Report of the

Joint HMA/EMEA Meeting on Promoting Prudent and Responsible Use of Antimicrobials in Veterinary Medicine

Marienbad, Czech Republic

19 – 20 May 2009

EXECUTIVE SUMMARY AND KEY RECOMMENDATIONS

Introduction

The Heads of Medicines Agencies (HMA) under the Czech Presidency and the European Medicines Agency (EMEA) jointly organised a coordinatory meeting on the topic of 'Promoting Prudent and Responsible Use of Antimicrobials in Veterinary Medicine' which was held in Marienbad, Czech Republic 19-20 May 2009.

The general objectives of the meeting were to:

- give an overview of the current status and ongoing activities with respect to the issue of antimicrobial resistance (AMR) in the EU,
- learn about the expectations of different parties involved,
- identify the areas which need further action with respect to the current scientific knowledge and political expectations,
- identify possibilities for effective actions at the EU level, including effective co-ordination of activities

The specific objectives of the meeting were to:

- Review implementation of CVMP recommendations for fluroroquinolones
- Agree how best HMA can work with CVMP to implement recommendations on AMR in future (including cephalosporins)
- Discuss with HMA and stakeholders how best EMEA can coordinate collection of AM sales data by national competent authorities

Conclusions

The main conclusions drawn from each session have been collated and summarised as follows:

Prudent use in the veterinary context

- Regulatory requirements have to be balanced against the need for therapeutic treatments for animals
- There remains a need for new and more effective antimicrobials

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- Any consideration of the use of antimicrobials in animals is not complete without a parallel discussion of the use of antimicrobials in man and must therefore involve all interested parties and the measures to be taken should be proportionate to the contribution to the identified risks
- The 'one health' aspects of AMR should continually be emphasised in any discussion on AMR and this should include the need for antimicrobials to control disease in animals
- The availability of authorised veterinary medicines needs also to be included in any discussion on AMR not only from the "one health" perspective but also from the perspective of animal health and welfare
- More information is required on antimicrobial resistance (in general) and on use of antimicrobials in veterinary medicine e.g. knowledge of prescription practices and patterns
- Many factors other than professional knowledge (e.g. culture, history, cost, profit, availability etc) influence prescribing habits of veterinary surgeons and an understanding of these factors is important for effective implementation of prudent use guidelines
- All efforts to promote prudent use risk being undermined by market factors such as decreasing cost (e.g. there is evidence in some Member States of an increase in the use of fluoroquinolones once the advent of generics results in a drop in price)
- The shorter withdrawal periods of newer antibiotics make them particularly attractive in food producing species
- The AMR issue is highly complex and the whole scientific agenda and rationale can be adversely influenced by non-scientific factors such as pricing and withdrawal periods
- The environment in which the veterinary profession and farmers work is changing substantially – the most important changes / factors being liberalisation on the market, competition at the global level and pressure on the food price - and these factors need to be considered when decisions on prudent use are taken

Promoting the prudent use agenda

- Communication is key in any issue related to AMR and regulatory bodies must not only take appropriate action but must be seen to be taking appropriate action
- Communication needs to address more than just the message – also need to change the culture
- It is important to identify the appropriate drivers for engagement for each stakeholder rather than relying on altruism
- There is a need for continued training of veterinarians and farmers on AMR. Continuous professional development is an important communication mechanism to reach vets and influence their prescribing habits
- A lack of information should not be a reason to delay action
- There is a clear need for better dissemination to prescribers and users of antibiotics of knowledge on resistance patterns in target animal organisms and on the optimum choice of antibiotic and dosage regime per indication
- Early and continuous engagement of stakeholders is essential for successful implementation of prudent use guidelines. The existing forums, such as RUMA/EPRUMA, can serve as useful models

Ensuring and enhancing adherence to prudent use

- Extensive guidance from CVMP is in place but needs to be better communicated and implemented
- The CVMP strategy on antimicrobials is based on prudent and responsible use. There is a need to understand and measure the impact of recommendations from regulators and other bodies (e.g. veterinary associations) on the use of antimicrobials
- Many activities are currently ongoing in the field of AMR including e.g. HMA Action Plan under the Swedish Presidency, Joint Report to the Commission from EU Agencies, European Commission activities and also from the pharmaceutical industry, the need now is for better coordination
- HMA has a leadership and coordination role in the field of AMR and the HMA Strategic Plan should act as the catalyst for implementing this role.

- There is a need to ensure that the whole of industry respects prudent use in terms of advertising, promotion etc. It is not clear that the current mechanisms to control advertising are effective, particularly as they only affect members of participating trade associations
- Introduction of any change to product literature with respect to prudent use warning should be done according to a risk analysis and the costs incurred by the industry need to be considered so that the exercise is efficient but unnecessary side costs (e.g. labelling) are avoided.
- It may be too simplistic an approach to continue to consider that price/cost cannot be considered as part of the licensing process as these factors are key to the pattern of use of any antibiotic
- In any future review of legislation a way needs to be found to ensure that costs, withdrawal periods etc promote rather than undermine prudent use
- Discussions of prudent use must cover the whole spectrum of the topic including alternatives to antimicrobials and non-therapeutic interventions such as changing husbandry systems

