



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



Report of the “Progress in the area of Antimicrobial Resistance – Veterinary Medicines” meeting, organised by the EMA and the HMA (veterinary)

Thursday 15 & Friday 16 September 2011

**EMA
7 Westferry Circus, Canary Wharf,
London, E14 4HB**

“Progress in the area of Antimicrobial Resistance – Veterinary Medicines”

Thursday 15 September 2011

Summary

This was a well attended meeting with relevant stakeholders represented. The list of speakers and attendees can be found at Appendix 1. The presentations focused on the progress made in relation to veterinary medicines and antimicrobial resistance in the previous 18 months, current activities and plans for the future. The meeting discussed and agreed upon areas for prioritisation and greater collaboration, to ensure that existing antimicrobials remain effective, that antimicrobial resistance development is slowed and that animals can be treated with appropriate antimicrobials to ensure their health and safety, so contributing to the “One Health”¹ agenda. Common themes included:

- the need to examine the impact of existing initiatives, when deciding on future measures
- any measures should be science based and proportional to the risk
- the need for data to be directly comparable (surveillance and use) and a common definition for “resistance”
- the importance of clear, fact based communications
- antimicrobial resistance does not recognise political frontiers, any EU activity on antimicrobial resistance (AMR) should take place in a global context
- the need to differentiate between existing antimicrobials and new antimicrobials when authorising antimicrobial products
- the desire that the European Commission provides support, including funding, on the animal medicines side, as they have done for human medicines on key areas like training of veterinarians and farmers and campaigns to promote responsible use

1. Welcome and Introduction

Dr David Mackay and Professor Peter Borriello opened the meeting. It was recognised that the area of antimicrobial resistance is a very important one that many different stakeholders

¹ <http://www.onehealthinitiative.com/>

had an interest in, it is a matter of international concern and there is also a high level of political interest. Those attending the meeting had a common objective of minimising the risk of antimicrobial resistance developing through the use of animal medicines. It was recognised that changes to the EU legislation were under discussion and there is a strong desire for any changes to be proportionate and evidence based, although it was acknowledged that it was likely that proposals would have to be evidence informed, given the still remaining gaps in the scientific information.

2. “The Commission activities on AMR (focus on zoonotic issues)” Presentation by Mrs Rosa Peran i Sala on behalf of the European Commission, DG SANCO

Rosa Peran reminded the audience that there are different directorates in the Commission involved in antimicrobial resistance, with DG SANCO being responsible for co-ordinating this work. The need for a holistic approach to the problem was emphasised, taking into account not just medicines but other areas such as use of biocides. Reference was made to the 2009 Staff Working Paper, the 2010 public consultation, referrals, scientific opinions and the European Parliament resolution from May 2011 which called upon the Commission to develop a broad multi-annual plan and to update monitoring programmes and controls. The feedback and information gained from these are being used to help inform the proposed revisions to the EU legislation in the area of antimicrobials. The Commission aim to publish their 5 year strategy on antimicrobial resistance on 18 November 2011. The strategy will include concrete actions such as to promote appropriate use, develop new tools to fight microbial infections, investigate antimicrobial resistance and its sources, causes and consequences, improve communication, promotion of international co-operation.

3. “Progress in the Area of Antimicrobial Resistance – Veterinary Medicines” Presentation by Mrs Jackie Atkinson on behalf of HMA-Veterinary Taskforce

Jackie Atkinson provided an overview of the work undertaken by the HMA veterinary taskforce over the last 18 months. The HMA veterinary taskforce was formed in December 2010 to finalise an action plan on antimicrobial issues and to oversee its delivery. Work already completed by the taskforce included: identifying the different stakeholder groups and which to engage with, collection of information on national activities on antimicrobial resistance (responsibilities, collection of sales data/prescription data, factors affecting prescribing, advertising rules, surveillance, responsible use guidance, communication, national restrictions on use, targets to reduce use), and developing and finalising the HMA proposals for the revised veterinary medicines legislation in relation to antimicrobials. Next steps included, publishing an overview of the national activities, conducting a survey of EU vets to better understand the factors that influence antimicrobial prescribing habits, and developing communication materials. A copy of the action plan can be viewed at http://www.hma.eu/uploads/media/HMA_AMR_Action_Plan_Feb_2011.pdf.

