EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Veterinary Medicinal Products (CVMP)

Question and answer document on requirements for pre-clinical studies submitted in support of a marketing authorisation application for a veterinary medicinal product

Background

Section I.1.6. (General requirements) of Annex II to Regulation (EU) 2019/6 (as amended by Commission Delegated Regulation (EU) 2021/805) states that:
"*Pharmacological, toxicological, residue and **pre-clinical studies** shall be carried out in conformity with the provisions related to Good Laboratory Practice (GLP) laid down in Directives 2004/10/EC and 2004/9/EC of the European Parliament and of the Council"*.

Question 1:

Which pre-clinical studies conducted in support of an application for a veterinary medicinal product are required to comply with good laboratory practice (GLP)?

Answer:

The CVMP interprets the provision in section I.1.6. to mean that pharmacological, toxicological, residue and pre-clinical ***safety*** studies shall be carried out in conformity with the provisions related to Good Laboratory Practice (GLP) laid down in Directives 2004/10/EC and 2004/9/EC of the European Parliament and of the Council.

Rationale:

Directives 2004/9/EC[1] and 2004/10/EC[2] restrict the GLP requirements to non-clinical **safety** studies with respect to human health and/or the environment.

Recital (2) of the preamble to Directive 2004/9/EC also considers "*the application of standardised organisational processes and conditions under which laboratory studies are planned, performed, recorded and reported for the non-clinical testing of chemicals for the **protection** of man, animals and the environment."*

[1] Directive 2004/9/EC on the inspection and verification of GLP
[2] Directive 2004/10/EC on harmonisation of laws, regulations and administrative provisions relating to the application of the principles of GLP and the verification of their applications for tests on chemical substances

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Question 2:

What are the requirements for pre-clinical efficacy studies submitted in support of applications for veterinary medicinal products other than biologicals (i.e. pharmaceuticals)?

Answer:

In general, pre-clinical efficacy studies should be conducted in a manner that assures the reliability of the data generated, and should be performed according to validated and internationally accepted methods. Commission Delegated Regulation (EU) 2021/805, 'Annex II', section I.2.4. Part 4 provides general principles and requirements as regards to efficacy documentation:

"(5) All efficacy trials shall be conducted in accordance with a fully considered detailed protocol, which shall be recorded in writing prior to commencement of the trial. The welfare of the trial animals shall be subject to veterinary supervision and shall be taken fully into consideration during the elaboration of any trial protocol and throughout the conduct of the trial."

For some pre-clinical efficacy studies that are generally conducted in a laboratory environment, study conditions have been described in relevant guidelines (e.g. CVMP guideline for the demonstration of efficacy for veterinary medicinal products containing antimicrobial substances (EMA/CVMP/627/2001), CVMP guideline on the conduct of pharmacokinetic studies in target animal species (EMA/CVMP/133/1999), CVMP guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000), VICH GL52 Bioequivalence: blood level bioequivalence study (EMA/CVMP/VICH/751935/2013), VICH GL43 Target animal safety for veterinary pharmaceutical products (EMEA/CVMP/VICH/393388/2006)).

In the absence of detailed CVMP guidance for other types of pre-clinical efficacy studies, it is recommended that they should follow the requirements for Good Clinical Practice (GCP) and/or Good Laboratory Practice (GLP), as appropriate (depending on the nature of the studies). In case GCP and/or GLP is not applied (e.g. absence of certified GLP status), traceability, accuracy, integrity and correctness of data should be ensured, and the use of such data in pivotal studies should be justified.

Data in support of the dosing regimen were already required in support of dossiers submitted under Directive 2001/82/EC; however, the new Annex II of Regulation (EU) 2019/6 has now introduced a specific section on "dose determination and/or dose confirmation" in the "pre-clinical section". These studies can be performed under experimental (laboratory) conditions or under field conditions.

As outlined in the CVMP guideline on statistical principles for clinical trials for veterinary medicinal products (pharmaceuticals) (EMA/CVMP/EWP/81976/2010), confirmatory trials including dose determination and dose confirmation studies should be conducted in conformity with the VICH GL9 (Good Clinical Practice). However, exceptions to this general rule to comply to GCP will occur, for example, where a bioequivalence or other pharmacokinetic study is used for the purposes of dose determination or confirmation, or for the analytical part of a study only. In such cases, compliance with the principles of GLP would be considered to be appropriate (see also relevant guidelines for such studies).