Coordinating the collection of data on sales of antimicrobials at an EU level

- A co-ordinated approach to the collection of antimicrobial sales data as part of the HMA Strategic Plan will be vital to achieve success
- The main recommendations from industry in relation to the collection of antimicrobial sales data were
    - Keep the system simple, at least initially, and focus on sales of active (in Kg)
    - Ensure confidentiality of the data collected and that its collection does not breach competition law
    - Collect the data at national level and not centrally
    - Cross check data from several sources as it is essential to validate
    - Collect data from all marketers of antimicrobials (i.e. pioneer companies and generics)
    - Collect data from all Member States
    - Ensure an open, frank and constructive dialogue between industry as the providers of data and NCAs as the collectors and users of this data
    - Ensure collection of contextual data (production figures, numbers of animals, disease incidence, etc)
- The experience gained by Member States and from the industry survey will be highly beneficial for setting up a project for collecting data for the EU and their analysis
- It is important to communicate the reason why the data is required to motivate all players in its supply and collection
- Any system introduced must be stable and consistent i.e. not prone to frequent changes

Recommendations

The recommendations made at each session have been collated and summarisedas follows:

All Stakeholders (Regulators, industry, EU and International bodies)

- Stakeholders should be involved at all levels in discussions on AMR due to the need to ensure effective communication, cooperation, coordination and commitment
- Prudent and responsible use should be promoted and restrictions on the use of antimicrobials should be introduced only when there is a scientifically sound basis
- Stakeholders should promote the continued training on AMR of veterinarians and farmers
- Other measures, such as biosecurity, vaccination, and education on the use of antimicrobials should be promoted as an integral part of the 'prudent use' agenda
- Encourage the development of tools to assist with the selection of antimicrobials in terms of active substance and dose which are targeted at particular user groups (companion/farm vets, generalist/specialist)
- Consider how best to promote further development of the resistance surveillance programmes in the EU, particularly for target animal pathogens, including programmes providing appropriate data on the regional level.
- CVMP recommendations on fluoroquinolones, cephalosporins and MRSA should be implemented by all concerned parties

Regulators

- There is a need to 'map' responsibilities in terms of implementing the policy of prudent use and identify who should lead in each relevant area. This mapping should include an assessment of 10 June 2008 Council Resolution on AMR to identify any gaps in actions or responsibilities
- The HMA should include a survey of the prescription status of antibiotics and prescribing practices in Member States (i.e. who can prescribe, what controls and monitoring of prescription exits) as this will be useful to understand divergence in EU
- The HMA should consider carrying out a survey in association with the Federation of Veterinarians in Europe (FVE) to identify factors that influence the prescribing practices of vets and to determine what are the best methods of communicating to them
- The HMA and EMEA should create a communication plan that uses existing vehicles as much as possible (e.g. RUMA, EPRUME, professional associations)
    - Adopt a step wise approach to the collection of AM sales data, starting with the collection of sales volumes, and moving forward progressively to look to more details later on
    - Use the experience gained from data collection in other countries, and from industry, to refine the proposal
- In relation to coordinating the collection of AM sales data by national authorities, the EMEA should
    - Collect sales data at a national level, with the EMEA coordinating collection, validation and analysis of the collated data in a consistent manner
    - Include all marketing authorisation holders of antimicrobials in the data collection
- Apply all measures related to prudent use in an equal manner to all sections of the animal health industry
- Give careful consideration during the next revision of the veterinary legislation governing AMR to the special nature of the benefit risk assessment for antimicrobials, especially those used in both man and animals

DETAILED REPORT

The agenda for the meeting is at Annex 1 and a list of attendees at Annex 2.

Prof. A. Hera (Czech Republic) welcomed the participants to the meeting, and introduced the topics to be covered. He presented data from the Czech Republic demonstrating that the problem of AMR is a real one and the threat is growing. The threat, and its management, are complex and any solution must involve both human and veterinary medicines. He emphasised the need for coordination, cooperation and communication. Action was needed by HMA both in gathering data, or coordinating its collection, to ensure future decisions are based on sound information and in coordinating the implementation of those measures that are under the direct control of national competent authorities (NCAs).

SESSION 1 : UPDATE ON ACTIVITIES RELATED TO AMR AND EXPECTATIONS FOR THE MEETING

Presentations:

- Reduction and prevention of antimicrobial Resistance in the veterinary sector: from a global perspective to the field level usage - How may HMA contribute: P Dehaumont (France)

  P. Dehaumont highlighted the extensive existing international guidance on AMR that has built up over the last decade, during which AMR has been an issue with a high political profile. At an international level this includes, OIE guidance (http://www.oie.int/eng/normes/Mcode/en_sommaire.htm) on harmonisation of AMR surveillance and monitoring programmes; monitoring of the quantities of antimicrobials used in animal husbandry; responsible and prudent use of antimicrobials; and, risk assessment for AMR from the use of antimicrobials in animals. Under the auspices of OIE, there has been development of VICH GL 27 (pre-authorisation guidance) & GL 36 (microbiological ADI), the development of a collaborative approach with FAO and WHO for risk analysis, the development of the veterinary critical antimicrobials and the human critical antimicrobials lists, and the working group for the creation of Draft Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance.

  At a field level, there is a need for regulatory controls to avoid misuse of antibacterials. The HMA strategic plan should promote the responsible use of antibacterials to avoid the increase of AMR. There is a need for safe and efficient antibacterials, promoting responsible use without unnecessary restrictions. A special focus should be made on continuous training of those administering antibacterials and on communication of AMR risks.

  Dr Dehaumont emphasised the HMA Strategic Plan on antimicrobials as an important milestone from the perspective of NCAs in the EU, particularly in terms of setting out how HMA coordinates its action with those of the European Commission, the EMEA/CVMP and stakeholders and how activities at HMA can complement those at national level. He considered that implementation of the action plan was a test of the credibility and leadership of the HMA in this important area

- CVMP/SAGAM recommendations on antimicrobials: K. Törneke (SAGAM chair, Sweden)

  K. Törneke reported on the many previous and ongoing activities of the CVMP and SAGAM which are guided by the recommendations of the CVMP strategy on antimicrobials 2006-2010. The CVMP Scientific Advisory Group on Antimicrobials (SAGAM) is well established and involved in the assessment of marketing authorisations for centrally authorised antimicrobials. The CVMP recommendations on (fluoro)quinolones, 3rd and 4th generation cephalosporins and MRSA (Meticillin Resistant *Staphylococcus Aureus*) were summarised.

