EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Veterinary use (CVMP)

Concept paper introducing a review and update of existing EU guidelines on residues studies to bring these into line with the VICH metabolism and residues guidelines GL46 to 49

Agreed by Safety Working Party	November 2011
Adoption by CVMP for release for consultation	09 February 2012
Start of public consultation	15 February 2012
End of consultation (deadline for comments)	31 May 2012

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

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1. Introduction

According to Directive 2001/82/EC (as amended) an application for marketing authorisation of a Veterinary Medicinal Product (VMP) which is intended for one or more food producing species cannot be made unless the pharmacologically active substances, which the product contains, appear in Table I of the Annex of Regulation (EU) No 37/2010 [which replaced Annexes I, II or III of Regulation (2377/90/EC]. To that end, an application for the establishment of MRLs should be submitted to the European Medicines Agency (EMA) at least six months prior to the submission of the marketing authorisation application.

Volume 8 of the publication "The rules governing medicinal products in the European Union" provides guidance on the presentation and content of the application for the establishment of MRLs, while Volume 6B is concerned with the structure and content of the application dossier for marketing authorisation of veterinary medicinal products.

2. Problem statement

Residues studies should be performed both for the establishment of MRLs and for the determination of withdrawal periods (WPs), and a number of guidance documents relating to the need for, and performance of, residues studies have been published at a European level. In February 2012 the VICH metabolism and residue kinetics guidelines, GL46 to 49, formally come into effect. These VICH guidelines provide internationally agreed guidance that now supersedes any parallel European guidance. Consequently there is a need to review the available EU guidance documents and, where these address issues also addressed in VICH GL46 to 49, to ensure consistency with the newly implemented VICH guidelines.

In addition, it has been noted that the existence of a number guidance documents on different aspects of residues studies can be confusing for both applicants and assessors. With a view to providing additional clarity on the aims of the different guidance documents and the issues covered in each, a document will be created that lists the different guidance documents available and briefly outlines the circumstances to which each relates.

3. Discussion (on the problem statement)

Requirements for residue studies have been set for both MRL establishment and withdrawal period determination. However, in both cases requirements may vary depending on the animal species concerned and/or the type of application submitted. Existing guidance relating to residues studies is distributed across a number of documents, with the most recent and up to date guidance provided in the VICH metabolism and residues kinetics guidelines GL46 to 49, which were adopted in March 2011 and formally come into effect in February 2012. Existing EU guidance covering topics also covered by VICH GL46 to 49 now needs to be updated to bring it into line with the VICH guidance. In addition, the opportunity will be taken to develop a document that clarifies when the different guidance documents need to be consulted.

4. Recommendation

The CVMP recommends reviewing existing EU guidance documents on residues studies and amending these as appropriate to ensure consistency with VICH GL46 to 49. The CVMP further recommends that a new document should be developed, listing all guidelines relevant to residues studies and clarifying the issues to which each relate.

5. Proposed timetable

February 2012:	Concept paper released for consultation
31 May 2012:	Deadline for comments on consultation paper
September 2012 to February 2013:	Review and update of residues guidelines by SWP
May 2013:	SWP agreement on revised residues guidelines where appropriate
May 2013:	SWP agreement on a draft document listing all residues guidelines and clarifying the circumstances under which each applies
July 2013:	Expected adoption of revised draft guidelines.

6. Resource requirements for preparation

The preparation of this guideline will require one rapporteur and one co-rapporteur from the SWP.

7. Impact assessment (anticipated)

Impact assessment for Regulatory Authorities and Industry

The review and update of existing residues guidelines to bring them in line with VICH GL46 to 49 will help avoid confusion in relation to the standards to be applied when evaluating residues studies, and the development of a separate document listing the existing guidelines and clarifying when each should be applied will further facilitate to the application of agreed and consistent standards in residues evaluation.

8. Interested parties

Regulators, veterinary pharmaceutical industry.

9. References to literature, guidelines, etc.

- Directive 2001/82/EC of the European Parliament and of the Council as amended by Directive 2004/28/EC and Directive 2009/9/EC, available at http://ec.europa.eu/health/documents/eudralex/vol-5/index_en.htm
- Regulation (EC) No 470/2009 of the European Parliament and of the Council laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council, available at http://ec.europa.eu/health/documents/eudralex/vol-5/index_en.htm
- Commission Regulation (EU) No 37/2010 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin, available at http://ec.europa.eu/health/documents/eudralex/vol-5/index_en.htm
- Rules Governing Medicinal Products in the EU: Notice to applicants Veterinary medicinal products, Volume 6B 'Presentation and Content of the Dossier', available at http://ec.europa.eu/health/documents/eudralex/vol-6/index_en.htm

- Rules Governing Medicinal Products in the EU: Notice to applicants and note for guidance, Volume 8 'Establishment of MRLs of veterinary medicinal products in foodstuffs of animal origin', available at http://ec.europa.eu/health/documents/eudralex/vol-8/index_en.htm
- VICH GL46: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: metabolism study to determine the quantity and identify the nature of residues, available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000384.jsp&mid=WC0b01ac058002dd37#ResiduesWithdrawalperiods
- VICH GL47: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: laboratory animal comparative metabolism studies, available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000384.jsp&mid=WC0b01ac058002dd37#ResiduesWithdrawalperiods
- VICH GL48: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: marker residue depletion studies to establish product withdrawal periods, available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000384.jsp&mid=WC0b01ac058002dd37#ResiduesWithdrawalperiods
- VICH GL49: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: validation of analytical methods used in residue depletion studies, available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000384.jsp&mid=WC0b01ac058002dd37#ResiduesWithdrawalperiods