European Medicines Agency
Veterinary Medicines and Inspections

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EMEA/CVMP/1034/04- Consultation

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS (CVMP)

CONCEPT PAPER ON FURTHER GUIDANCE ON INTERPRETATION OF THE DATA FROM VICH GL27 (GUIDANCE ON PRE-APPROVAL INFORMATION FOR REGISTRATION OF NEW VETERINARY MEDICINAL PRODUCTS FOR FOOD PRODUCING ANIMALS WITH RESPECT TO ANTIMICROBIAL RESISTANCE) (CVMP/VICH/644/01)

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1. INTRODUCTION

The former Ad hoc Group on Antimicrobial Resistance (AGAR) of the CVMP and the VICH Expert Working Group on Antimicrobial Resistance simultaneously developed two guidelines: Guideline on Pre-authorisation Studies to assess the Potential for Resistance Resulting from the Use of Antimicrobial Veterinary Medicinal Products (EMEA/CVMP/244/01-FINAL) which has been in operation since January 2003 and VICH GL27 Guidance on Pre-approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals with respect to Antimicrobial resistance (CVMP/VICH/644/01-FINAL) focussed at pre-approval data supplied by the industry in order to demonstrate the potential of the active substance in the given formulation to select for antimicrobial resistance of public health concern. The VICH guideline GL27 was adopted in 2003 and replaced the CVMP guideline in December 2004. The mandate of the Scientific Advisory Group on Antimicrobials (SAGAM), that provides expertise to the CVMP on all matters relating to antimicrobial resistance, requests the group to provide further guidance on how to interpret the data requested by the VICH guideline on pre-approval information for the registration of new veterinary medicinal products for food-producing animals with respect to antimicrobial resistance.

The objective of the intended guideline is to provide more guidance to applicants and to assessors on how to interpret and assess the data requested by VICH GL27.

Specifically, the document will provide further guidance on:

- When to provide additional information;
- Which information to provide;
- To have a harmonised approach for the requirement of data particularly for mutual recognition and decentralised procedures.

2. PROBLEM STATEMENT

The VICH GL27 is limited to 'characterisation of the potential resistance development as it might occur in the food-producing animal under the proposed conditions of use of the product'. The VICH GL27 does not include recommendations or guidance on an assessment of these data and on the level of detail of the data to be provided.

- **Anticipated benefit to:**
  - **Industry and Other Interested Parties**

    Consistency and transparency in the interpretation of data requirements.
  - **Regulatory Authorities**

    Consistency and transparency in the interpretation of pre-approval data.

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3. DISCUSSION

Internationally antimicrobial resistance is an ongoing subject for discussion. Recently at FAO/OIE/WHO meetings in Geneva (2003)[1] and Oslo (2004)[2], the existing knowledge on the risks of non-human use and the potential risk management's options were discussed. It was concluded that antimicrobial agents are essential drugs for human and animal health and welfare and that antimicrobial resistance is a global public health concern that is impacted by both human and non-human antimicrobial usage. Antimicrobial agents are used in food-producing animals, aquaculture, companion animals and horticulture to treat or prevent disease. The types of antimicrobials used are frequently the same as, or closely related to, antimicrobials used in humans. It was also concluded that clear evidence exist of the human health consequences due to resistant organisms (zoonotic pathogens) resulting from non-human usage of antimicrobials.

A human safety assessment of new marketing authorisation applications for antimicrobial veterinary medicinal products intended for food-producing animals is implemented by the adoption of VICH GL27. The proposed use conditions of a veterinary medicinal product, the potential exposure of animal gut flora to the antimicrobial agent, the potential exposure of humans to resistant bacteria or their resistance genes, and the perceived importance of the drug (or related drugs) to human medicine are factors that influence the level of detail of data to be provided by applicants (VICH GL27). However, this guideline is focussed at the characterisation of the potential of a drug to select for resistance of public health concern. Guidance for the assessment of the data provided is not included. The concept of 'critically important' classes of antimicrobials is already used on an ad hoc basis when assessing antimicrobial product applications. Transparent criteria for classification of antimicrobial agents are necessary for the human safety assessment. These criteria are being developed by international bodies (e.g., WHO/OIE) and may affect data requirements for different types of antimicrobial products intended for use in food-producing animals.

4. RECOMMENDATION (POINTS TO BE ADDRESSED)

It is important to clarify when there is a need to provide more information or even study data and when requirements are less demanding. Taking into account the data included in the dossier according to VICH GL27, this document will give more guidance to the applicant and the assessor for the level of detail of data provided.

A possibility to develop a -tiered approach or decision-tree to describe the dossier requirements for different types of application will be considered.

Guidance will be developed to carry out an assessment, including interpretive criteria for the assessment of the potential of the drug to select for resistance of concern to human health. These criteria include:

- Exposure assessment (gut flora of food-animals to the veterinary medicinal product);
- Exposure assessment of humans to resistant bacteria and resistance genes;
- Interpretation of criteria developed by international bodies (e.g., WHO/OIE) for categorisation of the importance of antimicrobials to public health;
- The potential impact of these resistant strains or resistance genes on public health[3].

[1] http://www.who.int/foodsafety/publications/micro/nov2003/en/
[2] http://www.who.int/foodsafety/publications/micro/mar04/en/
[3] Impact analysis is a tool to assess the potential impact on human health of resistant bacteria or resistance genes that are selected by use in animals and can be transmitted to humans.

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5. TIMETABLE

A draft timetable is intended to be released for consultation during the last quarter of 2005 or the beginning of 2006.

6. RESOURCE REQUIREMENTS FOR PREPARATION

It is proposed that the SAGAM develops the guideline, the input of the SWP-V might be required.

7. IMPACT ASSESSMENT

This guidance document will be complementary to the VICH GL27 which sets the dossier requirements for the applicants.

- **Impact for Industry and other Interested Parties**

  The guideline will provide a consistent approach on the preparation of data and assessment by applicants. It may have an impact on conditions of use of products as established by Marketing Authorisations.

- **Impact assessment for Regulatory Authorities**

  The guideline will provide a consistent and transparent approach on the assessment by regulators.

8. INTERESTED PARTIES

Regulators, veterinary medicines industry, veterinarians and consumers.

9. REFERENCES

CVMP-VICH GL27 Guidance on Pre-approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals with respect to Antimicrobial resistance (CVMP/VICH/644/01-FINAL)

Guideline on Pre-authorisation Studies to assess the Potential for Resistance Resulting from the Use of Antimicrobial Veterinary Medicinal Products (EMEA/CVMP/244/01-FINAL)

Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial resistance: Scientific Assessment (Geneva Dec. 2003) and Risk Managements Options (Oslo, March 2004)

CVM guidance document 152. Evaluating the safety of Antimicrobial new Animal Drugs with regard to their microbiological effects on Bacteria of Human health Concern.

Further information on the CVMP policy on antimicrobials can be found at the EMEA web page (http://www.emea.eu.int), under the topic “antimicrobial resistance”.

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