  K. Törneke concluded that the CVMP believe in prudent use, in the need for transparency and close collaboration with other stakeholders and finally in the need of implementation of warning texts and compliance with recommendations. Finally she highlighted the need to further implement biosecurity, vaccination and education to reduce AMR.

- European Commission activities in the field of antimicrobials: M. Terberger (European Commission - DG ENTR)

  M. Terberger considered that a more complete understanding of the problems was required and that the Commission had therefore requested EFSA, ECDC, EMEA and SCENIHR to provide a common report on AMR. The HMA plan on AMR is considered a very positive step on the various activities on AMR. The Commission was taking both direct and indirect action in the area in terms of arranging for the collection of AM sales data by the EMEA, strengthening cooperation within the network, promoting and engaging fully in international cooperation and stimulating research and innovation. Where necessary, further direct action could include referrals, requests for further guidance development and new or amended legislation.

  There are a number of documents that will feed into the further development of Commission AMR policy including; the conclusions from this meeting, the Swedish Presidency results to be provided in Stockholm in September 2009, the previously mentioned report of the 4 agencies as well as the ECDC-EMEA report on AMR (gap analysis on trends of disease and pipeline of new antimicrobials).

  He concluded that AMR from human and veterinary use of antimicrobials is a key issue of high interest for the Commission and that there is a need for continuous communication with all stakeholders.

- EMEA activities to foster implementation of CVMP recommendations on antimicrobials: D. Mackay (EMEA)

  D. Mackay presented the EMEA activities on AMR. The role of the EMEA is to foster the development, maintenance and implementation of the CVMP Strategy for antimicrobials. This is achieved by a combination of direct measures, such as the publication of guidelines, reflection papers and decisions in relation to centrally authorised antimicrobials, and indirect measures, such as cooperation with other EU and international organisation and coordination with HMA, NCA, industry and other stakeholders.

In the discussion of this session, concern was expressed that there is a lack of clarity as to who 'leads' within the EU on the subject of AMR. Dr Terberger considered that it would be useful for the network to conduct a 'mapping' exercise between the HMA Action plan, the CVMP strategy on antimicrobials and the June 2008 Council Resolution on Antimicrobial Resistance with two objectives. First, to identify any gaps requiring additional action and, second, to identify and agree who has lead responsibility for each area. Dr Terberger considered that in such a complex area as AMR, there is no one organisation that will have overall responsibility but that each player should be clear as to their own area of responsibility and action.

The need for a communication strategy on AMR was emphasised. In this strategy there would be a key role for stakeholders in delivering messages on prudent use to their user communities.

Conclusions from Session 1

- Regulatory requirements have to be balanced against the need for therapeutic treatments for animals
- Communication is key in any issue related to AMR and regulatory bodies must not only take appropriate action but must be seen to be taking appropriate action
- Any consideration of the use of antimicrobials in animals is not complete without a parallel discussion of the use of antimicrobials in man and must therefore involve all interested parties
- Extensive guidance from CVMP is in place but needs to be better communicated and implemented
- Comprehensive CVMP reports on fluoroquinolones, cephalosporins and MRSA are available

- CVMP strategy on Antimicrobials is based on prudent and responsible use. Prudent use is still the preferred option, but there is a need to know the impact of recommendations from regulators and other bodies (e.g. veterinary associations) on the use of the antimicrobials

- CVMP should pursue and ensure implementation of its recommendations on AMR, including those from the informal CVMPs in Paris and Brno

- There is a need for continued training of veterinarians and farmers on AMR

- Responsibilities of different parties (HMA, EMEA...) on AMR have to be communicated and tasks distributed accordingly

- More information is required on antimicrobial resistance (in general) and on use of antimicrobials in veterinary medicine e.g. knowledge of prescription practices and patterns

- All stakeholders should not hide behind a lack of information to delay action

- Many activities are currently ongoing in the field of AMR including e.g. HMA Action Plan under the Swedish Presidency, Joint Report to the Commission from EU Agencies, Commission activities and also from the pharmaceutical industry, the need now is for better coordination

- There remains a need for new and more effective antimicrobials

Recommendations

- Stakeholders should be involved at all levels on AMR discussions highlighting the need for further communication and coordination on AMR

- Prudent and responsible use should be promoted, restrictions on the use of antimicrobials should be introduced only when there is a scientifically sound basis

- Continued training on AMR of veterinarians and farmers is required

- There is a need to 'map' responsibilities in terms of implementing the policy of prudent use and identify who should lead in each relevant area. This mapping should include an assessment of 10 June 2008 Council Resolution on AMR to identify any gaps in actions or responsibilities

- CVMP recommendations on fluoroquinolones, cephalosporins and MRSA should be implemented by all concerned parties

- Other measures like biosecurity, vaccination, and education on use of Antimicrobials should be promoted as an integral part of the 'prudent use' agenda

SESSION 2 : WORKSHOP ON PRUDENT USE

Presentations:

- National experience with implementation of the prudent use warnings in the SPCs: Lucie Pokludová (Czech Republic)

Dr Pokludová reported the results of a survey of the prescribing practices of veterinary surgeons carried out in the Czech Republic where prudent use warnings have been systematically introduced since the 1990s. The results showed that knowledge of prudent use was variable and that factors other than professional knowledge frequently influence prescribing practices (e.g. price, number of

administrations required, withdrawal period, advertising and promotion). Factors identified that would improve prescribing practices in line with prudent use guidelines include more information on resistance in target animal pathogens, appropriate package sizes for all species, removal of disincentives to use appropriate antibiotics and making SPCs readily available. Dr Pokludova concluded that vets should therefore be addressed directly, that communication was key and that the discussion had to go wider than merely providing technical information on resistance and susceptibility.

