EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper on proposed revision to the Guideline for the conduct of efficacy studies for NSAIDs (EMEA/CVMP/237/01)

Agreed by Efficacy Working Party	March 2010
Adoption by CVMP for release for consultation	19 May 2010
End of consultation (deadline for comments)	30 November 2010

The proposed guideline will replace guideline: "Conduct of efficacy studies for non-steroidal anti-inflammatory drugs (EMEA/CVMP/237/01)".

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu, or +44 20 7418 8447

Keywords	*Guideline, veterinary medicinal product, NSAID*

[1] The deadline for the submission of comments has been extended until 30 November 2010.

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1. Introduction

The guideline for the conduct of efficacy studies for non-steroidal anti-inflammatory drugs was prepared in 2001 and came into effect in 2002. Considerable experience of assessing applications has been gained since then and it has become apparent that similar, major questions arise repeatedly during the assessment of applications for NSAIDs, suggesting that the existing guidance is not adequately addressing issues concerned with the development of these products.

Therefore it seems appropriate that the guideline should be revised.

2. Problem statement

On the basis of their common denomination, NSAIDs are frequently considered to have clinical effects in common. However, increased knowledge on pharmacology (incl. COX-selectivity) as well as results from clinical studies indicate that substances from the various classes of NSAIDs can differ substantially with regard to clinical effects, the doses needed to produce such effects and adverse effects. A review of the guideline to consider the impact of this increased knowledge is appropriate. This may lead to increased options for the demonstration of efficacy of these substances. Furthermore, a number of issues relating to study design (choice of response variables, assessment time points, observation intervals, study duration, the choice of control group, the detection of poor-/non-responders and dose finding) that would benefit from more clear guidance have been identified by regulators and have been brought to the attention of the CVMP-Efficacy Working Party.

3. Discussion (on the problem statement)

NSAIDs have become an important class of VMPs for both major and minor species. In order to produce qualitatively sound data, recommendations for study design and dose finding should be adequate and specific. It is suggested that a revision of the guideline might be beneficial for the followings reasons:

a) The dose finding part of the current guideline could be updated. Especially areas related to animal model studies and PK-PD modelling have developed considerably during the last years. In particular, the importance of selecting clinical relevant PK and PD data needs to be emphasized.

b) More emphasis could be placed on the importance of aspects of study design, e.g. choice of response variables, assessment time points and observation intervals, in relation to the expected and clinically relevant effects. Study design should take into account the possibility to differentiate between treatment effect and spontaneous recovery. Also, the presence of poor and non-responders should be taken into account.

c) The current guidance on rating scales could be reviewed and the importance of validating such scales emphasised.

d) Internal validity of data is of particular concern since baseline values in relation to treatment effect might be difficult to establish as in case of e.g. peri-operative claims. Therefore, the ethical aspect of the use of an untreated or placebo-treated control group needs to be balanced against the risks of allowing unjustified claims. Consideration could be given to the use of untreated or placebo-treated control groups under experimental conditions including alternative clinical trial designs which might allow use of early withdrawal or rescue treatments where placebos are used.

4. Recommendation

The EWP/CVMP recommends a revision of the existing guideline to consider the above mentioned issues.

5. Proposed timetable

May 2010	Concept paper adopted by CVMP for release for consultation
31 August 2010	Deadline for comments
2-3 Q 2011	Expected date for adoption of the revised guideline by EWP
3-4 Q 2011	Revised draft guideline for discussion and adoption by CVMP for release for consultation

6. Resource requirements for preparation

Preparation of the revision would involve one rapporteur assisted by two co-rapporteurs.

Preparation of the draft guideline will require discussions at 2 – 3 EWP meetings.

7. Impact assessment (anticipated)

The revision of the Guideline is not intended to introduce additional data requirements, rather to update the existing guidance in line with recent scientific progress and experience. It is expected to have a positive impact on animal health and welfare through refinement of study design and provision of better information on dosing regimens and application.
No impact on public health is expected.

8. Interested parties

Pharmaceutical Industry and veterinary consultants.
FVE,
EAVPT