

# HMA strategic plan on antimicrobial issues

## I. Introduction

At the HMA meeting on 11th July 2008 in Villiers le Mahieu, France, it was decided, during the discussions on the implementation of CVMP recommendations regarding Quinolones and Fluoroquinolones, that the HMA management group should prepare a strategic plan about the issue of antimicrobial resistance.

In preparing this strategic plan, the HMA management group took into account the Council Conclusions on Antimicrobial Resistance (Luxembourg 10th June 2008), reviewed the CVMP strategy on antimicrobials 2006-2010 and status report on activities on antimicrobials published in 2005. The CVMP status report on activities was structured according to the Guideline for the responsible and prudent use of antimicrobial agents in veterinary medicine (responsibilities of regulatory authorities) published by OIE.

This document supports the CVMP strategy and takes into consideration other international recommendations in order to identify the areas where HMA, according to their particular areas of competence, could complement the CVMP's strategy.

HMA highlighted that antimicrobial resistance is a global public health issue and expressed the necessity for good coordination with the human sector.

## II. Vision

HMA considers maintaining the efficacy of antimicrobials and minimising the development of resistance to be one of the most important tasks in the field of veterinary medicine. The measures, which are considered to be necessary to reach these goals, should be balanced so that the availability of necessary antimicrobial veterinary medicinal products is not unreasonably restricted. This is especially important for medicinal products that are used for indications for which there are no other alternatives available for efficacious treatment.

The focus of all actions should be based on the prudent and responsible use of the antimicrobials in Veterinary Medicine, which is considered to be an essential tool for the control of antimicrobial resistance development. Better and coordinated communication in this field appears as an important issue, in particular, in international discussions.

HMA support the EMA/CVMP strategy and actions on antimicrobial resistance and is ready to actively contribute to their further development.

HMA recognise the need to consider the antimicrobial resistance issue in a global context taking into account both the use of antimicrobials in veterinary and human medicines and the ongoing international developments (Antimicrobial Resistance Codex Task Force).

### **III. Responsibilities of the National Competent Authorities (NCAs)**

Responsibilities in implementing strategies for antimicrobial resistance issues may fall under different bodies at the national level. It is recognised that HMA can only act in their field of competence, however, they should act as a catalyst for promoting antimicrobial related actions at the national level.

#### **1. Marketing authorisation - submission of data, marketing approval, registration procedures and assessment of the potential of antimicrobials to select for resistance**

While the EMA/CVMP is responsible for the Marketing Authorisation issued through the Centralised procedure, NCAs are responsible for the products authorised in the National, Mutual recognition and Decentralised procedure.

The responsibility of the NCAs is to implement the requirements included in Directive 2001/82/EC as described in the guidelines on quality, safety and efficacy as well as the specific guidelines related to antimicrobial resistance and, in particular, Guideline VICH GL27: Guidance on the pre-approval information for registration of new veterinary medicinal products for food producing animals with respect to antimicrobial resistance.

The NCAs should ensure that antimicrobial authorisations are given and maintained on the basis of scientific data following a benefit risk assessment. They should ensure that necessary risk management measures are taken in order to limit the risk of development of antimicrobial resistance including instructions on administration, dosages and dosing intervals, indications, responsible use warnings where relevant, legal classification. *Additional risk management measures shall be discussed for their relevance in decreasing AMR*

NCAs shall also promote harmonisation of SPCs for defined antimicrobial products in order to reduce differences among Member States in the key elements of the Marketing Authorisations which may influence development of resistance to the antimicrobials.

It must be underlined that the public responsibilities in the field of antimicrobial resistance in the veterinary sector are shared by different NCAs and with quite numerous other public institutions and authorities. These concerned institutions or authorities are depending on the national organisations (e.g.: food safety authorities; public reference laboratories; ministries in charge of agriculture or health...) and their views need to be considered.

#### **2. Quality control of antimicrobial agents**

The NCAs are involved in the control of veterinary medicines. They participate to the network of Official Medicines Control Laboratory (OMCL).

In order to improve efficiency of testing of medicinal products authorised via the Mutual Recognition Procedure and Decentralised Procedure, HMA decided to set-up a Working Group dedicated to testing of medicinal products.

Antimicrobial products administered by oral route should be considered as medicines with high priority for quality control. Homogeneity and stability of antimicrobials in feed or in water should be carefully addressed as they are important factors to consider in order to ensure that an appropriate level of antimicrobial product will be ingested by the animal.

### **3. Control of therapeutic efficacy**

The NCAs should ensure the implementation of *the Guideline for the demonstration of efficacy for veterinary medicinal products containing antimicrobial substances* (EMA/CVMP/627/01) in relation to the assessment of clinical data on antimicrobials.

The NCAs have also responsibilities in pharmacovigilance and should ensure that if a failure of therapeutic efficacy is identified, appropriate actions are implemented.

As a part of the post-authorisation surveillance, the NCAs should take into consideration the Reflection paper on Antimicrobial Resistance Surveillance as Post-marketing Authorisation Commitment.

Information from field use which calls into question the merits of any of the conditions attached to the Marketing Authorisation of an antimicrobial product should be carefully assessed.