- Responsible use of veterinary antimicrobials in the UK: John FitzGerald (Veterinary Medicines Directorate, UK)

John FitzGerald reported on the UK experience where the term 'responsible' rather than 'prudent' use is preferred. The term 'prudent' implies a continuing reduction in use which may not always be appropriate. In contrast, 'responsible' implies appropriate use whether or not this results in an overall decrease. The UK VMD had been active in the field for at least the last decade and had placed great emphasis on communication. A major step had been the creation of the Responsible Use of Medicines in Agriculture (RUMA) stakeholder consortium comprising farmers, agricultural training organisations, pharmacists, the animal health industry and welfare organisations. Regulators have an observer role in this consortium and include VMD, Defra and the FSA. RUMA produces species-specific guidelines separately for vets and animal carers which are available free of charge from its website. This concept had now been followed at the European level with the creation of EPRUMA.

In the discussion of this session the difficulty of interpreting data on sales of antimicrobials was discussed, for example a reduction in sales could reflect successful implementation of prudent use or merely a reduction in the overall numbers of animals. Any policy therefore needs to be accompanied by accurate means of measuring its success and events can overwhelm even the most successful campaigns (e.g. will the current flu pandemic lead to a massive increase in AM usage in man?). It would be useful to survey the factors influencing prescribing habits across the EU to identify the relative importance of 'non scientific' factors such as withdrawal periods, costs etc.

Workshop 1 : How to influence prescribing habits of users of antibiotics and effectiveness of prudent use phrases in SPCs?

As goals were identified:

- Making informed decisions on what antibiotic to use and when to use it
- Responsible/prudent use phrases should have the impact that they deserve
- It is recognised that veterinarians are under pressure to take into account what farmers want, including economic aspects. It is also recognised that cost issue of food production is a main problem (costs *vs* income). However, veterinarians, and also farmers, have responsibility for public health

What can/should regulators (HMA/CAs, EMEA, Commission) do to achieve their goal?

Within this framework, the main conclusions from the workshop are summarised below.

HMA/CAs – national level/network:

- Improve communication to veterinarians, farmers and others.
  - Tools: Website, hardcopies, national language, are there better ways? Questions asked were: Do veterinarians know what an SPC is? Is the SPC a good tool to communicate?
  - Direct communication seems preferred by veterinarians. A survey should be conducted to find out what is the best way to communicate with vets
  - Short messages should be given on how to use a product
  - Key messages we want to deliver should be well communicated: responsible use / consequences

- Professional responsibility should be stressed, already during university education, and later via National professional chambers as part of continuing professional development (CPD)
- Training veterinarians/vet students
- Feedback mechanisms
- Legal measures to restrict use: consider within the next revision of the veterinary legislation including the provision to allow rejection of applications for certain antimicrobials for veterinary use where this is in the overall interests of public health; possibly consider how to restrict generic antibiotics where their entry into the market is clearly not in the interests of prudent use; measures should be evidence based and controls in place for their correct implementation
- Precautionary measures may be necessary, e.g. to limit use of some products for veterinary use
- Surveillance programmes, accessible to all

EMEA, Commission:
Coordination role on EU level for actions

Industry:
Important role / responsibility in
- Advertising practices
- Education
- No gifts to veterinarians that could affect choices related to prudent use, no irresponsible influence of farmers
- Appropriate control of generics (e.g. FQs)

Veterinarians
- Important role, responsibility in prudent and appropriate use
- Change in practice in animal husbandry, e.g. liquid feed

Farmer and animal owners
- Important role, responsibility
- Previously not adequately recognised as a target for prudent use, particular when there is an integrated production chain (breeder, rearer, slaughterer, retail)

Workshop 2: What more can each responsible body do to promote prudent use (Medicines agencies, EMEA/CVMP/SAGAM, veterinary surgeons and their professional bodies, colleges and education establishments, farmers and owners of animals)

Discussion in this workshop focussed on the knowledge gap that exists in terms of prudent use and how best to bridge it. Best practice already exists amongst almost all stakeholders and what is required now is to identify that best practice and then disseminate it more widely. A good example is the RUMA and EPRUMA partnerships which emphasise the key role for stakeholders. Embedding prudent use as part of continuous professional development should be given priority and the cultural aspects influencing AM usage should not be ignored. National Medicines Agencies could promote prudent use to relevant national bodies and then actively take part through the supply of information in writing, on websites or at conferences.

Conclusions from Session 2

- HMA has a leadership and coordination role in the field of AMR and the HMA Strategic Plan should act as the catalyst for implementing this role

- Many factors other than professional knowledge (e.g. culture, history, cost, profit, availability etc) influence prescribing habits of veterinary surgeons and an understanding of these factors is important for effective implementation of prudent use guidelines

- A clear need was identified for better dissemination to prescribers and users of antibiotics of knowledge on resistance patterns in target animal organisms and on the optimum choice of antibiotic and dosage regime per indication

- Early and continuous engagement of stakeholders is essential for successful implementation of prudent use guidelines. The existing forums, such as RUMA/EPRUMA, can serve as useful models

- It is important to identify the appropriate drivers for engagement for each stakeholder rather than relying on altruism

- All efforts to promote prudent use risk being undermined by market factors such as