4. “Progress in the Area of Antimicrobial Resistance – Veterinary Medicines” Presentation by Mr Jordi Torren on behalf of the EMA

Jordi Torren introduced his presentation and provided an overview of the work carried out by the EMA on antimicrobial resistance. Much of this work involved supporting scientific groups who work on antimicrobial resistance, for example CVMP, the CVMP Scientific Advisory Group on Antimicrobials (SAGAM), ESVAC and collaborating with international organisations such as EFSA, OIE and Codex Alimentarius. The EMA is also responsible for the ESVAC project on sales of antimicrobials, these data should allow for a holistic analysis of data on sales and resistance in humans and animals. An overview of the activities of the sector in EMA responsible for human medicines was given. In the area of human antimicrobials the main area of interest relates to the need for new antimicrobials so that multi-drug resistance organisms can be combated. The activities of regulators in the process of authorising antimicrobials were presented.

5. “Progress in the area of Antimicrobial Resistance” Presentation by Dr Anja Holm on behalf of CVMP

Anja Holm provided an overview of the relevant work of the CVMP. The CVMP has had a strategy on antimicrobials for many years, the current strategy being the third five year strategy². The CVMP has dealt with a series of referrals relating to antimicrobial products and has prepared a number of reflection papers on AMR, for example on MRSA and MRSP. Most recently the CVMP has issued a question and answer document to clarify the meaning of the word ‘prevention’ when a centrally authorised product contains the indication for “prevention and treatment”. Current activities include the review of a number of relevant guidelines and new reflection papers on macrolides, lincosamides and streptogramins and on pleuromutilins. CVMP’s scientific advisory group on antimicrobials (SAGAM) is gathering information on the impact of off-label use of antimicrobials and of use in companion animals. Suggested areas for greater collaboration included identifying gaps in the antimicrobials available to treat certain species and then progressing the development of suitable veterinary formulations of these antimicrobials. The aim is to authorise “the right antimicrobials”. Dr Holm emphasised the need to understand better the link between use of antimicrobials in animals and AMR in man, to ensure that risks are viewed proportionately and risk management is focused on the important areas.

6. “The ESVAC project. Main deliverables and results” Presentation by Prof Kari Grave on behalf of ESVAC, EMA

Kari Grave provided an overview of the work on ESVAC. This is currently in the pilot phase. A considerable amount of work has been done in order to produce “standardised” overall sales data for antimicrobials. The challenges in agreeing on the correct approach to normalise the data to take account of different factors, for example differences in animal demographics, including cross-border movement of animal, was referred to. This has culminated in the publication of a report in which sales data for nine countries for the period 2005-2009 are presented (copies of the report were made available at the meeting and it is now available on the EMA web site³). The call for 2010 sales data has been made to 23

² http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/07/WC500109137.pdf

³ http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/09/WC500112309.pdf

countries that have stated that they are willing to provide the data. In the future, ESVAC will engage with non-EU partners such as FAO, OIE, WHO and FDA, with the view to sharing experience and agreeing common approaches where possible. In discussion the validity of the current “comparative” data was explored, with some comments that it was not appropriate to compare the data between countries without further factors being taken into account. However, it was noted the data does provide information on trends over time and that such information can be highly valuable.

7. “Antimicrobial resistance, the views of EGGVP” Presentation by Dr Elsa Vecino on behalf of EGGVP

Elsa Vecino set out the views of the EGGVP, expressing the organisations willingness to actively contribute in this area, but asking that initiatives did not increase the burden on industry. The EGGVP considered there were four pillars to consider, these were; Objective data and information, Rules and Regulations, Communication and Training. The importance of a global approach to the problem was highlighted. Their support to the need for new antimicrobials and better formulations of existing antimicrobials was given. They illustrated how the timing of authorisation of a particular antimicrobial had a major impact on the indications and proposed that a system of monographs based on active substances be developed as a way to harmonise Summary of Product Characteristics for existing antimicrobial products. In discussion reference was made to the use of PK/PD modelling and to a paper prepared by Professor Peter Lees on this topic. A copy of this paper was made available and can be found on the website with the presentations delivered at the meeting.

