European Medicines Agency
Veterinary Medicines and Inspections

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FOCUS GROUP MEETING ON USER SAFETY GUIDELINE

REPORT OF THE MEETING HELD ON 13 DECEMBER 2007

Background and introduction

The meeting was arranged to discuss concerns raised by industry relating to the Guideline on User Safety for Pharmaceutical Veterinary Medicinal Products (EMEA/CVMP/543/03-FINAL). In particular, the view had been expressed that certain sections of the guideline need clarification. Additionally, there was the desire to produce a report from the focus group meeting that could be shared with a wider audience. 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.

In preparation for the 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. The CVMP/SWP-V experts then asked questions to clarify the concern, and provided explanations for the wording used in the guideline. This exchange was very useful to both parties.

The key points of discussion and agreement are reported below and follow the numbering used in the guideline.

Sections 1 and 2 – Introduction and Scope

The scope of the guideline was discussed as this provided a good basis for later discussions on specific elements of the guideline. Industry representatives had no major issues with these two sections but clarified that it should be clear to all that the user safety assessment should be limited to the final product and not to safety during manufacture.

Section 3 - Principles of assessment

Industry representatives asked the CVMP/SWP-V experts to clarify the reasoning for 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). CVMP/SWP-V experts explained that the guideline deliberately starts with ‘exposure assessment’ because if there is no exposure there is no need to perform a risk characterisation. It was emphasised that the guideline is intended for the assessment of the final product, and is not meant to apply to the product development programme. It was suggested that the guideline could refer to ‘elements’ in the assessment process rather than ‘steps’, and that the guideline could avoid indicating an order in which to examine these elements. It was noted that there is no requirement in the legislation to perform any exposure studies.

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The second paragraph of this section specifies that "all relevant exposure scenarios should be considered". It was agreed that some further explanation could be provided to clarify the types of exposure scenarios that should be considered.

The third paragraph of this section talks about comparing the exposure levels to which the user may be exposed to those at which no adverse effects are expected to occur. There was a short discussion over whether data from chronic or acute studies are appropriate for this purpose, and it was agreed that some further text could be added to clarify the issue.

Section 3.1 - Professional and non-professional users

The guideline states that while professional users can be expected to read the package insert, the same cannot be expected of non-professional users. There was some discussion of the validity of this assertion. It was agreed that while it was important to make a distinction between professional and non-professional users, the existing assumptions about who will and who will not read the insert cannot be supported.

Section 4.3.4 - The likelihood of exposure

Industry representatives felt that the guideline is not clear about what is meant by "likelihood of exposure" – are companies expected to provide specific probabilities of exposure or only a more semi-quantitative assessment? The CVMP/SWP-V experts clarified that a numerical value is not expected and that the aim was to determine only whether exposure would be frequent or rare, and that this information can be used to establish whether the relevant toxicological data should be drawn from acute or chronic studies. CVMP/SWP-V experts agreed that some further detail could be provided to clarify this.

Section 4.3.5 - The rate, extent, duration, interval and frequency of exposure

This section makes reference to Directive 93/67/EEC and the Technical Guidance Document (TGD) published in support of the directive. Industry representatives argued that while the TGD may include some useful exposure models, much of the document is not relevant to veterinary medicinal products and it would be more helpful to directly identify the relevant models and possibly include additional details in an annex to the guideline.

The fourth paragraph of this section refers to the 95^{th} percentile of the distribution. Industry representatives asked for clarification on how CVMP wanted this applied, as there are many 'distributions' for various safety parameters that could be considered. The CVMP/SWP-V experts responded that this refers to the computer models that produce a distribution and agreed that this could be clarified in the guideline.

Section 5 - Hazard identification and characterisation

CVMP/SWP-V experts clarified that this section aims to explain that the amount of data and types of studies provided will need to relate to the degree and type of user exposure anticipated. For example, if there is no anticipated exposure by a particular route then there is no need to perform studies with administration by that particular route. On the other hand, if there are two possible routes of exposure then studies using each of those routes may be appropriate. It was agreed that the text could be amended to provide clarification on this point. Industry representatives also suggested that there should be consideration of the OECD stepwise process (as per OECD guidelines for dermal and ocular toxicity).

Sections 6.1 and 6.2 - Qualitative risk characterisation and Quantitative risk characterisation

Industry representatives suggested that a worked example of how risk characterisation could be performed would be useful. The CVMP guideline Environmental Impact Assessment for Veterinary Medicinal Products in support of the VICH guidelines GL6 (Phase I) and GL38 (Phase II) (EMEA/CVMP/ERA/418282/2005corr) was considered to provide a good example of guidance on work flow, as were a number of CVMP pharmacovigilance guidelines. Additionally, it was noted that in the Guideline on User Safety, section 8 (Risk Communication) provides a good example of a bullet point list used to illustrate requirements.

Conclusion of the focus group meeting

The CVMP/SWP-V experts agreed that they would report back to CVMP, recommending that the guideline should be revised. This would be discussed at the January 2008 CVMP meeting and, if the CVMP agrees to a revision, the CVMP Safety Working Party will start work on this project at its meeting at the end of January 2008.

It was noted that a report of the meeting and its conclusions would be presented at the Infoday scheduled for March 2008. Representatives from industry and the CVMP will further discuss the format of the presentation.

LIST OF PARTICIPANTS

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