    - decreasing cost (e.g. there is evidence in some member states of an increase in the use of fluoroquinolones once the advent of generics results in a drop in price)

    - the shorter withdrawal periods of newer antibiotics make them particularly attractive in food producing species

- Continuous professional development is an important communication mechanism to reach vets and influence their prescribing habits

- Communication is key and needs to address more than just the message – also need to change the culture

- There is a need to ensure that the whole of industry respects prudent use in terms of advertising, promotion etc. It is not clear that the current mechanisms are effective, particularly as they only affect members of participating trade associations

Recommendations arising from the Workshop

HMA, as part of creating their Action Plan, should

- Include a survey of the prescription status of antibiotics and prescribing practices in Member States (i.e. who can prescribe, what controls and monitoring of prescription exits) as this will be useful to understand divergence in the EU

- Consider carrying out a survey in association with the Federation of Veterinarians in Europe (FVE) to identify factors that influence the prescribing practices of vets and to determine what are the best methods of communicating to them

- Create a communication plan that uses existing vehicles as much as possible (e.g. RUMA, professional associations)

- Encourage the development of tools to assist with the selection of antimicrobials in terms of active substance and dose which are targeted at particular user groups (companion/farm vets, generalist/specialist)

SESSION 3 : COORDINATING ACTIVITIES RELATED TO THE RATIONAL USE OF ANTIMICROBIALS

Presentations:

- Implementation of the HMA Strategic Plan on Antimicrobial Issues: J. Bureš (Czech Republic)

  J. Bureš presented the HMA Strategic Plan on Antimicrobial Issues that was adopted by HMA the previous day. The strategy is aimed to maintaining the efficacy of antimicrobials and containing the development of resistance. The strategy recognizes that a global approach is needed, and that a risk based and proportionate approach for maintaining availability is required. The focus of all actions should be based on the prudent and responsible use of the antimicrobials in veterinary medicine, with better cooperation and coordination.

- Results of HMA survey of collection of data on sales and use of Antimicrobials in Member States: L Pokludová (Czech Republic)

  L Pokludová presented the outcome of the HMA survey on the collection of data on sales and use of antimicrobials in EU Member states based on the HMA Action Plan. The aim was to obtain information on the bodies in the Member States responsible for collection of data on sales and use of antimicrobial veterinary medicinal products, and on the basic characteristics / description of the systems used.

  The survey showed that while data are collected in most Member States the approaches applied vary. For the future there is a need for a close co-ordination of activities between MSs and EMEA.

- Industry Activities on Collection of Data on Volume (Sales) of Antimicrobials and Proposals for the Future: L. Klostermann (IFAH-Europe)

  L. Klostermann presented the activities by industry to date on the collection, analysis and use of data on sales on antimicrobials. Surveys under the umbrella of CEESA were initiated in 2002, 2004 and 2006. Data collections were on kg active substances basis. Data on sales or generics were not included. Species differentiation in terms of sales could not be ascertained.

  Challenges and lessons learned: Data do not always match with governmental surveys; collection of data on national level is an absolute necessity, although it may be validated centrally; dialogue between industry and regulators and coordination between authorities is essential; all marketers should be involved; simple and pragmatic systems are required. IFAH-Europe is committed to a fruitful dialogue and cooperation.

- National Experience on collection and analysis of data on AM sales and use: G. Moulin (France) and V.F. Jensen (Denmark)

  G. Moulin presented the French experience on collection and analysis of data on antimicrobials sales and use. The aim of the system is to have a picture of the use of antimicrobials and to see evolutions; this determines the level of detail required. Both monitoring of AM sales and use and resistance monitoring are essential for full risk analysis.

  The French system is based on a simple questionnaire to industry towards the end of each year, requiring data on each sale package of VMPs containing an AM to be submitted for the past year. 100% response and the confidentiality of data must be ensured. Data quality is checked. Also data on the number of animals in the country are collected.

  Output data are tons of antimicrobials, tons of antimicrobials/ potential body weight treated, number of treatments, DDD, DDA, DDA kg. Conclusions of the significance of figures need to be drawn with great care. An approach for the repartition by species has been developed and refined over the years that is considered adequate for the purpose. Any system should be simple, cost-effective, and fit for the needs.

  V.F. Jensen explained the Danish experience on collection and analysis of data on antimicrobial sales and use – VetStat, which was introduced following a decision in 1998 to establish a medicine consumption database based on ”end-user-data”. The implemented system is however based in practice on prescription level data. The aim is to optimise medicine use and prudent use guidelines.

Reporting of sales data is mandatory. VetStat uses existing electronic data system as far as possible for the collection of data. Veterinarians and farmers can get POMs only through pharmacies (except for POM medicated feed – from the feed mills), and the billings system for prescriptions is the main source of data collection. This is complemented by the information from feed mills and data collection from veterinarians, if they use another data system.

VetStat has given the potential of detailed multifactorial modelling of effect of usage on resistance, i.e. allowing to identify consumption patterns/high risk herds, and provides valuable information on usage patterns and factors affecting usage.

The National Defined Animal Daily Dose is considered superior to kg active compound – both for surveillance and research. An international DDDvet is considered superior for international surveillance and work has started at WHO to agree how this should be defined.

- Coordination of collection of data on sales of antimicrobials: J. Torren (EMEA)

J. Torren summarised the proposal of the EMEA for the collection of data on use of antimicrobial veterinary medicines in the EU following a request of the European Commission to collect such data. The purpose of the monitoring is to document variations in antibacterial medicine consumption, detect patterns of use and trends, to allow risk profiling, for setting risk management priorities and to assess the impact of prudent use recommendations, thus allowing to make evidence based recommendations.

