European Medicines Agency
Veterinary Medicines and Inspections

London, 21 November 2005
Doc. Ref. EMEA/CVMP/SWP/139646/2005-CONSULTATION

COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON GUIDANCE ON THE APPROACH ON HOW TO DEMONSTRATE WHETHER A SUBSTANCE IS CAPABLE OF PHARMACOLOGICAL ACTION OR NOT

DRAFT AGREED BY SAFETY WORKING PARTY	14 October 2005
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	9 November 2005
END OF CONSULTATION (DEADLINE FOR COMMENTS)	21 February 2006

Comments should be provided to Kornelia Grein, Head of Sector - Safety of Veterinary Medicines at kornelia.grein@emea.eu.int

Fax +44 20 7418 8447

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 86 60
E-mail: mail@emea.eu.int http://www.emea.eu.int

1. INTRODUCTION

Article 6 (1) of Council and Parliament Directive 2001/82/EC, as amended, requires that a veterinary medicinal product may not be subject of a marketing authorisation for food producing species unless the pharmacologically active substances which it contains appear in Annex I, II or III of Council Regulation (EEC) No 2377/90.

Council Regulation (EEC) No 2377/90 defines "residues of veterinary medicinal products" as "pharmacologically active substances, whether active principles, excipients or degradation products and their metabolites, which remain in foodstuffs obtained from animals to which veterinary medicinal product in question has been administered" and establishes the procedure for the establishment of maximum residue limits for pharmacologically active substances. Active principles of biological origin intended to produce active or passive immunity or to diagnose a state of immunity used in immunological veterinary medicinal products are excluded from the scope of the Regulation.

Position paper on the definition of pharmacological action

The CVMP agrees that the definition of "pharmacologically active substances", in particular the approach to be taken for excipients, is still valid as stated in a Position Paper on the definition of substances capable of pharmacological action in the context of Council Directive 2001/82/EC.

The Position Paper was updated in July 2004 (EMEA/CVMP/072/97- Rev.1) to take account of the changes in the legislation. In addition, the Committee took the opportunity to also clarify the approach to be taken for manufacturing materials with regard to the establishment of MRLs. Further considerations are still ongoing with regard to adjuvants and a further revision of the Position Paper is planned once the approach regarding adjuvants has been finalised.

List of substances considered not falling within the scope of Regulation 2377/90

The EMEA publishes a list of substances (EMEA/CVMP/046/00-Rev.7), which are considered not falling within the scope of Regulation 2377/90. This list includes only substances for which requests in this respect were made to CVMP. The list is in no way exhaustive.

2. PROBLEM STATEMENT

Background

None of the above-mentioned pieces of legislation provide a legal definition of pharmacological activity.

According to the CVMP Position Paper on the definition of substances capable of pharmacological action in the context of Directive 2001/82/EC, as amended, with particular reference to excipients and manufacturing materials (EMEA/CVMP/072/97-Rev.1 (Revised July 2004)), pharmacologically active substances should be interpreted as substances which are pharmacologically active at the dose at which they are administered to the target animals by means of veterinary medicinal product in which they are included.

The question on how to demonstrate whether a substance is capable of pharmacological action or not is often asked by applicants of Marketing Authorisations and in absence of guidance, inconsistent and often inadequate data, are provided. The CVMP therefore agreed that guidance on the approach on how to demonstrate whether a substance is capable of pharmacological action or not would be useful.

3. DISCUSSION

As a general principle the potential toxicity of any substance included in a veterinary medicinal product should be addressed in the safety file for applications for the granting of marketing authorisations.

Currently, in order to establish if an excipient can be considered excluded from the scope of Regulation 2377/90, appropriate data to demonstrate the absence of such activity at the dose at which it is included in the final formulation have to be provided with the application for the marketing authorisation or if independent of an application for a marketing authorisation, as a request of scientific advice to CVMP. Should the substance be shown to have pharmacological activity at the doses at which it is administered to the target animals, an MRL application would be required.

In order to develop a guideline there are some points that should be addressed:

- What are the criteria that define an ingredient as not pharmacologically active?
- What tests or studies are required to demonstrate that an ingredient is not pharmacologically active?

4. RECOMMENDATION

To develop a guideline to address the points above and if required to consider and review the current CVMP Position Paper. The guideline is not intended to increase the requirements but to clarify how to demonstrate whether a substance is capable of pharmacological action or not, as guidance on this issue is often asked by applicants.

5. TIMETABLE

November 2005 Concept paper to CVMP for adoption for release.

February 2006 End of consultation.

The work on the guideline is intended to be initiated early 2006 after consideration of comments received during the consultation period. A draft guideline is intended to be released for consultation during the third quarter of 2006.

6. RESOURCE REQUIREMENTS FOR PREPARATION

It is proposed that the SWP-V develops the guideline. A Rapporteur and Co-rapporteur will be nominated. Adequate time for discussions at the SWP-V will be required. The EMEA secretariat will manage the development of the guideline and consultation process. Discussions at CVMP prior final adoption are foreseen.

7. IMPACT ASSESSMENT

Impact assessment for Regulatory Authorities

For Regulatory Authorities the proposed revision of the position paper and a new guideline would be conductive to a uniform decision on the scope of Regulation 2377/90 throughout the EU and would thus facilitate the evaluation of applications.

Impact assessment for Industry and other Interested Parties

For industry and other interested parties, a guidance note or guideline would contribute to the predictability and harmonisation of data requirements for marketing authorisation applications.

8. INTERESTED PARTIES

Regulators, veterinary medicines industry, consumer associations, EFSA.

9. REFERENCES TO LITERATURE, GUIDELINES ETC

Position paper on "The definition of substances capable of pharmacological action in the context of Council Directive 2001/82/EC as amended, with Particular reference to excipients and manufacturing materials." (EMEA/CVMP/072/97/FINAL-Rev. 1)

Substances considered as not falling within the scope of Council Regulation (EEC) 2377/90 (EMEA/CVMP/046/00-Rev.7)

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

Council Regulation 2377/90, as amended.