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Committee for Veterinary Medicinal Products (CVMP)

Concept paper on the revision of the guideline on pharmaceutical fixed combination products (EMA/CVMP/83804/2005-Rev.1)

Agreed by Efficacy Working Party (EWP-V)	May 2026
Adopted by CVMP for release for consultation	16 July 2026
Start of public consultation	24 July 2026
End of consultation (deadline for comments)	31 October 2026

The proposed guideline will replace the current "Guideline on pharmaceutical fixed combination products" (EMA/CVMP/83804/2005-Rev.1).

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

Keywords	Veterinary medicinal products, fixed combinations, pharmaceuticals, combination packs

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1. Introduction

The CVMP guideline on pharmaceutical fixed combination products (EMA/CVMP/83804/2005) was initially adopted in December 2006. The last revision (Rev.1) was carried out in July 2021, with the purpose to implement administrative changes to update the guideline with the new definitions and terminology provided by Article 4 of Regulation (EU) 2019/6.

This concept paper addresses the need for a more thorough revision of the guideline, in line with Regulation (EU) 2019/6, the European Commission's Guidance to Applicants (C/2024/1443) and the CVMP guideline on the evaluation of the benefit-risk balance of veterinary medicinal products (EMA/CVMP/248499/2007-Rev.1). It also takes into consideration the experience gained in the assessment of data for fixed combination veterinary medicinal products. This experience has highlighted the need for further clarification and updating of certain aspects of the guideline to ensure alignment with current scientific knowledge and regulatory requirements.

2. Problem statement

The objective of the current guideline is to outline the conditions and clarify the data requirements for efficacy, safety and residues documentation for pharmaceutical veterinary medicinal products containing two or more active substances (so called "fixed combination products").

Although it is considered that the guideline is still relevant in most of its aspects, based on current scientific knowledge and regulatory experience certain sections would benefit from the inclusion of more detail to aid applicants in preparing applications and lead to a more predictable and consistent outcome, as detailed below.

The need to fully align the scientific content of this guideline with Regulation (EU) 2019/6 and the European Commission's Guidance to Applicants was identified. Furthermore, it should be ensured that the guideline remains in line with relevant CVMP guidance documents, such as the revised Guideline on the evaluation of the benefit-risk balance of veterinary medicinal products (EMA/CVMP/248499/2007-Rev.1) and Guideline on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.2), and takes account of the 3Rs principles (replacement, reduction and refinement).

Furthermore, it is noted that the existing 'Questions and answers on the CVMP guideline on pharmaceutical fixed combination products' document (EMA/CVMP/EWP/325284/2011-Rev.1) contains important clarifications and information on specific (antiparasitic) fixed combination products, which should be considered in the revised guideline.

3. Discussion (on the problem statement)

The wording of certain sections in the current version of the guideline is liable to misinterpretation, which can lead to confusion for applicants and regulators in relation to data requirements, and inconsistent decision making from a regulatory perspective. In particular, the guideline would benefit from revision of Section 6 - *Dossier requirement for combination products.*

The inclusion of meaningful examples in the guideline could aid in its consistent application, preventing potential misinterpretation and facilitating understanding of the terminology used. In particular, this would be useful in clearly identifying direct benefits and determining separately the additional benefits (if any) of these products.

While the guideline was updated (Rev.1) after Regulation (EU) 2019/6 came into force, this was solely an administrative update to align the regulatory content of the guideline with the new definitions and terminology provided by Article 4 of the Regulation. There are, however, some scientific concepts that still require alignment with Regulation (EU) 2019/6. In particular, in line with section IV.3.3 of Annex II to Regulation (EU) 2019/6, a sound justification based on valid therapeutic principles for the combination of active substances, including clinical data, shall be provided to demonstrate the need for and contribution of all active substances at the moment of treatment. The corresponding information in the guideline should be updated to better reflect these requirements.

One of the key points for discussion will be in relation to the justification of the combination and the current provision (in section 4 of the guideline) that a fixed combination product can only be justified if such a combination offers an advantage over its active substances, when used as single substance products. This aspect requires review and amendment to ensure that the guideline reflects current legislation.

Following the implementation of Regulation (EU) 2019/6 and as outlined in the European Commission's Guidance to Applicants, veterinary medicinal products that have been authorised under Article 20 (i.e. combination veterinary medicinal products) can be used as reference products in a generic/hybrid application. Therefore, the guideline would benefit from the inclusion of further information and clarification on the documentation to be presented by applicants in support of fixed combination products submitted as generic or hybrid applications.

In addition, it is intended to update the guideline in accordance with European Commission's Guidance to Applicants and provide further clarification where necessary. For instance, it is noted that at present, in relation to combination packs, the information in the European Commission's Guidance to Applicants and the CVMP guideline on fixed combination products is not consistent. This requires review and amendment of the guideline to ensure clarity for applicants and regulators alike.

Currently, the guideline is primarily focused on the positive aspects of fixed combinations. Nevertheless, the 'Guideline on the evaluation of the benefit-risk balance of veterinary medicinal products' (EMA/CVMP/248499/2007-Rev.1) includes some statements related to the potential risks of fixed combination products. It is intended that these risks are also addressed in the revised guideline to ensure a more complete view of the benefit-risk assessment.

In accordance with Annex II of Regulation (EU) 2019/6, all experiments on animals should be conducted in accordance with the 3Rs principles (replacement, reduction and refinement) as laid down in Directive 2010/63/EU on protection of animals used for scientific purposes, and the guideline should be updated to reflect this aspect.

In this regard, it is noted that the CVMP guideline on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.2) has been updated to reflect the 3Rs principles, providing options in the interest of reducing testing requirements in animals. The necessity to test the final formulation to justify the safety for the user has been reviewed for fixed combination products. Therefore, the guideline should be updated in line with these amendments.

Finally, the information included in 'Questions and answers on the CVMP guideline on pharmaceutical fixed combination products' document (EMA/CVMP/EWP/325284/2011-Rev.1) will be taken into consideration for the revision and incorporated into the guideline as necessary.

4. Recommendation

The CVMP recommends the revision of the existing guideline on pharmaceutical fixed combination products to provide clearer guidance and to align the guideline with current scientific and regulatory requirements, taking into account the considerations outlined above.

5. Proposed timetable

July 2026	Concept paper released for public consultation
31 October 2026	Deadline for comments from interested parties
Q2 2027	Expected date for adoption of the draft revised guideline by CVMP for release for consultation
Q4 2027	Expected end of consultation on the draft revised guideline
Q2 2028	Expected date for adoption by CVMP and publication of the revised guideline

6. Resource requirements for preparation

Revision of the guideline will involve a number of rapporteurs and co-rapporteurs from EWP-V and SWP-V, as appropriate.

Preparation of the draft revised guideline will require discussion at several EWP-V and SWP-V plenary meetings. Drafting group meetings (virtual) will be organised, as needed.

7. Impact assessment (anticipated)

The revision of the guideline is expected to improve the guidance for applicants as well as for regulatory authorities. It is not intended to increase the requirements for marketing authorisation applications for such veterinary medicinal products.

8. Interested parties

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

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

European Commission’s Guidance to Applicants (C/2024/1443)

Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes

Guideline on the evaluation of the benefit-risk balance of veterinary medicinal products (EMA/CVMP/248499/2007-Rev.1)

Questions and answers on the CVMP guideline on pharmaceutical fixed combination products document (EMA/CVMP/EWP/325284/2011-Rev.1)

Guideline on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.2)