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Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper on the provision of field efficacy studies in support of marketing authorisation applications for immunological veterinary medicinal products and on indications for veterinary vaccines

Agreed by Immunologicals Working Party	17 December 2020
Adopted by CVMP for release for consultation	20 January 2021
Start of public consultation	29 January 2021
End of consultation (deadline for comments)	31 March 2021

The proposed guidelines will replace the 'Note for guidance – Field trials' with veterinary vaccines' (EMEA/CVMP/852/99-FINAL) and the 'Revised position paper on indications for veterinary vaccines' (EMEA/CVMP/042/97-Rev.1-FINAL)

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

Keywords	Field efficacy, indications, veterinary vaccines

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1. Introduction

To date, field efficacy data is generally expected to be provided in support of a marketing authorisation application for a vaccine. This requirement is based on existing legislation. However, currently the draft Annex to the Commission Delegated Regulation amending Annex II to Regulation (EC) 2019/6 (still to be adopted or endorsed by the European Commission) states in section IIIb, Requirements for Immunological Veterinary Medicinal Products:

"In general, pre-clinical studies shall be supported by trials carried out in field conditions.

When pre-clinical studies fully support the claims made in the summary of product characteristics, trials carried out in field conditions are not required.

Unless otherwise justified, results from pre-clinical studies shall be supplemented with data from clinical trials, using batches representative of the manufacturing process described in the marketing authorisation application. Both safety and efficacy may be investigated in the same clinical trials."

The existing "Note for Guidance - Field trials with Veterinary Vaccines" EMEA/CVMP/852/99-FINAL lists a number of situations when the omission of field efficacy data may be accepted. In particular, vaccines against notifiable and/or exotic diseases, vaccines against rare or sporadic diseases and vaccines for minor species are listed.

Assuming Annex II to Regulation (EU) 2019/6 comes into force as it is drafted today, further vaccine types or indications may be considered exempt from the requirement for field efficacy data, in addition to those currently listed in the existing guideline. This would lessen the administrative and practical burden placed on applicants to complete a marketing authorisation dossier.

Absence of field efficacy data may have implications for the description of indications for veterinary vaccines in product literature, for this reason the position paper on indications for veterinary vaccines may need to be updated.

The Immunologicals Working Party has been tasked to reflect on the requirement to provide efficacy clinical trials in support of marketing authorisation applications for veterinary vaccines and to review the already existing guidance on this issue.

2. Problem statement

A Joint European Medicines Agency (EMA)/Heads of Medicines Agencies (HMA) focus group meeting with invited stakeholders was held in June 2017 to examine the relevance of efficacy clinical trials in the context of an EU authorisation for veterinary vaccines. Based on the outcome of the Focus Group meeting the joint EMA/HMA Steering Group on veterinary vaccine availability recommended that CVMP consider how best to provide predictability to applicants as to those situations in which a justification to omit field efficacy data will be accepted by regulators and how best to reflect in the SPC of veterinary vaccines the efficacy data that have been provided.

As stated in the introduction, Annex II to Regulation (EU) 2019/6 has now been drafted to include a statement that field efficacy data may be omitted under particular conditions ("*When pre-clinical studies fully support the claims made in the summary of product characteristics, trials carried out in field conditions are not required.*").

Currently, the guideline "Field trials with Veterinary Vaccines" EMEA/CVMP/852/99-FINAL includes a section on 'deviations from the basic principle'. However, this section lists only a few exceptional circumstances when field efficacy data are not required (Minor Use Minor Species products, vaccines

against notifiable diseases, vaccines against sporadic diseases). In order to provide clarity and predictability on the need for provision of field efficacy data, also in light of the statements on clinical trials in Annex II to Regulation (EU) 2019/6, a revision of the guideline is proposed.

The revised guideline should be updated to include further guidance on the type of products that would or would not require field efficacy data.

The position paper on indications for veterinary vaccines may need to be updated as a consequence of changes to the guideline on field trials with veterinary vaccines. This update should provide clear guidance on how efficacy data is to be reflected in the SPC.

