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Veterinary and Inspections Unit

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON THE REVISION OF THE GUIDELINE ON USER SAFETY FOR PHARMACEUTICAL VETERINARY MEDICINAL PRODUCTS

AGREED BY SAFETY WORKING PARTY	April 2008
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	17 April 2008
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 May 2008

The proposed guideline will replace guideline EMEA/CVMP/543/03-FINAL

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1. INTRODUCTION

Council Directive 2001/82/EC as amended by 2004/28/EC, establishes the requirement for user safety to be evaluated. Annex I, states that

The safety documentation shall show:

1. *the potential toxicity of the medicinal product and any dangerous or undesirable effects which may occur under the proposed conditions of use in animals, these should be evaluated in relation to the severity of the pathological condition concerned.*

Details of the documentation required are given in the Notice to Applicants Volume 6B and the CVMP Guideline on User Safety [EMEA/CVMP/543/03-FINAL] was adopted in July 2005.

2. PROBLEM STATEMENT

Background

A presentation on Industry's perspective of the Guideline on User Safety given at the EMEA/IFAH-Europe Info Day in November 2006, raised concerns that certain aspects of the guideline needed clarification.

CVMP agreed Industry's request for a meeting to discuss the Guideline on User Safety and a focus group meeting was arranged in December 2007. The meeting was attended by expert representatives from the Committee for Medicinal Products for Veterinary Use (CVMP), its Safety Working Party (SWP-V), and the veterinary pharmaceutical industry as well as members of the EMEA secretariat. The meeting discussed the concerns raised and a report was made at the EMEA/IFAH-Europe Info Day in March 2008.

In preparation for the focus group meeting industry representatives had circulated documentation highlighting the areas of the guideline that they wished to focus on. This documentation was used to structure the discussions. Industry representatives presented each issue in turn, providing further explanations where appropriate and the CVMP/SWP-V experts asked questions to clarify the concerns. The exchange of information was constructive and will provide a basis for the revision of the guideline.

The CVMP agreed that the guideline should be revised and requested the SWP-V to prepare the concept paper for the revision of this guideline.

3. DISCUSSION (on the problem statement)

The key points of discussion that will form the basis of the revision are:

- **Scope**: clarification of the scope of the guideline and that user risk assessments are on final formulations and are not required for safety during manufacture
- **Principles of assessment**: review of the order given in the guideline for the risk assessment process (i.e. exposure assessment followed by hazard identification and characterisation followed by risk characterisation followed by risk management) and consideration of introducing different terminology (such as elements rather than steps) to avoid the indication that there is an "order" to follow; clarify the types of exposure scenarios that should be considered and also clarify the use of data from chronic or acute studies
- **Professional and non-professional users**: revision of the distinctions between professional and non-professional users and the assumption that professional users are expected to read the package insert, but non-professional users are not.
- **The likelihood of exposure**: clarification of "likelihood of exposure".

- **The rate, extent, duration, interval and frequency of exposure**: revise the reference to Directive 93/67/EEC and the Technical Guidance Document (TGD) published in support of the directive and include relevant exposure models and consider additional details in an annex to the guideline; clarification of the reference to "the 95th percentile of the distribution".
- **Hazard identification and characterisation**: clarification of the amount of data and types of studies required and how they need to relate to the degree and type of user exposure anticipated; consideration of the OECD stepwise process (as per OECD guidelines for dermal and ocular toxicity).
- **Qualitative risk characterisation and Quantitative risk characterisation**: revision to include a worked example of how risk characterisation could be performed

To also consider comments, suggestions and information collected from the discussions at the EMEA/IFAH-Europe Info Day in March 2008 and from the consultation exercise.

4. RECOMMENDATION

To revise the current guideline to address the points above.

5. TIMETABLE

Proposed draft timetable. There has already been consultation with interested parties in the form of a focus group meeting in December 2007 and a presentation and discussion at the 2008 EMEA/IFAH-Europe Info Day, which was also attended by other interested parties. The standard consultation period has therefore been reduced from 2 months to 1 month for the concept paper and a reduced consultation period of 4 months is proposed for the revised guideline.

April 2008	Adoption of Concept paper by CVMP for release for 1 month consultation
November 2008[1]	CVMP to discuss/adopt draft revised guideline drafted by SWP-V. Draft revised guideline to be released for 4 months consultation
April 2009	SWP-V to start reviewing the comments and revise guideline
September 2009[1]	CVMP final adoption

6. RESOURCE REQUIREMENTS FOR PREPARATION

The SWP-V to revise the guideline

7. IMPACT ASSESSMENT (Anticipated)

Impact assessment for Regulatory Authorities
For Regulatory Authorities the proposed revision of the guideline would clarify the procedure and data requirements for user risk assessments for marketing authorisation applications and would thus facilitate the evaluation of applications.

Impact assessment for Industry and other Interested Parties
For industry and other interested parties, the proposed revision of the guideline would clarify the procedure and data requirements for user risk assessments for marketing authorisation applications.

8. INTERESTED PARTIES

[1] The adoption may be earlier, dependant on whether 1 or 2 SWP-V meetings are necessary for revision and /or review of comments

Regulators, veterinary medicines industry, consumer associations.

9. REFERENCES TO LITERATURE, GUIDELINES ETC

CVMP Guideline on User Safety for Pharmaceutical Veterinary Medicinal Products [EMEA/CVMP/543/03-FINAL]

Council Directive 2001/82/EC as amended by 2004/28/EC

The Rules Governing Medicinal products in the EU; Volume 6B, Notice to Applicants, VMPs Presentation & Contents of the Dossier.