'guideline on user safety for pharmaceutical veterinary medicinal products (EMEA/CVMP/543/03-Rev.1)' taking into account the issues identified above.

5. Proposed timetable

26 July 2024	Concept paper released for consultation

[1] Paragraph I.1.7 of Annex II of Regulation (EU) 2019/6 states that "All experiments on animals shall be conducted taking into account the principles laid down in Directive 2010/63/EU, notwithstanding the place of conduct of the experiments".

31 October 2024	End of consultation of the concept paper (deadline for comments)
Q1/Q2 2025	Draft guidelines adopted by CVMP and released for 3-month consultation
Q2/Q3 2025	End of consultation of the guidelines (deadline for comments)
Q4 2025 /Q1 2026	Final guidelines adopted by CVMP and published

6. Resource requirements for preparation

The revision of the guideline mentioned above will involve the SWP-V, the 3RsWP, including a drafting group composed of 3 SWP-V members and 1 3RsWP member, and the CVMP.

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

7. Impact assessment (anticipated)

The revision will update the references to the legislation and to the 3Rs. No adverse impact on industry or regulators with respect to either resources or costs is foreseen.

8. Interested parties

Veterinary pharmaceutical industry, EU competent authorities, consultants

9. References to literature, guidelines, etc.

Commission Delegated Regulation (EU) 2021/805 of 8 March 2021 amending Annex II to Regulation (EU) 2019/6 of the European Parliament and of the Council https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32021R0805&qid=1715784665500

Guideline on user safety for pharmaceutical veterinary medicinal products (EMEA/CVMP/543/03-Rev.1) https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-user-safety-pharmaceutical-veterinary-medicinal-products_en.pdf

Guideline on user safety of topically administered veterinary medicinal products (EMA/CVMP/SWP/721059/2014) https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-user-safety-topically-administered-veterinary-medicinal-products_en.pdf

Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches (EMA/CHMP/CVMP/JEG-3Rs/450091/2012) https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-principles-regulatory-acceptance-3rs-replacement-reduction-refinement-testing-approaches_en.pdf

Reflection paper providing an overview of the current regulatory testing requirements for veterinary medicinal products and opportunities for implementation of the 3Rs (EMA/CHMP/CVMP/3Rs/164002/2016) https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-providing-overview-current-regulatory-testing-requirements-veterinary-medicinal-products-and-opportunities-implementation-3rs_en.pdf

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