3. Discussion (on the problem statement)

At the focus group meeting in 2017, preliminary data from a review of immunological products authorised via the centralised route were presented. The findings suggest that, for some vaccines, field efficacy trials were pivotal in defining some indications and, in addition, field studies may provide data that increases understanding of the appropriate use of a vaccine and informs other sections of the SPC. However, for the majority of immunological products considered in the review, field data appeared to be of limited value from an efficacy perspective and was only generally supportive to the claims.

Veterinary vaccines represent a very wide range of products, all having specific properties with regard to safety and efficacy. In general, it is difficult to cover all the vaccine types using a limited set of criteria. In addition, it is challenging to list all vaccines for veterinary use, including future solutions. This makes it difficult to define upfront those vaccines for which field efficacy data would not be required, either by defining a set of criteria or by providing a list.

The introduction of uncertainties concerning data requirements should be avoided as much as possible. It may therefore be possible to approach the problem described above by defining or describing both the types of vaccines for which field efficacy data would not be required, as well as those for which field efficacy data would be required. In this way, it may not be possible to cover all future veterinary vaccines, but it would provide clarity in many cases. For any vaccines falling outside these categories, there is always the option to request scientific advice.

The revision of the guideline should encompass the following:

- To provide guidance for which vaccines/indications omission of efficacy clinical trials may be justified.
- To provide guidance for which vaccines/indications field efficacy data should be provided and the type of data required.

The revision of the position paper on indications for veterinary vaccines should provide clear guidance on how efficacy data, generated in the laboratory and/or in the field, is to be reflected in the product literature.

4. Recommendation

The Committee for Medicinal Products for Veterinary use (CVMP) recommends the Immunologicals Working Party (IWP) to revise the Note for guidance on field trials with veterinary vaccines, taking into account the issues identified above.

The guidance should be updated to clarify for which vaccines/indications applicants could be exempted from providing clinical efficacy data, apart from those vaccine types already exempted in the current

guidance. In addition, it is foreseen that guidance should be included for which vaccine indications clinical efficacy data would be required. In addition, the format of the guidance needs to be updated to the current standard e.g. guideline.

The Committee for Medicinal Products for Veterinary use (CVMP) also recommends the Immunologicals Working Party (IWP) to revise the position paper on indications for veterinary vaccines, following the update of the guidance on field trials with veterinary vaccines. The position paper should be updated to provide guidance on how efficacy data (in the presence or in the absence of field efficacy data) is to be reflected in the product literature. In addition, the format needs to be updated to a current standard (e.g. guideline, reflection paper) that needs to be defined.

5. Proposed timetable

29 January 2021	Concept paper released for consultation
31 March 2021	Deadline for comments from stakeholders
May 2021	Discussion in IWP
July 2021	Adoption of the draft guideline by CVMP and release for consultation
October 2021	Expected end of consultation
January 2022	Expected date for adoption by CVMP and publication of the guideline

It is expected that the guideline will come into operation earlier than six months after adoption, coinciding with the date of application of the veterinary medicines Regulation (EU) 2019/6 (28 January 2022).

6. Resource requirements for preparation

The revision of each of the existing guidance will involve the IWP (including a drafting group composed of rapporteur, co-rapporteur and 1-2 IWP members).

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

7. Impact assessment (anticipated)

It is anticipated that the guideline would provide clarity and predictability to both industry and regulators on the need to perform efficacy clinical trials. It would result in a more consistent assessment of efficacy data. The guidance should result in reduction of requirements and thereby reduce the use of resources for industry and contribute to the enhanced availability of vaccines.

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.

Annex to the Commission Delegated Regulation amending Annex II to Regulation (EC) No 2019/6 of the European Parliament and of the Council (draft published on 10 November 2020).

Note for Guidance on field trials with veterinary vaccines (EMEA/CVMP/852/00-FINAL).

Revised Position paper on indications for veterinary vaccines for veterinary vaccines (EMEA/CVMP/042/97-Rev.1-FINAL).

Report on the Focus Group meeting with invited stakeholders on field efficacy trials in the context of an EU authorisation for veterinary vaccines (EMA/405642/2017).