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SCIENCE MEDICINES HEALTH

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Committee for Veterinary Medicinal Products (CVMP)

Concept paper on the revision of the guideline on dossier requirements for anticancer medicinal products for dogs and cats

Agreed by Efficacy Working Party (EWP-V)	June 2024
Adopted by CVMP for release for consultation	18 July 2024
Start of public consultation	26 July 2024
End of consultation (deadline for comments)	31 October 2024

The proposed guideline will replace the current 'CVMP guideline on dossier requirements for anticancer medicinal products for dogs and cats' (EMA/CVMP/28510/2008-Rev.1).

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

Keywords	*Cancer, companion animals, (non) cytotoxic substances, chemotherapy*

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

1. Introduction

The CVMP guideline on dossier requirements for anticancer medicinal products for dogs and cats (EMA/CVMP/28510/2008) was initially adopted by the CVMP in 2009. The guideline outlines the conditions and data requirements for the demonstration of quality, safety (user, environmental, target animal), and efficacy of anticancer veterinary medicinal products used in dogs and cats.

So far, four anticancer veterinary medicinal products have been authorised by the centralised procedure (three for dogs and one for cats). Currently, there are no anticancer veterinary medicinal products authorised via the decentralised procedure.

Although the CVMP encourages the authorisation of anticancer products for veterinary use, and though it is expected that interest for anticancer products (in particular for dogs and cats) is increasing, there were no changes to the scientific content of the guideline since its development in 2009 (NB the guideline was revised in 2021 (Rev. 1) to align it to 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, focusing on the scientific content.

2. Problem statement

The objective of the current guideline is to outline the data requirements for the demonstration of quality, safety (user, environmental, target animal), and efficacy of anticancer veterinary medicinal product used in dogs and cats.

In general, most of the recommendations included in the existing guideline are still relevant. However, following recent experiences during the authorisation procedures of anticancer veterinary medicinal products, the need to revise the current guideline (in particular with regards to quality, user safety, target animal safety and efficacy data requirements) was recognised. Some sections are not considered sufficiently detailed (i.e. use of several definitions, such as cytotoxicity), whilst other sections require updating by focussing more clearly on the regulatory nature of this guideline (i.e. executive summary, introduction, scope).

Also, the scope of the guideline, which currently appears to focus primarily on previously known active substances, will be reconsidered. Whereas the current guideline focuses on the development for veterinary use of chemotherapeutic substances used in human medicine, it is considered appropriate that the guideline should be revised to take account of the development of all chemotherapeutic products intended for veterinary use.

In addition, given the nature of these products, it is considered appropriate to review the suitability and appropriateness of currently recommended risk mitigation measures and warnings to ensure such guidance reflects experience gained in the use of such products in the veterinary field. Furthermore, it is considered appropriate to review the guidance provided for substances that are intended to be used as part of a protocol as opposed to administration as a single chemotherapeutic agent.

Moreover, as several other related guidelines have been revised in recent years, consistency with these guidelines should be ensured. Finally, it is noted that the guideline does not make specific reference to 3Rs principles.

3. Discussion (on the problem statement)

The need for a thorough revision of this guideline was identified. In particular, the 'Introduction (background)" section requires an update. This section currently provides very detailed background information. However, this level of detail is considered unnecessary for the purpose of a guideline. The 'Introduction (background)" section should instead provide a short description of relevant information regarding the development of this particular guideline, as well as to inform about the purpose and content of the guideline.

The 'Executive summary' should focus on providing a short summary of relevant information (including reference to the disease and therapy), including a short description of the information that will be outlined in the following sections (which is now placed under the 'scope' of this guideline).

With regards to the section 'Scope', whilst the guideline has been specifically written with dogs and cats in mind, the principles and approaches outlined may be extrapolated to other companion animal species where appropriate. Also, the current guideline appears to focus primarily on the situation where a previously known active substance, for which data on the mode of action and off-target toxicity are already available and documented according to CHMP guidelines, is developed for veterinary use. However, as the anticancer veterinary medicinal products authorised during the last years were not previously documented according to CHMP guidelines, that is they were not 'known', guidance for new active substances that are not yet documented should be included. The 'Scope' should be updated to include potential new active substances as well.

It is also considered appropriate that the guideline is updated to include reference to the 3Rs principles (replacement, reduction and refinement) when designing/conducting relevant studies.

The **quality** documentation (Part 2) will be reviewed to ensure compliance with the requirements of Annex II of Regulation (EU) 2019/6. The need for further guidance would also be considered in relation with the scope of the revised guideline.

It is considered that the **safety** documentation (Part 3) will need to be amended to reflect the current guidelines on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.1 and EMA/CVMP/SWP/721059/2014) where appropriate, including harmonisation of the terminology relating to user risk assessment. Moreover, it is intended to update the safety documentation section based on the current insights and knowledge/experiences gained, including to delete information which is already covered in the guidelines on user safety.

As for the **efficacy** documentation (Part 4), some sections would benefit from revision in order to better clarify the guidance provided and several sections could benefit from the addition of (sub)headings (such as a separate section on 'resistance'), others from subdivision of the information presented (e.g. section on pharmacological data). Improvements and clarifications on terminology, such as reference to target animal 'tolerance' or 'safety', could also be implemented. Some of the content currently included in the introduction would be more suitably located in the efficacy section of the guideline, such as the information on cytotoxic/non-cytotoxic compounds in particular. Also, based on regulatory experience, the paragraph describing these terms is considered to require some rewording. Additional guidance could also be helpful when deviation from some of the requirements is necessary. In certain unconventional products, such as products intended for intratumoural use, current requirements for dose escalation and dose finding are not considered appropriate.

In addition, in light of experience gained to date, it is considered appropriate to review the current guidance for substances intended to be administered as part of a treatment protocol and consider what, if any, updates to the guidance might be required.

Ultimately, the need for further guidance would also be considered in relation with the scope of the revised guideline.

4. Recommendation

The CVMP recommends the revision of the existing guideline on dossier requirements for anticancer medicinal products for dogs and cats in order to provide clearer guidance and to align the guideline with current scientific and regulatory requirements, taking into account the issues identified above.

5. Proposed timetable

July 2024	Concept paper released for public consultation
31 October 2024	Deadline for comments from interested parties
Q3/Q4 2025	Expected date for adoption of the draft revised guideline by CVMP for release for consultation
Q1/Q2 2026	Expected end of consultation on the draft revised guideline
Q2/Q3 2026	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, QWP and SWP-V, as appropriate.

In addition, the preparation of the draft revised guideline will require discussion at several EWP-V, QWP 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, e.g. Federation of Veterinarians in Europe (FVE).
- Veterinarians in oncology practice.
- Scientific veterinary associations, e.g. European College of Veterinary Internal Medicine-Companion Animals (ECVIM-CA).

9. References to literature, guidelines, etc.

CVMP Guideline on dossier requirements for anticancer medicinal products for dogs and cats (EMA/CVMP/28510/2008-Rev.1)

Oncology Focus Group Meeting – minutes of the meeting, 25 April 2007 (EMEA/CVMP/EWP/180579/2007)

CHMP Guideline on the clinical evaluation of anticancer medicinal products (EMA/CHMP/205/95 Rev.6)