



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 8 December 2016
2 EMA/CVMP/EWP/707573/2015
3 Committee for Medicinal Products for Veterinary Use (CVMP)

4 **Concept paper on the revision of the guideline for**
5 **veterinary medicinal products for zootechnical purposes**
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Agreed by the CVMP's Efficacy Working Party (EWP-V)	September 2016
Adopted by the Committee for Medicinal Products for Veterinary Use (CVMP) for release for consultation	8 December 2016
Start of public consultation	16 December 2016
End of consultation (deadline for comments)	31 March 2017

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9 The proposed guideline will replace the "Guideline for veterinary medicinal products for zootechnical
10 purposes" ([NtA Volume 7, 7AE7a](#)).

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12 Comments should be provided using this [template](#). The completed comments form should be sent
to vet-guidelines@ema.europa.eu

Keywords	veterinary medicinal products for zootechnical purposes, embryos transfer, oestrus synchronisation, fixed time artificial insemination
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1. Introduction

The current guideline for veterinary medicinal products for zootechnical purposes (7AE7a) was adopted in March 1992 and came into force in September 1992. The guideline concerns the documentation of the efficacy of zootechnical products and in particular the conduct of clinical trials in the target animal. The guideline gives the following definition of a veterinary medicinal product for zootechnical purposes: a product applied to a healthy animal for non-pathologic, i.e. non therapeutic claims to: synchronise oestrus, terminate unwanted gestation, prepare donors and recipients for the implantation of embryos, and improve fertility. The guideline therefore concerns, essentially, products active on the reproductive system (see also Directive 96/22/EEC, article 1(2)(c)).

Products applied to a healthy animal in order to influence favourably the yield and/or quality of animal produce and/or nutritional efficiency and/or growth of the animal are not covered in this guideline; for those products, the guideline on performance enhancers should be followed (7AE6a, 1991).

2. Problem statement

Overall, the recommendations included in the existing guideline are still relevant. Based on regulatory experience it is observed that the recommendations are not sufficiently detailed regarding requirements for the conduct of the studies according to current quality standards (Good Clinical Practices / Good Laboratory Practices), number of laboratory/field trials, design of the trials, etc.). Also, the requirements are not related to the type of product or of claimed indication.

Moreover, in 2015 the CVMP, through EWP-V, answered a question from the CMDv about the necessity and acceptability of adding oestrus synchronisation protocols onto Summary of Product Characteristics (SPCs) of cattle hormonal products. The discussion around this issue highlighted a need for harmonized requirements for the addition of protocols to product literature.

Given that veterinary medicinal products for zootechnical purposes have no therapeutic benefit, particular attention should be given to the justification that the target animal safety and welfare are not adversely affected by the use of the product. The text may also benefit from clarification on the different parameters to be considered when designing the trials that will permit to confirm this aspect.

Furthermore, the guideline should be modified considering the more recent reference to GCP (*i.e.* VICH GL9 adopted by CVMP in 2000) and adapted according to the revised guideline on statistical principles for veterinary clinical trials (EMA/CVMP/EWP/81976/2010).

3. Discussion (on the problem statement)

Considering the need for requirements for oestrus synchronisation protocols, where the concerned VMP is used in combination with other active substances and for fixed time artificial insemination, EWP considered that protocols should be only mentioned in section 4.9 of the product literature (SPC) and that they have to be supported by appropriate data e.g. peer reviewed literature or own clinical studies. Such recommendations could be included in the revised guideline. The extent to which the efficacy of such protocols that are mentioned in the SPC should be documented, has to be specified in more detail and the possibilities of extrapolation between different formulations and molecules of the same class should be addressed.

Preclinical trials on target animal pharmacology (and in particular pharmacokinetic studies)

The recommendations on this part of the current guideline should be further detailed with a reference to the Guidelines for the conduct of pharmacokinetic studies in target animal species (EMA/CVMP/133/99).

Dose determination studies and clinical trials

It is recommended to conduct clinical studies according to GLP and/or GCP. If GLP and/or GCP are not applied, the traceability and integrity of data should be adequately guaranteed by other means. For clinical field trials, GCP status is required. Statistical principles for veterinary clinical trials should be followed (see guideline CVMP/EWP/81976/2010). The guideline should be therefore updated with regard to current requirements on conduct of clinical studies.

The guideline should also be expanded based on the experience gained from recently authorized products. The minimum data necessary to obtain a claim should be indicated: dose determination, treatment regimen determination, and dose confirmation under laboratory and/or field conditions.

Regarding target animal safety demonstration through clinical trials, the requirements in the current guideline are not detailed enough and more guidance should be provided on the different parameters that have to be considered and reported to confirm the clinical safety of the product.

4. Recommendation

The CVMP recommends the revision of the existing guideline in order to provide clearer guidance on the conduct of preclinical and clinical studies, in particular for oestrus synchronisation protocols, and for the aspects to be considered in regard to target animal safety and welfare. Also, the guideline should be updated in line with current quality standards (GCP, GLP) and current regulatory documents.

5. Proposed timetable

8 December 2016	Concept paper adopted by CVMP for release for consultation
31 March 2017	Deadline for comments from interested parties
Q2-Q3 2018	Expected date for adoption of the revised guideline by EWP-V
Q3-Q4 2018	Expected date for adoption of the revised guideline by CVMP for release for consultation

6. Resource requirements for preparation

Preparation of the revision would involve one rapporteur assisted by co-rapporteur(s).

Preparation of the draft guideline will require discussion at EWP-V plenary meetings, and drafting group meetings (virtual), 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 usual requirements for veterinary dossiers.

8. Interested parties

Veterinary pharmaceutical industry and consultants

Regulatory authorities

- 90 Veterinary organisations, e.g. Federation of Veterinarians of Europe (FVE)
- 91 Scientific veterinary associations, e.g. European Society for Domestic Animal Reproduction (ESDAR)
- 92 **9. References to literature, guidelines, etc.**
- 93 CVMP guideline on statistical principles for veterinary clinical trials (CVMP/EWP/81976/2010)
- 94 Directive 96/22/EEC concerning the prohibition on the use in stockfarming of certain substances having
95 a hormonal or thyrostatic action and of beta-agonists and repealing Directives 81/602/EEC,
96 88/146/EEC and 88/299/EEC
- 97 Good Laboratory Practice (GLP) (see Council Directive 88/320/EEC as amended)
- 98 Guideline for Veterinary Medicinal Products for Zootechnical Purposes (NtA Volume 7, 7AE7a)
- 99 *'Should regulatory authorities be accepting the addition of oestrus synchronisation protocols onto SPCs*
100 *of cattle hormonal products?'* (EMA/CVMP/EWP/41051/2015-final)
- 101 VICH guideline 9 (GL 9): Good Clinical Practice (CVMP/VICH/595/1998)