First, the existing data/surveillance systems in the Member States have been identified in collaboration with HMA. Now a harmonised approach for data collection is being developed for the collection and reporting of data for estimations of usage in at least major groups of species (poultry, pigs, cattle, other ruminants, fish and major companion animal species).

For defining the minimum requirements for the collection of data a meeting with responsible Member State bodies will be held in autumn 2009. The analysis of existing data for 2009 is planned by November 2010, the first phase of a coordinated data collection involving all MS is scheduled for 2010.

The system should be simple, feasible and respect confidentiality. It is proposed that the data should be reported by e.g. the pharmaceutical industry, wholesalers and feed mills and all antimicrobials used in animal husbandry and in companion animals should be reported. Currently it is considered applying the ATCvet code, but further discussions on the required detail are required. Also animal population data are proposed to be included in the data collection, e.g. the number of animals/species slaughtered.

Further discussions are required of the details required for future data collection to obtain data on the use of antimicrobials, and to include details on age groups, type of animal production, and usage at herd or farm level to be carefully considered, including resources required and objectives of obtaining data per species. This would require reporting by veterinarians, pharmacies and feed mills (when relevant).

It is proposed that a step-wise, simple approach is applied with first coordinating the collection of sales data on national level, and collating such data for the EU. The approach can be refined later and more details collected. The task of the EMEA would be to collect the data from Member States and manage the database, to draft a summary annual report with the data from Member States and to analyse the data.

Conclusions from Session 3

- A co-ordinated approach to the collection of AM sales data as part of the HMA Strategic Plan will be vital to achieve success

- The data collection on sales and use of antimicrobials varies between EU Members States. For the future there is a need for a close co-ordination of activities between Members States and EMEA

- The industry project on data collection was presented highlighting obstacles and lessons learned. IFAH-Europe expressed their commitment for cooperation. The main recommendations from industry were

    - Keep the system simple, at least initially, and focus on sales of active (in Kg)
    - Collect the data at national level and not centrally
    - Cross check data from several sources as it is essential to validate (central vs national; industry vs wholesalers etc)
    - Collect data from all marketers of Antimicrobials (i.e. pioneer companies and generics)
    - Collect data from all Member States
    - Ensure an open, frank and constructive dialogue between industry as the providers of data and NCAs as the collectors and users of this data
    - Ensure collection of contextual data (production figures, numbers of animals, disease incidence, etc)

- The examples of data collection systems by France and Denmark were presented in detail and discussed

- The experience gained by these countries and from the industry survey will be highly beneficial for setting up a project for collecting data for the EU and their analysis

- The project proposal for the collection of sales/use data for EU level and their analysis by the EMEA and the possible mechanisms for data collection was presented

- There was general support for collecting data for the EU; the EMEA should have the coordinating role

- It is important to communicate the reason why the data is required to motivate all players in its supply and collection

- Any system introduced must be stable and consistent i.e. not prone to frequent changes

- Reassurance must be given, and confidence built, that systems are confidential and secure

Recommendations

- A step wise approach should be applied to the collection of AM sales data, starting with the collection of sales volumes, and moving forward progressively and to look to more details later on

- The experience available from data collection in other countries, and from industry, should be used to refine the EMEA proposal

- It is considered most appropriate to collect sales data on national level, with the EMEA to coordinate collection, validation and analysis of the collated data

- It is important that all marketing authorisation holders of antimicrobials are included in the data collection

- Data must be collected in a consistent manner at national level

SESSION 4 : EXPECTATIONS AND ACTIONS IN THE AREA OF PRUDENT USE

Objective(s) of the session:

- The objectives of this session were to share with stakeholders their experience and views in the wider area of prudent use and the implementation of prudent use, including harmonisation of SPCs
- Hear from the DG SANCO about the Commission activities and perspective on AMR

Presentations:

➢ EPRUMA – turning aspiration into reality: D. O'Brien (IFAH-Europe)

The mission of this activity established in 2005 is to promote responsible use of medicines in animals in the European Union. It covers all medicines, not only antimicrobials. The initiative includes active participation of different stakeholders (COPA-COGECA, EISA, FEFAC, FESASS, FVE, IFAH-Europe) covering the whole production chain up to the point where the products leave the farm gate. The platform works by agreeing what are the issues of concern in particular with respect to public health, animal health and welfare and the environment, providing an informed consensus on these issues. The aim is to agree on best practice and to implement such best practice in field conditions. The first production of this initiative is a booklet summarising the consensus view on the best practice framework. The framework is adaptable to the Member States level. Translation into several languages has been prepared and the steps to follow are translation to more languages, dissemination of the information, and assurance that the principles are implemented in practice. A stepwise approach is taken. A key part of the process is education, both pre-graduate education and continuous professional development programmes. Aspiration needs to move to reality and steps on this are in place.

In summing up, industry recognises that

- antimicrobials are very important veterinary medicines with beneficial effects in animals husbandry

- responsible use is needed

- engagement of all stakeholders is needed

- delivery of best practice principles to the practice, including development of the continuous professional development, leading to real change is needed

Integrators operating at the Member State level need to be considered as stakeholders (i.e. 'farm to fork' operations)

- Experience and Observations on Implementing Prudent Use of Fluoroquinolones: L. Klostermann (IFAH-Europe)

History of the prudent use, international (WHO, OIE) as well as EU activities were mentioned. In addition, an overview of the guidelines produced by different associations was given. In relation to SPCs harmonisation for FQs, industry mentioned that the warnings have been included in a number of countries since the first authorisations of the products. The impact on the costs related to changes of product literature was mentioned as well as the possibility to use existing stocks of the packaging materials. Administrative difficulties in a few countries resulted in the delay in the introduction of the changes. An example was given on the possible influence of market competition on consumption of FQs. In summary, the industry expressed the view that the prudent use principle has a long history in the European Union, the principle is very well established and understood and implementation and effects ran successfully. Measures are most effective if all MAH as well as all NCAs are fully committed. It is very important that the timely and complete inclusion of the prudent use warning into the product literature is implemented. Update of the product literature has been mentioned as a first step in the prudent use.

