European Medicines Agency
Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON THE REVISION OF THE NOTE FOR GUIDANCE ON STABILITY TESTING OF EXISTING ACTIVE SUBSTANCES AND RELATED FINSIHED PRODUCTS

AGREED BY QUALITY WORKING PARTY	March 2007
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	18 April 2007
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 July 2007

The proposed revised guideline will replace the Note for Guidance on "*Stability testing of existing active substances and related finished products (EMEA/CVMP/846/99)*".

Comments should be provided to QWP@emea.europa.eu
Fax + 44 20 74 18 84 47

KEYWORDS	Stability, existing active substances.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 84 47
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

1. INTRODUCTION

This concept paper addresses the need to update the CVMP Note for Guidance on Stability Testing of Existing Active Substances and Related Finished Products (EMEA/CVMP/846/99) (1). This Guideline was originally adopted in November 2000 as an extension of the VICH Guideline on Stability Testing of New Veterinary Active Substances and Medicinal Products (VICH GL 3) (2). The VICH Guideline has recently been updated (finally adopted by VICH SC in January 2007) (3) and therefore an update of the CVMP Guideline is now necessary.

2. PROBLEM STATEMENT

A revision of the CVMP Note for Guidance on Stability Testing of Existing Active Substances and Related Finished Products (EMEA/CVMP/846/99) is necessary as there are now some inconsistencies between it and the newly revised VICH Stability Guideline GL 3(R) and these are not scientifically justified. Also, the Note for Guidance on Declaration of Storage Conditions in the Product Information of Pharmaceutical Veterinary Medicinal Products and for Active Substances (EMEA/CVMP/422/99-Rev 2) (4), which is an annex to the guideline under consideration, includes already testing conditions which are now officially introduced by the revised VICH Guideline. Moreover, the corresponding guideline for human medicinal products, the Note for Guidance on Stability Testing of Existing Active Substances and Related Finished Products (CPMP/QWP/122/02, rev. 1) (5), contains elements of the new VICH stability testing conditions since 2003. As there are a lot of active substances which are used in both human and veterinary medicinal products, testing conditions for stability studies should be adapted to avoid unnecessary double testing (at only slightly different storage conditions).

3. DISCUSSION (ON THE PROBLEM STATEMENT)

The current Guideline was developed in 1999 and came into force in July 2002.

The major issues identified for revision are as follows:

- According to the newly revised VICH guideline, long term stability studies can be carried out not only at 25°C $\pm$ 2°C / 60% RH + 5% RH, but alternatively also at 30°C $\pm$ 2°C / 65% RH $\pm$ 5% RH. It is up to the applicant to decide the conditions used. If stability studies at 30°C $\pm$ 2°C / 65% RH $\pm$ 5% RH are chosen, there is no testing at intermediate conditions. This principle has already been accepted in the CVMP Guideline on Declaration of Storage Conditions (4).

- Conditions proposed for intermediate conditions changed from 30°C $\pm$ 2°C / **60**% RH $\pm$ 5% RH to 30°C $\pm$ 2°C / **65**% RH $\pm$ 5% RH in the revised VICH guideline.

- Testing conditions for active substances and finished products in specific cases have to be added in line with the revised VICH guideline (e.g., testing conditions for active substances to be stored in a freezer, testing conditions for finished products in impermeable or semi-permeable containers).

- The requirements concerning the selection of batches for stability studies, and the minimum time period covered by stability studies at time of submission of an application, should be reviewed.

4. RECOMMENDATION

Based on the above mentioned discussion, the CVMP recommends the QWP revise the current Guideline in line with the revised VICH Guideline GL 3(R) and also any other necessary revisions.

5. PROPOSED TIMETABLE

- March 2007 Concept paper to be discussed and adopted in QWP
- April 2007 Concept paper to be adopted by CVMP for release for 3 months consultation
- end July 2007 Deadline for comments
- Q III/IV 2007 Comments and draft revised guideline to be discussed in QWP
- Q IV 2007 if possible / Q I 2008 Draft revised guideline to be adopted by CVMP for release for consultation

RESOURCE REQUIREMENTS FOR PREPARATION

Rapporteur to prepare the draft revised Guideline. Member States to provide input via QWP. EMEA to provide secretarial support.

6. IMPACT ASSESSMENT (ANTICIPATED)

The anticipated benefit both to industry and regulatory authorities of the revised Guideline is the clarification it will provide on these stability study requirements for the EU. Especially, for active substances used in human as well as in veterinary medicine, unnecessary double testing at two slightly different testing conditions can be avoided.

7. INTERESTED PARTIES

The following interested parties are regarded stakeholders in the revision process of the Guideline: QWP interested parties (Veterinary), Regulatory Authorities.

8. REFERENCES TO LITERATURE, GUIDELINES ETC

1. Stability Testing of Existing Active Substances and Related Finished Products (EMEA/CVMP/846/99)
2. VICH Guideline 3 - Stability Testing of New Veterinary Drug Substances and Medicinal Products (CVMP/VICH/899/99)
3. VICH Guideline 3 (R) - Stability Testing of New Veterinary Drug Substances and Medicinal Products (Revision) (CVMP/VICH/899/99-Rev.1) Adopted by VICH SC in January 2007. Effective date January 2008
4. Note for Guidance on Declaration of Storage Conditions in the Product Information of Pharmaceutical Veterinary Medicinal Products and for Active Substances (EMEA/CVMP/422/99-Rev 2)
5. Stability Testing of Existing Active Substances and Related Finished Products (CPMP/QWP/122/02, rev. 1)