Friday 16 September 2011

8. “Progress in the area of Antimicrobial Resistance – activities of IFAH-Europe” Presentation by Mr Declan O’Brien on behalf of IFAH-Europe

Declan O’Brien speaking on behalf of IFAH-Europe reviewed the recommendations on antimicrobials which have been made by various bodies and put forward IFAH - Europe’s own recommendations. These formed part of their four strand strategy which also covered: target pathogen monitoring programmes, responsible use guidance and research into gene transfer mechanisms. Good progress has been made on the target pathogen monitoring programme that involves a number of countries in a pilot. The plan is to publish the first set of data from this programme in the middle of 2013. There are plans to expand the programme in the light of experience. IFAH-Europe indicated that policies and SPC changes need to be scientifically driven and not by the Precautionary Principle by default. IFAH-Europe’s views were sought on the incentives that would be necessary in order to stimulate the development of new antimicrobials for use in animals. IFAH-Europe advised that uncertainty regarding future restrictions on use of antimicrobials might stop new antimicrobials coming into the market. Reference was made to incentives being considered for human medicines, although more thought was required to set out the more effective incentives for animal medicines. Currently the available antimicrobials are considered sufficient to treat animals but it was emphasised this situation might change. At this stage it

was not possible to say for which species and conditions the need for new antimicrobials may arise. It was pointed out that some antimicrobials that are too toxic for use in man may be suitable for use in animals without causing problems of resistance.

9. **“Progress in the area of Antimicrobial Resistance in Veterinary Medicines”
Presentation by Dr Christophe Buhot on behalf of FVE**

Christophe Buhot gave a presentation on behalf of FVE. By having the necessary knowledge, being familiar with the local situation and working under the supervision of a licensing body, veterinarians are part of the solution in the prevention and control of antimicrobial resistance. FVE promotes a number of concrete actions, e.g. further research in the origin of resistance, improving animal health management, strengthening surveillance and creating a stronger relation between the veterinarian, the animals under his care and their owners. They promote the use of “old” antibiotics to safeguard the effectiveness of “new” ones. A campaign to stimulate companion animal vets to have a critical look at the use of antimicrobials will be launched. FVE indicated its support for certain restrictions on the use of fluoroquinolones and 3rd and 4th generation cephalosporins in animals. It was highlighted that the cascade is indispensable. A change in the order of the cascade was advocated to have medicines authorised in other EU countries for the intended species and indication higher up in it. According to FVE the price per dose should be independent from the pack size. FVE is revising the European Veterinary Code of Conduct, giving special attention for the responsible use of medicines. Reference was made to the FVE seminar on 18th November, supported by the Polish Presidency. During the discussion the practicalities of prescribing of antimicrobials at farm level being entered into an EU database were explored.

10. **“Antimicrobial Resistance – the role of European farmers and European Agricooperatives” Presentation by Dr Klaas Johan Osinga on behalf of COPA-COGECA**

Klaas Osinga gave a presentation on behalf of COPA-COGECA. A clear message to farmers is that prevention is better than cure, but if animals become sick they need to be treated. In this regard it was hoped that the revised EU Welfare Strategy for 2011-2015 expected in December this year will state that sick animals have the right to be treated. COPA-COGECA has been involved in a number of national information campaigns to farmers on antimicrobials. The importance of the whole food chain working together was emphasised and the key role of large supermarkets was referred to. COPA-COGECA stated their support for: the promotion of practical disease prevention measures, eradication programmes, voluntary quality schemes, responsible use guidance, evidence based and pragmatic policy. They emphasised the importance of a co-ordinated communication strategy to farmers and consumers and their willingness to help deliver this. The financial pressures on farmers was referred to as was a desire for the European Commission to provide funds which will allow farmers to change the way in which they operate so allowing a reduction in the use of antimicrobials. He considered the EU2020 initiative could be used to fund projects that link science to farming practices. To summarise: three key messages:

- A food chain approach is needed, from farmers to retail and consumers

- We need to build bridges between science, policy and farmers by creating tools through EU2020 (Horizon2020), The Common Agricultural Policy (CAP) etc
- We need a co-ordinated communication strategy: one clear message for farmers and consumers. The 18th of November provides a first opportunity.