- Prudent use of cephalosporins, Experience and observations: V. Thomas (IFAH-Europe)

IFAH-Europe expressed full support for responsible use of antimicrobials. Industry consider that it has taken a very positive approach to ensuring responsible use for modern antibiotics. Prescription only status has been stressed to be very important as well as the role of the veterinarians at the farm with local knowledge. Parenteral administration / individual treatment were also mentioned as important aspects for such valuable antibiotics. The importance of susceptibility testing and surveillance both at national and European level were mentioned. With respect to cephalosporines, the industry is not completely in agreement with the current reflections formulated in the CVMP Reflection Paper on Cephalosporins, namely to consider them as reserve antibiotics and to have only restricted indications on the SPC. In accordance with the industry opinion and experience, the volume (amount) used is an important indicator with respect to resistance development and the overall volume of cephalosporins used is low relative to other antibiotics. This view was challenged in the subsequent discussion by regulatory speakers saying that the number of animals actually treated may be more important than the relative percentage of the compound / class used as the specific activity of the active is an important factor. In addition it has been stressed in the discussion that because of their potency, including potency to select for AMR, these molecules need careful consideration. The importance of surveillance and susceptibility testing was stressed by the industry as a tool for improving prescription practice. All MAHs should participate in the surveillance programmes. In the opinion of the industry the level of resistance to cephalosporins is very low and the main focus should be development of the (regional) surveillance programmes with further research into what other measures might be taken.

- Resistance against anti-microbial resistance: veterinarians' goals and initiative: J. Vaarten (FVE)

One of the key policies is promotion of "One Health" linking human and animal health together. AMR is a part of the One Health concept. Biosecurity was a topic of the November 2008 Veterinary Week – it was emphasized that biosecurity includes not only avoiding introduction of new pathogens on to the farm but also to control the on-farm infection pressure at a low level.

Veterinary profession initiatives can be divided into the initiatives taken at the EU level and initiatives taken at the national level. At the EU level a MRSA conference was mentioned that resulted in several publications in veterinary journals and increased awareness and discussions at the national level.

A European Code of Conduct has been developed, which includes the issue of antimicrobial resistance.

FVE is involved in the ERRUMA initiative. UEVP (Union of European Veterinary Practitioners) is going to have this issue at their agenda as well.

The new European Animal Health law, which is now under discussion, should also include the issue of containment of antimicrobial resistance.

There are important differences in the organisation of the veterinary profession regulatory bodies across the EU with different roles and responsibilities. This results in limitations as to what the regulatory bodies do and what they can do.

Concerning the measures at the Member States level, a survey has been done across the EU and in general a broad range of activities and initiatives can be seen, with different effects in the practice. The focus is in particular to food producing animals, especially intensive farming. The different activities include dissemination of information, promotion of prudent use, national guidelines on prudent use, farm management, health plans, biosecurity, evaluation and audits, stimulation of the farmer – vet relations. Initiatives in the pre- and post- graduate training exist. In some countries the right to dispense medicines may be subject to extra training and/or a quality assurance scheme. Some countries apply "de-coupling", i.e. separation between prescription and sale. The environment in which veterinarians work is changing substantially – the most important changes being liberalisation on the market, competition at the global level, and pressure on food prices.

The veterinary profession is committed and willing to take actions, stricter rules alone will not solve the problem, they are seen as a part of the measures. A change of the culture is needed with ensuring more compliance with engagement of the full food chain.

- Reduction of antimicrobial use and resistance: any other options than reducing triggers for bacterial disease?: K. Hellmann

K. Hellmann on behalf of AVC challenged whether the correct approach was being adopted at a fundamental level. Modern production systems inevitably lead to higher levels of disease and therefore a greater risk for infectious disease. He hinted at potential factors increasing infectious disease including increased trade and transport, deficient housing and management. Therefore animal producers have to be included in any discussion on AMR. For the producers, cost effectiveness is the key factor in deciding whether to opt for improvement of housing and management including biosafety, vaccination or the use of antibiotics to control infectious disease. He also stressed the need for better diagnostics and post-mortem facilities to achieve more accurate use of antimicrobials in infectious disease.

- European Commission activities in the field of antimicrobial resistance: K. De Smet (European Commission - DG SANCO)

An overview of the problem from the public health perspective was made, including recognition of the role of human as well as veterinary medicine. It has been stressed that each sector (human and veterinary) takes its own responsibilities. Examples of selected animal species and of the zoonotic pathogens which are of concern with respect to public health protection, including overview figures were mentioned. The aim is to develop an EU risk based strategy on zoonotic antimicrobial resistance in line with the international standards. For this, different elements need to be considered. Data collection is the first step to establish the prevalence of AMR and to gather data on the use of antimicrobials which will be further used for scientific risk assessment and as the basis for consequent risk management measures. An overview of the EU monitoring programmes and data resources were made. The new initiative – Commission (ENTR/SANCO) request to EMEA/EFSA/ECDC/SCENHIR common short report on AMR focusing on zoonotic infections was explained. The first phase is concentrated on the public health problems. The importance of different sources of AMR (use of antibiotics in humans, animals, other sources) should be addressed in the report. As a second term of reference, priorisation of zoonotic species/agent/antimicrobial combinations of highest concern should be given. Identification of alternatives for prevention or treatment of animal diseases should be a part of this exercise. The purpose of this activity is to inform ongoing initiatives and to start reflections on additional management options that might be needed. Risk management measures taken in the human and veterinary medicine were overviewed. Evaluation of trends and results of actions shows that more actions need to be taken as the prevalence of AMR is not reducing. Concerning communication, a number of co-ordinated activities are running within DG SANCO to cover all different areas. Because of the complex nature of the issue of AMR, mutual communication is of utmost importance. The most dangerous position would be to take actions based on limited information available to individual

parties involved. Concerning international impact, it must be noted that FQs were banned by one of the biggest EU trading partners, the US. This requires that the EU looks seriously into the problem. In conclusion, the Commission tries to develop a comprehensive strategy on AMR in zoonotic infections in collaboration with DG ENTR and relevant EU agencies.

