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Committee for Medicinal Products for Veterinary Use (CVMP)

# Concept paper for the revision of the guideline on requirements for production and control of immunological veterinary medicinal products

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| Agreed by Immunologicals Working Party | 27 May 2021 |
| Adopted by CVMP for release for consultation | 17 June 2021 |
| Start of public consultation | 25 June 2021 |
| End of consultation (deadline for comments) | 30 September 2021 |

The proposed guideline will supersede 'Guideline on requirements for the production and control of immunological veterinary medicinal products' (EMA/CVMP/IWP/206555/2010 Rev. 1).

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

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| Keywords | Production, control, immunological veterinary medicinal products |

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# 1. Introduction

The 'Guideline on requirements for production and control of immunological veterinary medicinal products' (EMA/CVMP/IWP/206555/2010-Rev.1) provides information on items to be considered for the production and control of all immunological veterinary medicinal products (IVMPs).

The guideline outlines important items related to the quality, safety and efficacy parts of the marketing authorisation dossier that were not sufficiently defined in the requirements of Annex I of Directive 2001/82/EC and the European Pharmacopoeia (Ph. Eur.).

Regulation (EU) 2019/6 of the European Parliament and of the Council on veterinary medicinal products is repealing Directive 2001/82/EC. In line with Art. 8(1) of this Regulation, an application for a marketing authorisation of veterinary medicinal product shall contain the information set out in Annex I (administrative documentation) and Annex II (technical documentation). The requirements in Annex II to Regulation (EU) 2019/6 were revised, updated and adapted to scientific and technical progress because the original Annex II took over the dossier requirements set out in Annex I to Directive 2001/82/EC, without updating them at the time of adoption of Regulation (EU) 2019/6. This update concerns also requirements for IVMPs.

The Commission Delegated Regulation (EU) 2021/805 of 8 March 2021 amending Annex II to Regulation (EU) 2019/6 describes in section IIIb the requirements that shall apply to IVMPs.

With regard to the Annex 2 of the aforementioned guideline 'The approach to demonstrate freedom from extraneous agents as part of the production and control of IVMPs for mammalian species, salmonids and other finfish', a revised testing approach was included in the Ph. Eur. texts. Updated and new monographs are published on the management of extraneous agents in IVMPs, other monographs were deleted.

The Immunologicals Working Party has been tasked with the revision of the existing 'Guideline on requirements for production and control of immunological veterinary medicinal' to adapt the guideline to the new veterinary regulation and Ph. Eur. monographs.

# 2. Problem statement

Until now, the guideline outlines important items related to the quality, safety and efficacy parts of the marketing authorisation dossier that are not sufficiently defined in the requirements of Annex I of Directive 2001/82/EC and the European Pharmacopoeia (Ph. Eur.).

The requirements in Annex I of Directive 2001/82/EC have been taken over in Annex I and Annex II of Regulation (EU) 2019/6 and were revised considering scientific and technical progress.

Annex I of Regulation (EU) 2019/6 contains administrative details that need to accompany an application for a marketing authorisation of veterinary medicinal product.

Annex II of Regulation (EU) 2019/6 provides details on the technical data to be provided by the applicants for marketing authorisations of veterinary medicinal products. In particular, it details the technical documentation necessary for demonstrating the quality, safety and efficacy for the different types of products. Section IIIb details data set requirements for quality, safety and efficacy for IVMPs.

In addition, freedom from extraneous agents (EA) is a high priority for any medicinal product. For any IVMP placed on the market in the EU, the requirement to test IVMPs for potential infectious contaminants is specified in Directive 2001/82/EC and in Regulation (EU) 2019/6 repealing the Directive as well as in Ph. Eur. general and specific monographs.