11. “EPRUMA – Presentation to HMA/EMA” Presentation by Mr Declan O’Brien on behalf of EPRUMA

Declan O’Brien reminded the audience of the aims and work of EPRUMA. They support a holistic approach to the problem, with disease control and prevention being essential tools. There is a need to convince everyone to follow the EPRUMA guidelines on responsible use of antimicrobials, but it was recognised that specific measures might be required to get everyone to conform. EPRUMA’s antimicrobial framework document is now available in twelve different languages and further language version are being finalised. EPRUMA’s focus is on communicating the message of responsible use. They are using a number of different communication tools, including leaflets, videos and a website. They also have plans to ensure that every veterinary student learns about their responsible use guidance during their training, and for qualified professionals they plan to use continuous professional development (CPD) events. EPRUMA specifically asked the HMA to help communicate responsible use at a national level. It was agreed that the HMA would consider this.

12. “Status quo and current challenges related to antimicrobial resistance: Veterinary consultants view” Presentation by Dr Klaus Hellmann on behalf of AVC

Klaus Hellmann expressed his concern that despite the issue of antimicrobial resistance being one that has been spoken about for more than 20 years, very little progress has been made, although the recent efforts reported by previous speakers were noted. Concern was voiced regarding reports where recommendations, for example restrictions, were proposed but the body of the report acknowledges that sufficient evidence does not exist to inform the most appropriate recommendations to make in order to reduce the development on antimicrobial resistance. AVC indicated their support for any schemes which would promote innovation in the area of antimicrobials, for example faster approval processes. The AVC also expressed their support in areas such as: improving target animal pathogen monitoring, improving the understanding of how resistance develops. The AVC does not support the banning of use of antimicrobials in the absence of scientific evidence to support this. In discussion the meeting expressed strong reservations regarding the European Parliament’s recent decision to fund research into homeopathy and phytotherapy as alternates for antimicrobials as it was felt that such funding could be better spent investigating alternatives for which there is a recognised evidence base.

13. “Overview of areas for collaboration and prioritisation” Presentation by Jackie Atkinson on behalf of HMA-Veterinary

In this final session a series of areas for prioritisation and collaboration were set out based on the previous presentations. These were discussed and amended in light of the

discussions - see Appendix 2. It is now hoped that these will form the basis for future collaborative work.

Those attending:

Chairmen:

European Medicines Agency (EMA): Dr David Mackay
Veterinary Medicines Directorate (VMD): Professor Peter Borriello

Speakers:

The European Commission, DG SANCO: Mrs Rosa Peran i Sala
VMD: Mrs Jackie Atkinson
EMA: Mr Jordi Torren
Committee for Medicinal Products for Veterinary Use (CVMP): Dr Anja Holm
EMA: European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): Prof Kari Grave
European Group for Generic Veterinary Products (EGGVP): Dr Elsa Vecino
International Federation for Animal Health Europe (IFAH-Europe): Mr Declan O'Brien
Federation of Veterinarians in Europe (FVE): Dr Christophe Buhot
COPA-COGECA: Dr Klaas Johan Osinga
European Platform for the Responsible Use of medicines in Animals (EPRUMA): Mr Declan O'Brien
Association of Veterinary Consultants (AVC) – Dr Klaus Hellmann

Delegates:

A J Trees, University of Liverpool
Alasdair King, MSD Animal Health
Alison Glennon, NOAH
Amy Gray, National Farmers Union (NFU)
Ana Mateus, RVC
Andrew Hillan, Norbrook Laboratories Ltd
Anya Thurgood, Dechra Technical Services
Bruno Urbain, CVMP
Catherine McLaughlin, National Farmers Union (NFU)
Chris Van den Eede, PFIZER
Christophe Buhot, FVE
Claire Chauvin, CVMP
Clare Collins, VMD
Clare Tapsfield-Wright, RCVS
Consuelo Rubio Montejano, CVMP/HMA-V Member
Cris Madavo, VMD
Cristina Munoz, CVMP/HMA Member
David Burch, Octagon Services Ltd
David Hurd, David Hurd Consultancy
Dawn Howard, British Agriculture Bureau (BAB)
Declan O'Brien, IFAH Europe/EPRUMA
Despoina Iatridou, FVE
Donal Murphy, NOAH
Edward Ferguson, Pfizer Animal Health
Ellen-Margrethe Vestergaard, CVMP

