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Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON FATE OF VETERINARY MEDICINAL PRODUCTS IN MANURE[1]

AGREED BY WORKING PARTY ON ENVIRONMENTAL RISK ASSESSMENT	22 January 2009
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	12 February 2009
END OF CONSULTATION (DEADLINE FOR COMMENTS)	30 April 2009

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KEYWORDS	*Degradation, fate, manure, non-extractable residues, environmental risk assessment*

[1] In this document the term manure should be considered to mean manure, slurry and poultry litter

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1. INTRODUCTION

Recently, the EMEA released the guideline *Environmental Impact Assessment for Veterinary Medicinal Products in support of the VICH guidelines GL6 and GL38* (EMEA/CVMP/418282/2005-Rev.1) which gives further technical support to the implementation of the VICH guidelines GL6 and GL38 on the environmental risk assessment (ERA) of veterinary medicinal products (VMPs). Besides algorithms, models and default values for the determination of the predicted environmental concentration (PEC) of VMPs in the environment, the guideline provides a number of options for refinement of the PEC. One of these options is to refine the PEC based on degradation in the manure of the target animal(s).

2. PROBLEM STATEMENT

No validated or standardised method for assessing the fate of veterinary medicines in manure at either laboratory or field level has been developed. Consequently the CVMP guideline provides only limited advice on this aspect of the risk assessment which concentrates on the use of degradation studies as part of the Phase I assessment. Since the release of the CVMP guideline it has become clear that there is a need for guidance on how fate studies in manure should be conducted and how the result should be evaluated and used in the ERA which is provided in support of an application for a marketing authorisation.

The CVMP recognises that there is an urgent need to develop further guidance on the design and the evaluation of studies intended to elucidate the fate of VMPs in manure and as a consequence has prepared this concept paper.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

Recently a technical protocol for laboratory tests on degradation of VMPs in cattle and pig manures has been produced by the Institute of Ecological Chemistry and Waste Analysis in the framework of the UBA (Umweltbundesamt) funded project on Methodological Aspects of Laboratory Tests of VMP and Biocides in Manures and Manured Soils. This protocol was discussed at an international workshop at the Technical University in Braunschweig in April 2008.

Using the information provided at this workshop and following discussion of the issue by the CVMP Environmental Risk Assessment Working Party (ERAWP), the following were identified as key points which need to be addressed in order to develop an accepted study design and agreed interpretation of the data:

STUDY DESIGN

- Selection and handling of the test manure (e.g. origin, storage, reference manure, tank manure)
- Matrix characterisation of the manure (parameters to be measured)
- Establishing test conditions (e.g. temperature, aerobic, anaerobic, moisture, duration, sterile, non-sterile)
- Test substance (e.g. labelled, non-labelled) and spiking procedure
- Extraction and determination of the test substance, metabolites and non-extractable residues (e.g. validation of analytical methods, setting criteria for recovery)
- Data analysis (e.g. kinetics)

EVALUATION AND USE OF THE TEST RESULTS

- Extrapolation of biotic and abiotic transformation of VMPs within and between manure types of different target species
- Defining realistic and representative storage conditions for standardisation of test results (e.g. temperature, time)
- Use of test results to refine PECs (e.g. dealing with non first-order dissipation interpretation of non-extractable residues)
- Identification of relevant metabolites

4. RECOMMENDATION

There is a need to develop further guidance on the design and the evaluation of studies intended to elucidate the fate of VMPs in manure. It is intended to obtain views of all interested parties by the circulation of this concept paper.

Following this consultation it is the intention for the CVMP ERAWP to hold a focus group meeting in June or July 2009 in order to exchange the views and experiences of researchers, industry and authorities in this area.

The objective is to prepare a CVMP guideline to provide guidance on the design, execution and interpretation of studies on the fate of VMPs in manure which can be used in the preparation of the ERA by the applicant for a Marketing Authorisation and in the evaluation of the studies by the competent authorities.

5. PROPOSED TIMETABLE

Adoption by CVMP for release for consultation: February 2009

End of consultation: April 2009

Focus group meeting: June/July 2009

Preparation of draft guidance by ERAWP: Third quarter 2009

Adoption by CVMP for release for consultation: End of 2009

End of consultation: Second quarter 2010

Discussion of comments received at ERAWP: Second/third quarter 2010

Adoption of revised guideline by CVMP: Third quarter 2010

6. RESOURCE REQUIREMENTS FOR PREPARATION

The development of the guidance will require one focus group meeting with specialists from third parties. The guidance will be prepared using the standard ERAWP meeting and virtual meetings as required.

7. IMPACT ASSESSMENT (ANTICIPATED)

It is foreseen that the guidance document will enable applicants to design, carry out and report on fate studies in manure based on agreed criteria. This will provide applicants with a better predictability of requirements and acceptability of their applications and will enhance harmonisation of the design and interpretation of such studies by applicants and regulators and by consequence enhance agreement between Member States with the possible benefit of fewer referrals.

8. INTERESTED PARTIES

Industry, clinical research organisations and regulators.

9. REFERENCES TO LITERATURE, GUIDELINES ETC

- CVMP/VICH Topic GL6 (Ecotoxicity Phase I) Guideline on environmental impact assessment (EIAS) for veterinary medicinal products – Phase I, CVMP/VICH/592/98-FINAL
- CVMP/VICH GL 38 Environmental impact assessment for veterinary medicinal products - Phase II, CVMP/VICH/790/03-FINAL
- Guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38, EMEA/CVMP/ERA/418282/2005-Rev.1
- UBA (Umweltbundesamt) project on Methodological Aspects of Laboratory Tests of VMP and Biocides in Manures and Manured Soils. Veterinary medicinal products in manure and manured soils: development of a technical protocol for laboratory tests (FKZ 20467455, http://www.umweltdaten.de/publikationen/fpdf-l/3343.pdf) and Technical guidance: degradation of biocides in manure (FKZ 370867403, publication in preparation).