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Committee for Veterinary Medicinal Products (CVMP)

Concept paper for the revision of the Guideline on the requirements for combined vaccines and associations of immunological veterinary medicinal products (IVMPs) (EMA/CVMP/IWP/594618/2010)

Agreed by Immunologicals Working party	22 October 2024
Adopted by CVMP for release for consultation	5 December 2024
Start of public consultation	13 December 2024
End of consultation (deadline for comments)	13 March 2025

The proposed guideline will replace the guideline on the requirements for combined vaccines and associations of immunological veterinary medicinal products (IVMPs) EMA/CVMP/IWP/594618/2010.

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

Keywords	Veterinary vaccines, combined vaccines, association claims

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Introduction

The "Guideline on the requirements for combined vaccines and associations of immunological veterinary medicinal products (IVMPs)" (EMEA/CVMP/IWP/594618/2010) was adopted in July 2013 and came into effect on 1 February 2014. This document intends to outline items to consider in relation to marketing authorisation applications for combined vaccines and applications where an association between two or more different IVMPs, each with its own separate marketing authorisation, is claimed by the applicant. It provides guidance on the data requirements

- for combined vaccines

  - which are intended for immunisation against more than one disease **or**
  - which contain multiple strains of a causative agent of the same disease

- for the associated use of vaccines, administered

  - after mixing,
  - at the same time and different sites **or**
  - at different times and at different sites

This concept paper addresses the need to revise the guideline, which is based on the requirements of Directive 2001/82/EC. The focus of the revision of the guideline is to reflect current knowledge and the experience gained from the assessment of association claims ince the guideline first came into force in 2014, and to align with Regulation (EU) 2019/6.

1. Problem statement

It was agreed that the impact of the "Guideline on the requirements for combined vaccines and associations of immunological veterinary medicinal products (IVMPs)" should be assessed by the European Medicines Agency two years after coming into effect. This report should involve a consultation of the interested parties that provided comments. However, the proposed assessment of the impact of the guideline was not done up to now.

In recent years, the topic of combination and compatibility between vaccines was identified by stakeholders as one of their current main priorities. The stakeholders' foremost concern is the requirement to re-demonstrate efficacy claims for the associated use by additional studies requiring challenges. They consider this too demanding in regard to costs and efforts and not in line with 3Rs aspects. Furthermore, they claim to have developed an alternative approach, which focuses on the demonstration of absence of major interference on immune responses during associated use instead of demonstrating the efficacy of each antigen by challenge studies.

Therefore, the experience gained after use of the guideline shall be reflected in the revision and some requirements may be regarded defusable due to data (omission) acceptance in past applications. Also, the alternative approach proposed by stakeholders should be taken into consideration.

In addition, since the guideline came into force, the product range of recombinant live vector vaccines carrying one or more antigen inserts has been further developed by several applicants and the use of vector vaccines has increased considerably. These vector vaccines are often used as part of a vaccination schedule (e.g. in poultry) and their associated use with other vaccines of the schedule can raise special issues, which should be reflected in the revision of the guideline.

Vector vaccines are amenable to the use of vaccine platform technology master files (vPTMF). One question coming up during the authorisation procedures is, if, or under which conditions, data from earlier marketing authorisations (or data included in a vPTMF) can be taken into account for the assessment of association claims for a new vector vaccine based on the same vector platform or on a certified vPTMF.

2. Discussion (on the problem statement)

Based on the issues described above, the following points will be considered during the revision:

- Alignment to Regulation (EU) 2019/6.
- Content based amendments according to approaches accepted in past applications. (e.g. possible omission of data on duration of immunity, demonstration of efficacy based on serology).
- Reconsideration of some requirements (discontinuation of association claim in case of product changes, threshold requirements for follow-up markers to be *at least equal* to the threshold established for each individual IVMP).
- Considerations to association claims for vector vaccines, including those based on a certified vPTMF.
- Extrapolation of associated use claims from larger presentations (or from vector vaccines with more inserts) to smaller presentations (or to vector vaccines with less inserts).
- Inclusion of a summary table for easier overview.
- Definition of the requirements that have to be fulfilled for a (test-)parameter to qualify as marker of protection.
- Clarification on the wording for SPC and package leaflet in case alternatives to challenges are used for studies on associated use.

The goal of the revision is to allow the consideration of existing information on already authorised vaccines, wherever regarded supportive, but as well to still get meaningful assurance on the possible impact of different antigens on each other by suitably designed studies, whilst ensuring the safety and efficacy of combined vaccines or when IVMPs are used in association.

3. Recommendation

The Immunologicals Working Party (IWP) recommends revising the "Guideline on the requirements for combined vaccines and associations of immunological veterinary medicinal products (IVMPs)" (EMA/CVMP/IWP/594618/2010) to consider scientific and regulatory developments since the guideline came into effect as well as the experiences that were gained by the use of the guideline. The issues listed above shall be considered in the revision.

4. Proposed timetable

December 2024	Concept paper released for consultation
March 2025	Deadline for comments from stakeholders
Q4 2025	Adoption of the draft revised guideline by CVMP and release for consultation
Q2 2026	Deadline for comments from stakeholders

Q4 2026	Expected date for adoption by CVMP and publication of the revised guideline

5. Resource requirements for preparation

The revision of the guideline will involve the IWP (including a drafting group composed of rapporteur, co-rapporteur and 2-3 IWP members).

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

6. Impact assessment (anticipated)

The revision of the guideline is expected to benefit new applications, including variations for combined vaccines and/or vaccines with a claim of associated use, especially in case of vector-based vaccines. It is envisaged to provide clearer guidance on which information on associated use can be derived from other vaccines of the same vPTMF platform or from the corresponding vPTMF itself. Clearer guidance could result in a tailored data set on associated use to avoid superfluous studies and unnecessary use of animals (3R).

Overall, it is anticipated that the revision of the guideline will have a positive impact on the authorisation procedure of any new product with more than one antigen or with an association claim as well as on variations procedures for already authorised products of this kind, that will be submitted under the new legislation (Regulation 2019/6). It is expected that it will facilitate the submission and authorisation of veterinary vaccines (with more than one antigen or with an association claim) and to contribute to increased availability of veterinary vaccines, and thereby benefit public and animal health.

7. Interested parties

Veterinary pharmaceutical industry and consultants, EU regulatory authorities involved in assessment of marketing authorisation and variation applications.

References

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