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Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper for the revision of residues guidelines to align with the definitions for withdrawal periods provided in Regulation (EU) 2019/6

Agreed by SWP-V	June 2021
Adopted by CVMP for release for consultation	17 June 2021
Start of public consultation	25 June 2021
End of consultation (deadline for comments)	31 July 2021

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

Keywords	Consumer safety, withdrawal period, tissues, milk, injection site residues

1. Introduction

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 entered into force on 28 January 2019 and is applicable from 28 January 2022 onwards.

Article 4 of this regulation introduces a new definition for withdrawal period (WP), differing from the definition currently used in residues guidelines. This new definition triggers a revision of the relevant residues guidelines.

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2. Problem statement

Article 4 of Regulation (EU) 2019/6 provides the following definition:

"(34) 'withdrawal period' means the minimum period between the last administration of a veterinary medicinal product to an animal and the production of foodstuffs from that animal which under normal conditions of use is necessary to ensure that such foodstuffs do not contain residues in quantities harmful to public health"

This definition differs from the one provided by article 1 of Directive 2001/82/EC:

"9. Withdrawal period: The period necessary between the last administration of the veterinary medicinal product to animals, under normal conditions of use and in accordance with the provisions of this Directive, and the production of foodstuffs from such animals, in order to protect public health by ensuring that such foodstuffs do not contain residues in quantities in excess of the maximum residue limits for active substances laid down pursuant to Regulation (EEC) No 2377/90."

The major alteration is that in Directive 2001/82/EC it is explicitly mentioned that residues in foodstuffs of animal origin should be below the maximum residue limits (MRLs), whereas in Regulation (EU) 2019/6 residues in foodstuffs of animal origin should not be harmful to public health. The latter, therefore, provides opportunities for alternative approaches to ensuring consumer safety, in addition to compliance with relevant MRLs.

Since Regulation (EU) 2019/6 introduces a new definition for withdrawal period, there is a need to review and revise, as appropriate, the following residues guidelines in order to align them with the new definition:

- guideline on determination of withdrawal periods for edible tissues (EMA/CVMP/SWP/735325/2012)
- note for guidance for the determination of withdrawal periods for milk (EMA/CVMP/473/1998)
- guideline on injection site residues (EMA/CVMP/542/2003)

3. Discussion (on the problem statement)

Due to the definition introduced by Regulation (EU) 2019/6, the revision of relevant guidelines is considered necessary:

- Guideline on determination of withdrawal periods for edible tissues (EMA/CVMP/SWP/735325/2012)

  This guideline has been developed during the period of 2016 -2018 and came into effect on 1 April 2019.

  The guideline is considered up-to-date and already addresses approaches, other than compliance with relevant MRLs, such as injection site residue reference value (ISRRV) and/or acceptable daily intake (ADI).

  No major changes are considered necessary.

  It only needs introducing the new definition with some minor amendments related to this introduction when applicable. This may include additional guidance on what approach should be the standard way (MRL) and what are the alternative ways, if no MRL is set.

- Note for guidance for the determination of withdrawal periods for milk (EMA/CVMP/473/1998)

  This note for guidance has been developed during the period of 1998-2000 and came into effect on 8 September 2000.

  This is a rather old guidance document. In addition to alignment with the new definition, references need to be updated. For instance, it refers to guideline EMEA/CVMP/036/95-FINAL instead of EMA-CVMP-SWP-735325-2012 (guideline on determination of WP for edible tissues).

- Guideline on injection site residues (EMA/CVMP/542/2003)

  This guideline has been developed during the period of 2003-2004 and came into effect on 13 April 2005.

  This is a rather old guidance document. Next to alignment with the new definition, references need to be updated. For instance, it refers to guideline regulation 2377/90 instead of 470/2009, to Vol 8 instead of 2018/782 and to guideline GL EMEA/CVMP/036/95-FINAL instead of EMA/CVMP/SWP/735325/2012 (WP meat).

  Moreover, the new definition for withdrawal period provides opportunities for alternative approaches. The possibility for establishment of an Injection Site Residues Reference Value (ISRRV) is mentioned in the Commission Regulation (EU) 2018/782 (referring to Regulation (EC) No 470/2009). The ISRRV is already being mentioned in the Guideline on determination of withdrawal periods for edible tissues (EMA/CVMP/SWP/735325/2012), however, it is currently not mentioned in the Guideline on injection site residues. The current revision provides an opportunity for update to also briefly reflect on this aspect in that the ISRRV can be introduced in accordance with the Guideline on determination of withdrawal periods for edible tissues. Subsequently no new technical information will be introduced, though it will be harmonised. In future, the Guideline on injection site residues could be combined with the 'Guideline on determination of withdrawal periods for edible tissues'.

To implement the new definition, the revision of the relevant guidelines will in principle be of editorial nature including the update of references. Significant changes of the technical guidance are not foreseen due to the short timeline. The ISRRV could be easily introduced in the guideline on injection site residues.

4. Recommendation

The Committee for Medicinal Products for Veterinary Use (CVMP) recommends that the Safety Working Party (SWP-V) revises the following guidelines to address the problems above:

- guideline on determination of withdrawal periods for edible tissues (EMA/CVMP/SWP/735325/2012)
- note for guidance for the determination of withdrawal periods for milk (EMA/CVMP/473/1998)
- guideline on injection site residues (EMA/CVMP/542/2003)

The revision is expected to be mainly editorial to align with the new definition and update the references. Also, the ISRRV could be easily introduced in the guideline on injection site residues.

5. Proposed timetable

17 June 2021	Concept paper released for consultation
31 July 2021	End of consultation of the concept paper (deadline for comments)
October 2021	Draft guidelines adopted by CVMP and released for 2-month consultation
December 2021	End of consultation of the guidelines (deadline for comments)
March 2022	Final guidelines adopted by CVMP and published

Considering the nature of the changes foreseen (mostly editorial), it is expected that the revised guidelines will come into operation earlier than six months after adoption.

6. Resource requirements for preparation

The revision of the 3 guidelines mentioned above will involve the SWP-V (including a drafting group composed of 2 SWP-V members) and the CVMP.

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

7. Impact assessment (anticipated)

In principle, the revised guidelines are not intended to increase or change the requirements for marketing authorisation applications regarding the type or amount of data. The revisions are considered mainly of an editorial nature and are only intended to provide clarity by aligning the existing guidelines with the new definition provided by Regulation (EU) 2019/6.

8. Interested parties

- Veterinary pharmaceutical industry and consultants.
- EU Regulatory authorities involved in assessment of marketing authorisation applications for veterinary medicinal products.
- Scientific associations and professional bodies.

9. References to literature, guidelines, etc.

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

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

https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02001L0082-20090807&from=EN

Commission Regulation (EU) 2018/782 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 (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/PDF/?uri=CELEX:32009R0470&from=EN