EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper for the revision of the CVMP guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2)

Agreed by Efficacy Working Party (EWP-V)	February 2016
Adopted by CVMP for release for consultation	21 April 2016
Start of public consultation	29 April 2016
End of consultation (deadline for comments)	31 July 2016

The proposed guideline will replace the current guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2).

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

Keywords	pharmacokinetics, generic veterinary medicinal product, acceptance limits, biowaiver, *in-vitro* dissolution test, bioequivalence

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1. Introduction

The current CVMP guideline for the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2) was first adopted in January 2001 and revised in April 2011. The objective of the guideline is to specify requirements for the design, conduct and evaluation of bioequivalence studies for pharmaceutical forms with systemic action, and in addition to give guidance on how *in vitro* data in specific cases may be used to allow bridging of safety and efficacy data.

In November 2015, the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Steering Committee adopted a new VICH guideline, VICH GL52 Bioequivalence: blood level bioequivalence study (EMA/CVMP/VICH/751935/2013), which comes into effect in the EU in August 2016. This guideline is intended to harmonise the data requirements associated with *in vivo* blood level bioequivalence (BE) for veterinary pharmaceutical products and provides internationally agreed guidance that may supersede the existing European guidance. Consequently, there is a need to review the current CVMP guideline.

2. Problem statement

The revision of guideline EMA/CVMP/016/00-Rev.2 is considered necessary to ensure consistency with the new VICH GL52 where the current CVMP guideline addresses issues also addressed in VICH GL52. The revision will therefore concern the following topics:

- A harmonised definition of bioequivalence, as agreed by the VICH.
- Recommendations for study design, conduct and evaluation of bioequivalence studies:

Most of guidance given VICH GL52 is the same as in the current CVMP guideline. The concerned text will remain unchanged in the new revision of the CVMP guideline.

For any identified difference in the recommendations between both VICH GL52 and CVMP guideline (e.g. GLP/GCP status of the studies, choice of the reference product, criteria of data exclusion from analysis, prandial state, acceptance criteria for area under the concentration curve (AUC) and the concentration at peak (C_{max}), more clarity should be provided in the foreseen revision of the CVMP guideline.

Overall, as the VICH requirements prevail, the text of the CVMP guideline will be adapted to the international recommendations.

Where VICH GL52 contains more details on specific points (e.g. situations where the parallel design is preferred, alternative study designs, nonlinear kinetics and dose selection, sample size determination) than the current CVMP guideline that can be useful for the applicants, the CVMP guideline will be extended to include such information, or cross-reference to the VICH guideline will be made.

On the contrary, when the current CVMP guideline gives more elaborated guidance regarding the study design, conduct and evaluation of bioequivalence studies that is not contradictory to the VICH guideline, the text should remain unchanged.

Considering other topics/areas addressed in the current CVMP guideline, but not in the VICH GL52, the text will remain unchanged.

3. Discussion (on the problem statement)

Given that the definition of bioequivalence should be updated, and that recommendations for study design, conduct and evaluation of bioequivalence studies are in some aspects either redundant, different or insufficient in the current CVMP guideline compared with VICH GL52, there is a need for revision. Topics that are not addressed in VICH GL52 and already included in the current CVMP guideline are not expected to be affected by the revision.

4. Recommendation

The CVMP recommends revising the CVMP guideline on conduct of bioequivalence studies EMA/CVMP/016/00-Rev.2 as appropriate to ensure consistency with VICH GL52 Bioequivalence: blood level bioequivalence study (EMA/CVMP/VICH/751935/2013).

5. Proposed timetable

April 2016	Concept paper adopted by CVMP for release for consultation
July 2016	Deadline for comments from interested parties
3-4 Q 2017	Expected adoption of the revised draft guideline by EWP-V
4Q 2017-1Q 2018	Expected date for adoption of the revised draft 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 revised CVMP guideline will require discussion at EWP-V plenary meetings, and drafting group meetings (virtual), as needed.

7. Impact assessment (anticipated)

The revised CVMP guideline is not intended to increase the requirements for marketing authorisation applications. The review and update of the current CVMP guideline for the conduct of bioequivalence studies for veterinary medicinal products to bring it in line with VICH GL52, will help to bring clarity and consistency in relation to the standards to be applied.

8. Interested parties

Veterinary pharmaceutical industry and consultants.

Regulatory authorities.

Scientific veterinary associations, e.g. European College of Veterinary Pharmacology and Toxicology.

9. References to literature, guidelines, etc.

CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2).

VICH GL52 Bioequivalence: blood level bioequivalence study (EMA/CVMP/VICH/751935/2013 – Corr.).