Erik De Ridder, ELANCO
 Ernesto Liebana Criado, European Food Safety Authority (EFSA)
 Fia Westerholm, CVMP
 Françoise Leblanc, Vetoquinol
 Frank Verheijen, College ter Beoordeling van Geneesmiddelen/HMA-V Member
 Gemma Adam, VMD
 Giles Coley, Dechra Technical Services
 Giles Davis, VMD
 Helen Jukes, VMD/CVMP Member
 Isaura Duarte, EMA
 J G Beechinor, Irish Medicines Board/HMA-V Member
 Jack Kay, VMD/DARC Member
 Jamie Day, Animal Pharm
 Jan Dahl, Danish Agriculture and Food Council
 Jan Vaarten, FVE
 Jean-Pierre Orand, French Agency for veterinary Medicinal Product/HMA-V member
 Jill Moss, The Bella Moss Foundation
 Jiří Bureš, CVMP/HMA-V Member
 Karin Kraus, The European Commission
 Karolina Törneke, CVMP
 Katherine Gray, VMD
 Ken Stapleton, VMD
 Klaas van Aken, Eurovet Animal Health
 Kornelia Grein, EMA
 Ludwig Klostermann, BAYER
 Malcolm Flanagan, Animal Pharm
 Maria Szabo, Directorate of Veterinary Medicinal Products Hungary/HMA-V Member
 Marie Agerso, European Reference Laboratory
 Marie-Anne Barthelemy, SIMV
 Mario Nagtzaam, The European Commission
 Mark Doshier, The Bella Moss Foundation
 Max Thomas, Animal Pharm
 Mike Overend, Huvepharma NV
 Olivier Espeisse, ELANCO
 Pascal Butty, CEVA
 Peter Jinman, RCVS
 Peter Jones, British Veterinary Association (BVA)
 Peter Lees, The Royal Veterinary College
 Peter Silley, MB Consult Limited
 Phil Sketchley, NOAH
 Philippe Naber, Pfizer Animal Health Europe Middle East and Africa
 Richard Young, Soil Association
 Rob Joosten, EGGVP
 Robin Maynard, Compassion in World Farming
 Suzanne Eckford, VMD
 Trish Logie, VMD
 Valérie Thomas, MSD Animal Health
 Wilhelm Schlumbohm, CVMP

Overview of areas for prioritisation and collaboration

1) Monitoring and Sales of Antimicrobials

EMA/ESVAC/ Industry/	Collection and reporting of sales data (at a species level) from across the EU in a uniform way. Reconsider the extent to which existing data e.g. PSUR, commercially available data on sales which is segmented by regions etc, might be used, bearing in mind the ongoing discussions regarding PSURs as part of revising the veterinary medicines legislation.
EMA/ESVAC	Develop/agree common units of measurement of use with others (e.g. WHO Collaborating Centre for Drug Statistics Methodology/FDA)
EMA/ESVAC	Share experiences on collection and interpretation of data on sales of antimicrobials with others (e.g. FDA)

Remarks:

- It is desirable to consider the species farmed in different member states when interpreting data.
- It is important to examine the data on use of antimicrobials in third countries, if available, as well as AMR surveillance data from these countries, if available, as the import of products represents a potentially very important factor.

2) Understanding of Prescribing and Dispensing Habits

EMA/HMA	Map out how antimicrobials are made available to end users in the different member states.
EMA/HMA/ FVE	Developing together a questionnaire for vets across the EU to better understand prescribing of antimicrobials in terms of both legal frameworks (NCAs) and habits (vets). Consider initially running this as a pilot restricted to antimicrobials supplied in medicated feed and drinking water for food animals.
EMA/HMA/ FVE	Analysing the questionnaire data and identify the area where greatest leverage can be placed to modify prescribing habits.