The 'Guideline on requirements for the production and control of IVMPs' was supplemented by Annex 2 'The approach to demonstrate freedom from extraneous agents as part of the production and control of IVMPs for mammalian species, salmonids and other finfish' which should be taken into account. This Annex 2 laid down the EU approach to move away from prescribing the test methodology that must be used for a particular agent or substrate and to move towards describing the general approach in order to demonstrate suitability of tests applied to show freedom of the relevant substrate from specified EA. This Annex includes a reference list of extraneous agents for mammalian species, salmonids and other finfish that must be taken into account when considering which testing for EA is appropriate. This list was established in accordance with the existing knowledge at the time of writing this guideline.

This approach for management of EA - moving from a prescriptive, mainly relying on extensive laboratory testing, to a scientifically-sound and targeted risk-based approach - is now included in Ph. Eur. monographs. It is restricted to living replicative EA, covers all starting materials of animal or human use and includes the entire production process, from the sourcing of raw materials to the final product stage. The approach based on risk management including risk assessment and risk control allows the use of any suitable culture or other fit-for-purpose method capable of detecting specified EA but with a focus on in vitro methods. Furthermore, it provides an updated single reference list of EA for mammalian and poultry species, salmonids and other finfish to be considered in the risk assessment.

# 3. Discussion

Due to the revision of Annex II to Regulation (EU) 2019/6 on veterinary medicinal products and new, updated and deleted Ph. Eur. monographs, mainly on the management of EA in IVMPs, it is necessary to review the current guideline on requirements for production and control of IVMPs.

The following issues should be addressed:

- Update of references.
- Revise/amend the information provided in section II and III of the guideline according to Annex I and II of Regulation (EU) 2019/6 considering the specifics for IVMPs detailed mainly in section IIIb of Annex II to Regulation (EU) 2019/6.
- Update Annex 2 - The approach to demonstrate freedom from extraneous agents as part of the production and control of immunological veterinary medicinal products for mammalian species and finfish – considering the revision of the Ph. Eur. texts on the management of extraneous agents in IVMPs.

# 4. Recommendation

The Immunologicals Working Party recommends revising the CVMP guideline on requirements for production and control of immunological veterinary medicinal products in order to take into account the revision of Annex II to Regulation (EU) 2019/6 on veterinary medicinal products, updated and new texts of the Ph. Eur., mainly on the management of extraneous agents.

# 5. Proposed timetable

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| 25 June 2021 | Concept paper released for consultation |
| 30 September 2021 | Deadline for comments |
| November 2021 | Discussion of the revised guideline by IWP |

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| December 2021 | Discussion and adoption the draft guideline by CVMP and release for consultation |
| March 2022 | Expected end of consultation |
| June 2022 | Expected date for adoption by CVMP and publication of the revised guideline |

# 6. Resource requirements for preparation

The revision of the guideline will involve the IWP (including a drafting group composed of rapporteur, co-rapporteur and 2 IWP members).

The IWP drafting group will meet virtually as required (e.g. 2-3 virtual meetings). Discussion is foreseen at 1-2 IWP plenary meetings.

# 7. Impact assessment

It is anticipated that the guideline would provide clarity and predictability to both industry and regulators on the data requirements for submission of marketing authorisation application. The guideline is intended to supplement Annex I and II to Regulation (EU) 2019/6, Ph. Eur. monographs and relevant VICH guidelines and to clarify requirements that are not covered by these. It will also result in a more consistent assessment of the provided data for a marketing authorisation application by regulators. Therefore, the guidance would benefit both industry and regulators and will contribute to increase veterinary vaccine availability.

# 8. Interested parties

Veterinary pharmaceutical industry and consultants.

EU Regulatory authorities involved in assessment of marketing authorisation applications for immunological veterinary medicinal products.

# 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

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

Ph. Eur. monograph 0062 'Vaccines for veterinary use'

Ph. Eur. monograph 2.6.37 'Principles for the detection of extraneous viruses in IVMPs using culture methods'

Ph. Eur. monograph 5.2.4 'Cell cultures for the production of vaccines for veterinary use'

Ph. Eur. monograph 5.2.5 'Management of extraneous agents in IVMPs'