### **4. Establishment of acceptable daily intake, maximum residue limits (MRLs) and withdrawal periods for antimicrobial compounds**

While the responsibility of EMA/CVMP is to establish MRLs, the NCAs have the responsibility to agree on withdrawal periods for products in National, Mutual recognition and Decentralised procedures.

The NCAs have also to ensure the validity of withdrawal periods within the framework of the pharmacovigilance system and the residues surveillance plan.

### **5. Protection of the environment**

Regarding the assessment of the risks for the environment the NCAs should ensure the implementation of the VICH guidelines on Environment Impact assessments (VICH GL6 and VICH GL38). The NCAs should ensure that appropriate risk management measures are in place so as to mitigate any potential adverse environmental effects.

The NCAs have also to assess and take any necessary measures regarding any potential reported environmental problem in the framework of the pharmacovigilance system.

## **6. Establishment of a summary of product characteristics (SPC) for each veterinary antimicrobial product (VAP)**

The SPC contains the information necessary for the appropriate use of veterinary medicinal products and constitutes the official reference for the labelling and package leaflet for such products. The SPC and other product information should include all the necessary warnings and instructions for responsible use in accordance with the CVMP guideline on SPC for antimicrobials products.

The NCAs in close cooperation with the EMA/CVMP should implement the recommendations for harmonisation of SPC wording on antimicrobials previously set out by the EMA.

Such recommendations have already been made for products containing Quinolones and Fluoroquinolones and 3rd and 4th generation cephalosporins for systemic action.

Further proposals for other antimicrobial classes considered as important in treating critical diseases in humans may follow. At the time when the NCAs are requested to implement such proposals, a specific work plan and deadlines should be defined. A regular follow up of the implementation should also be put in place. In case of difficulties of implementation, a referral to EMA/CVMP may be envisaged.

## **7. Post Marketing surveillance**

A survey of consumption of antimicrobials and of antimicrobial resistance in all member states of the EEA is considered an essential tool for risk assessment and risk management of antimicrobials in the Community. The NCAs should ensure that a survey of the consumption of antimicrobials is done at a national level each year.

The NCAs should ensure that the data are presented in a format to be agreed between the NCAs and the EMA. In those Member States where NCAs are not directly responsible for survey, the NCAs shall actively promote implementation of such surveys and exchange of data.

Contacts should be established with EMA in order to agree arrangements for coordinating this survey.

HMA should coordinate the collection of data on the prescribing practices in different member states and how this influences the sales and use of antimicrobials.

## **8. Supply and administration of the antimicrobial agents used in veterinary medicine.**

The NCAs have a pivotal role in deciding the prescription status of a medicine. They should ensure that all antimicrobials are restricted to prescription only medicines.

Any derogation for a particular product intended for companion animals should be based on up-to-date requirements related to veterinary medicinal products and fully justified by the benefit:risk analysis of the product concerned.

## **9. Control of advertising**

The NCAs have a role in ensuring that the advertising practices for antimicrobials products are in line with the national and European legislation.

## **10. Training of antimicrobials users**

Training of users of antimicrobials is a shared responsibility with other stakeholders. An action plan for communication on responsible use of antimicrobials should be initiated with the EMA and other stakeholders as The European Platform for the Responsible Use of Medicines in Animals (EPRUMA)

## **11. Research**

Improvement of diagnostic tools and finding alternative measures to the use of antimicrobials are to be supported.

## **IV. The responsibility of HMA**

HMA, as an informal network, has no direct responsibilities in the implementation of the NCAs' duties. HMA should play the role of facilitator in this area. The below mentioned strategic plan could be further elaborated in order to:

- Help its members identifying areas and ways of actions
- Organise the follow up of implementation of the agreed measures
- Assist, when necessary, the members of the network, for instance, by putting in place centres of resource or work sharing in this area.
- Help develop a comprehensive communication strategy within and outside the network. HMA should strengthen its actions with regards to availability of medicines according to the HMA Task Force Report on Availability of Veterinary Medicines published in April 2007.

## **V. Strategic Plan**

In order to implement the vision and taking into account the responsibilities of the HMA, the following steps are proposed or have already been carried out:

First Step

- It is important to put in place an adequate coordination with the EMA. A specific meeting was co-arranged by the Czech Presidency and the EMA in May 2009 involving the HMA and stakeholders. This was done in order to coordinate and prioritise the actions to be implemented. The report and recommendations from the meeting have been published.
- It is important to ensure that all antimicrobials are prescription only medicines.

Any derogation for a particular product intended for companion animals should be based on up-to-date requirements related to veterinary medicinal products and fully justified by the benefit:risk analysis of the product concerned. A questionnaire has been sent to HMA members in order to ensure that it is the case.

- Use of the results of the surveys of consumption and of resistance, in both animal and human medicines, should be ensured. These results can be used as elements to be considered in risk assessments but also in the communication strategy to users/prescribers of antimicrobials.

#### Second step

- The establishment of an HMA action plan should not be finalised without further discussion and coordination with the EMA. A draft action plan has been discussed during the second HMA meeting under the Czech presidency in May 2009 and further elaborated under the Swedish presidency in 2009.