Conclusions from Session 4

- Different parties in the EU (official bodies / authorities, industry, professional asociations) have taken actions in the area of AMR both at the EU level and nationally and the different stakeholders now need to work more closely with each sector (human and veterinary) taking its own responsibility with respect to AMR.

- The 'one health' aspects of AMR should continually be emphasised in any discussion on AMR and this should include the need for Antimicrobials to control disease in animals that has the potential for transmission to man

- The inclusion of the prudent use warning for FQs was supported by all stakeholders, but this requires complete and timely actions from all MAHs and NCAs

- Introduction of any change to product literature with respect to prudent use warning should be done according to risk analysis principles and the costs incurred to the industry need to be carefully considered so that such exercise is efficient but unnecessary side costs (e.g. labelling) are avoided

- Market competition may play a role in the implementation of the responsible / prudent use policy

- Continuing profession development is a key tool to implement prudent use

- Discussions of prudent use must cover the whole spectrum of the topic including alternatives to antimicrobials and non-therapeutic interventions such as changing husbandry systems

- The environment in which the veterinary profession and farmers work is changing substantially – the most important changes / factors being liberalisation of the market, competition at the global level, and pressure on food prices, and these factors need to be considered when decisions on regulatory actions are taken

Recommendations

- Ensure that different parties are informed about the progress in the initiatives taken by the other parties on regular basis and that the activities are co-ordinated accordingly

- Facilitate implementation of different activities in practice (e.g. help to the industry with the translation of the EPRUMA to help to have the information available in all EU languages)

- The market competition issue and its influence to the prudent use policy may need to be taken into account when future changes to the veterinary pharmaceutical are considered

- To think about further development of the resistance surveillance programmes in the EU, including programmes providing appropriate data on the regional level

- Involve and motivate stakeholders from an early stage

- Apply all measures related to prudent use in an equal manner to all section of the animal health industry

SESSION 5: FINAL CLOSED SESSION FOR AUTHORITIES

Conclusions from Session 5

- The AMR issue is highly complex and the whole scientific agenda and rationale can be de-railed by non-scientific factors such as pricing and withdrawal periods

- It may be too simplistic an approach to continue to consider that price/cost cannot be considered as part of the licensing process as these factors are key to the pattern of use of any antibiotic

- A way needs to be found to ensure that costs, withdrawal periods etc promote rather than undermine prudent use

Recommendations

- Careful consideration will need to be given during the next revision of the veterinary legislation governing AMR to take into account
    - The special nature of the benefit risk assessment for antimicrobials, especially those used in both man and animals
        - The need to take cost to the user into account
        - The need to take the impact of withdrawal periods into account

ANNEX: LIST OF ATTENDEES

European Medicines Agency	Dr David Mackay Dr Kornelia Grein Mr Jordi Torren Edo
International Federation of Animal Health (Europe)	Mr Declan O'Brien Dr Ludwig Klosterman Dr Valerie Thomas Dr Marie-anne Barthelemy
European Group for Generic Veterinary Products (EGGVP)	Dr Rob Joosten
Federation of Veterinarians in Europe (FVE)	Dr Jan Vaarten
Association of Veterinary Consultants (AVC)	Dr Klaus Hellmann
European Commission DG ENTR/F2	Dr Martin Terberger Dr Karin Krauss
European Commission DG SANCO E - Safety of the Food Chain	Dr Kris De Smet
Chair of CVMP	Dr Gérard Moulin
Chair of CMDv	Dr Esther Werner
Chair of SAGAM	Dr Karolina Törneke
Community Reference Laboratory for Antimicrobial Resistance	Dr Vibeke Jensen
Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)	Dr Cornelia Ibrahim
Latvian State Agency of Medicines	Ms Inguna Adovica
Veterinary Medicines Directorate	Ms Jackie Atkinson Mr John FitzGerald
Austrian Medicines and Medical Devices Agency	Mr Eugen Obermayr
Ministry for Labour, Health and Social Affairs, Italy	Ms Alessandra Perrella
Federal Ministry for food, agriculture and consumer protection, Germany	Dr Thomas Schneider
Danish Medicines Agency	Prof. Per Helboe

Medicines Evaluation Board, the Netherlands	Mr Frank Verheijen
The European Group for Generic Veterinary Products (EGGVP)	Dr Inge Sandberg
National agency for veterinary medicinal products (AFSSA)	Dr Patrick Dehaumont
Medicinal Products Agency, Sweden	Dr Henrik Holst
Agency for medicinal products and medical devices of the Republic of Slovenia	Ms Martina Cvelbar
Irish Medicines Board	Dr J. Gabriel Beechinor
Institute for State Control of Veterinary Biologicals and Medicaments, Czech Republic	Prof. Alfred Hera Dr Jiří Bureš Dr Leona Nepejchalová Dr Lucie Pokludová Ing. Josef Suchý