European Medicines Agency
Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

REFLECTION PAPER ON THE PUBLICATION OF THE CVMP'S NEGATIVE OPINION AND REFUSAL TO RECOMMEND THE GRANTING OF A MARKETING AUTHORISATION FOR VETERINARY MEDICINAL PRODUCTS[1]

ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	14 December 2006
END OF CONSULTATION (DEADLINE FOR COMMENTS)	28 February 2007
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[1] By analogy, similar information would be made available for MRL applications

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REFLECTION PAPER

Publication of Negative Opinion and Refusal of Marketing Authorisation Applications

1. INTRODUCTION

This document defines the scope, content and format of the documents on negative opinions and refusals to be published, taking into account commercially confidential information and the different stages of the evaluation procedure.

2. LEGAL BASIS AND SCOPE

Article 37 (3) of Regulation (EC) No. 726/2004, obliges the EMEA to publish information on refusals: "*Information about all refusals and the reasons for them shall be made publicly accessible"*.

A refusal of an application for marketing authorisation takes place by a European Commission decision following an opinion of the scientific committee of the EMEA.

According to transparency measures adopted by its Management Board, the EMEA publishes a summary of opinion for initial applications and also for certain post-authorisation applications (e.g. variations related to extension of new therapeutic indications). A summary of opinion is published irrespective if the opinion is positive or negative, immediately after the Committee meeting.

The publication of information about refusal concerns initial Marketing Authorisation applications, as well as applications for extensions of marketing authorisations as set out in Annex II to Regulation (EC) No 1085/2003[2].

In addition, on the basis of Article 80 of Regulation (EC) No 726/2004[3], the EMEA Management Board decided at its September 2006 meeting, in the context of a further strengthening of the transparency of EMEA processes and with a view to maintaining consistency on related processes, to extend the publication of information to refusals of applications for new indications via a Type II variation for medicinal products for human use; by analogy in the veterinary sector, this would apply to changes to or additions of a non-food target species as well as to new indications.

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[2] Changes requiring an extension application are listed below:

1. Changes to the active substance(s):

(i) replacement of the active substance(s) by a different salt/ester complex/derivative (with the same therapeutic moiety) where the efficacy/safety characteristics are not significantly different,

(ii) replacement by a different isomer, a different mixture of isomers, of a mixture by an isolated isomer (e.g. race mate by a single enantiomer) where the efficacy/safety characteristics are not significantly different,

(iii) replacement of a biological substance or product of biotechnology with one of a slightly different molecular structure. Modification of the vector used to produce the antigen/source material, including a new master cell bank from a different source where the efficacy/safety characteristics are not significantly different,

(iv) a new ligand or coupling mechanism for a radio-pharmaceutical,

(v) change to the extraction solvent or the ratio of herbal drug to herbal drug preparation where the efficacy/ safety characteristics are not significantly different.

2. Changes to strength, pharmaceutical form and route of administration:

(i) change of bio-availability;

(ii) change of pharmaco-kinetics e.g. change in rate of release,

(iii) change or addition of a new strength/potency,

(iv) change or addition of a new pharmaceutical form,

(v) change or addition of a new route of administration (1).

3. Other changes specific to veterinary medicinal products to be administered to food-producing animals: Change or addition of target species.

[3] Article 80 of Regulation (EC) No 726/2004: *"To ensure an appropriate level of transparency, the Management Board, on the basis of a proposal by the Executive Director and in agreement with the Commission, shall adopt rules to ensure the availability to the public of regulatory, scientific or technical information concerning the authorisation or supervision of medicinal products which is not of a confidential nature."*

3. DOCUMENTS TO BE MADE AVAILABLE TO THE PUBLIC

- The negative opinion will be announced in the Press Release of the CVMP meeting during which the opinion is adopted. A negative Summary of Opinion will be attached.

- In the case of a request for re-examination of the opinion, the Applicant's request will be published. If the re-examination is followed by a negative CVMP opinion, the European Commission publishes the Commission Decision and grounds for refusal in all languages. If the re-examination is followed by a positive CVMP opinion recommending a marketing authorisation, the negative Summary of Opinion, published at the time of the initial opinion, will be immediately removed and replaced by a (positive) Summary of Opinion.

- Following a negative opinion and Commission decision, a Refusal EPAR will normally be published 2-3 months later. In the case of a request for re-examination of the opinion, where the re-examination confirms the refusal, the re-examination steps will be clearly identified and described in the Refusal EPAR.

4. STRUCTURE AND CONTENT OF THE REFUSAL EPAR

The preparation of the Refusal EPAR preparation will follow the same procedure as the preparation of an EPAR for positive opinions.

The draft Refusal EPAR will be sent to the applicant who will usually be asked to verify the deletion of commercially confidential information within 10 working days (See Principles to be applied for the Deletion of Commercially Confidential Information for the Disclosure of EMEA Documents - EMEA/45422/2006). It should, however, be noted that it is the EMEA's responsibility whether or not to accept further proposed deletions of text.

The Refusal EPAR will highlight the main concerns raised by the CVMP which will be clearly explained. The CVMP will adopt the Refusal EPAR at a subsequent meeting.

The applicant will be provided with the final Refusal EPAR for information prior to its publication.

In case of a refusal of a post-authorisation application, this information will be made public through an EPAR update.

Starting date of the implementation

Implementation is from 20 November 2005 (the entry into force of Title 3 of Regulation (EC) No. 726/2004) and only for applications refused from that day onwards.