EMA/HMA/ FVE	Promote the development of national or regional formularies to agree and advise on best prescribing practice.
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Remarks:

- Experience gained in collecting information in the human medicine sector may provide some insight to the planned work, although it is acknowledged that the supply of human medicines is complex and follows a different model to veterinary medicines.
- Areas to explore in the questionnaire might usefully include: the drivers to prescribe and supply larger quantities of antimicrobials than necessary and leaving these on farm, the extent of wastage, the level of compliance, whether the terms prophylaxis and metaphylaxis are widely understood.
- A debate is required if, in some situations, the prophylactic use of antimicrobials may be justified on a benefit risk basis. For example, use of intramammary antimicrobials during the dry cow period or for the prevention of shipping fever. Development of a common understanding of when prophylactic antimicrobials are justified would be helpful.

3) **Surveillance for Resistance**

HMA/ Industry	Developing more co-ordinated EU programmes for surveillance of target animal pathogens, sharing findings, considering their significance.
EMA/HMA/ Industry/Vets	Encouraging reporting of suspected lack of efficacy of antimicrobials.

4) **Marketing Authorisations for Antimicrobials**

CVMP/EMA/HMA (+CMDv)/Industry	Harmonisation of SPCs for <u>certain</u> antimicrobial veterinary medicines + prioritisation.
EMA/HMA/ Industry	Implementation of Commission Decisions e.g. Adding warnings relating to responsible use.
CVMP/EMA/HMA/ Industry	Ensure revised EU legislation encourages the development of both new antimicrobials and of improved formulations of old but effective antimicrobials where the risk to man can be shown to be acceptable.
CVMP/EMA/HMA/ Industry/Vets	Identifying and encouraging the availability of the right authorised antimicrobials for first line treatment options, including those for minor species/minor use.
CVMP/EMA/HMA/ Industry	Consider innovative solutions e.g. monographs or other means to promote harmonisation, making an appropriate differentiation for existing antimicrobials and new ones.

Industry (IFAH/EGVVP)	Consider pooling of available data.
Academia/EMA/ Industry	Exploring the use of PK/PD modelling to optimise dose for antimicrobials and promoting its use in regulatory procedures where appropriate.

Remarks

- An early dialogue between industry and regulators during the early stages of development of a new antimicrobial is strongly encouraged.
- It would be helpful if industry set out what type of incentives would actually encourage them to develop new antimicrobials and more convenient formulations of existing antimicrobials which remain effective.
- The Commission is active in supporting work in the area of new antimicrobials for humans, considering “One Health” it would seem appropriate for the Commission to also support the development of appropriate antimicrobials for use in animals.

5) **Communication with stakeholders**

EMA/ EPRUMA / HMA	Co-ordinated, consistent communication to a range of stakeholders (including vets, consumers, large supermarkets).
COPA- COGECA /EPRUMA/ HMA/Industry	Co-ordinated, consistent communication to farmers through a shared communication strategy, co-ordinating national projects where these exist already.
ALL	Promote the message of proportionality in terms of relative risk from animal-derived antimicrobial resistance and stimulate research in this area so there is more relevant evidence available to allow for informed decisions, in particular in the area of the transmission routes for spread of antimicrobial resistance.

Remarks

- Liaise with FVE/EC to ensure effective communication on veterinary issues at the 18 November Antimicrobial Resistance Awareness Day.

6) **Education (for prescribers and animal owners)**

HMA/EPRUMA/ Industry/Vets	Provide clear training materials highlighting what responsible use is and why it is important. Helping with the delivery of training.
COPA- COGECA/EPRUMA/Industry	Provide information to farmers on measures which can reduce the need for antimicrobials (disease prevention).

Remarks

- Funding for educational activities is necessary. Institutions and the European Commission are considered to have a role to play in this respect.

7) Other

EMA/HMA	Encourage and follow appropriate developments in the area of antimicrobials for <u>human</u> use.
Academia/ Industry/ (SAGAM) CVMP	Concerning gene transfer, take into account literature and as appropriate perform risk analysis
ALL	Ensure the revisions to the legislation (veterinary medicines, medicated feed, Animal Health) strike the correct balance and are coordinated to have the maximum impact