Workshop on the Economics of Antimicrobial Use in the Livestock Sector and Development of Antimicrobial Resistance: Implications for future work on Health, Food and Agriculture

Meeting: 12th October 2015, Organisation for Economic Co-operation and Development (OECD),

The purpose of the workshop was to focus on the following:

(i) The level of usage of antimicrobials
(ii) The use of antimicrobials for therapeutic, prophylactic and growth promotion purposes
(iii) Resistance associated with use of Antimicrobials (AMs)
(iv) Cost to society of Antimicrobial Resistance (AMR)
(v) Cost of switching to a more targeted use thereby reducing levels of usage and productivity gain in livestock production

Overview of OECD work –Dr Michele Cecchini

An overview of OECD work highlighted that development and spread of Antimicrobial Resistance (AMR) is largely driven by issues in the human sector such as inappropriate use in humans, insufficient hygiene, global trade and travel. However, inappropriate use in animals is also a factor. Statistics show that one in five human infections in G7 countries are resistant to antibiotics, with 700,000 deaths per year globally, 50,000 in Europe and North America due to AMR. Figures show that hospitalised patients with AMR infections cost an additional 10-40k US Dollars, and this figure does not capture what is happening in the Community. AMR has been shown to have a negative economic impact on productivity with losses of 38k US Dollars per patient.

The OECD review has shown that individual countries such as Canada, the Netherlands, Denmark, France and UK have made significant progress in terms of having comprehensive national action plans which implement AMR strategies using the One Health approach. The National action plans focus on enforcement, targets for reduction of use, evaluation of the AMR issue and taking ownership of appropriate actions. On the human side to avoid emergence of AMR there has been development of stewardship programmes, price policies, improved hygiene and early detection. In relation to stimulating research and development of new human antibiotics there has been a proposed initiative to de-link incentives to develop new drugs from sales.

The OECD has recommended that the G7 countries efforts to address AMR be upscaled into global actions, in particular with regard to strengthening surveillance and monitoring, with an emphasis on globally measurable targets on AMR incidence and use of antibiotics. Essentially OECD stated that all countries should be working towards a National action plan with Health sector being the main driver.

'Global Action plan on Antimicrobial Resistance' – Dr Marc Sprenger World Health Organisation

In some countries, treatment for some disease, such as gonorrhoea and pneumonia caused by *Klebsiella pneumonia* is at a post antibiotic stage as there is no longer an effective antibiotic

treatment option. The global action plan with its five strategic was adopted at the World Health assembly in May 2015 with a focus on developing global antibiotic awareness campaigns, good infection control, improved surveillance systems, antibiotics to be only available on prescription and investment in research and development of new disease treatments.

The nine work streams of the global action plan work to:

(i) Support MS in developing their own national plan

(ii) Launching and maintaining a global communication campaign

(iii) Global surveillance

(iv) Improving infection prevention and control

(v) Monitoring use and enhancing stewardship

(vi) Encouraging R & D, and exploring new business models

(vii) Improving point of care diagnostics

(viii) Addressing environmental drivers

(ix) Engaging the UN General Assembly

Dutch perspective on AMR

In 2014 the Netherlands maintained its number one position at the top of the annual Euro health consumer index (EHCI), which compares healthcare systems in Europe. The Netherlands has been in the top three countries in each report published since 2005; therefore there has been a focus on the veterinary sector as opposed to the health sector with regard to antibiotic usage, particularly since 2008 when a person died from *ESBL E. coli* of poultry origin.

The Dutch parliament adopted a 5 year action plan for countering antibiotic resistance in June 2015 where the primary focus is on the well being of human health. In this overall plan, agreements with public health care organisations, research into alternatives, international collaboration and the One Health approach are mentioned as crucial factors. The integrated approach is initiated and supported by both the Ministries of Health, Welfare and Sports and Economic Affairs. Two targets are: to decrease of the amount of health related infections by 50% and to reduce incorrectly prescribed antibiotics by 50% in the entire health care chain.

In the Netherlands, there is a large support base from several disciplines to contribute to the development of new antibiotics, alternatives to antibiotics and innovations in prevention. The focus will be on strengthening the research infrastructure while adhering to existing initiatives. The Dutch government has put antibiotic resistance high on the agenda for the first half of 2016, the period of its European chairmanship. During this period, a Ministers conference will be organised

with the EU Ministers of Agriculture and Health to come to a joint action plan, with a 'One Health 'leadership and a commitment to EU action with solid national action plans.

In relation to usage of antibiotics in animal production, the Netherlands are proposing a ban on use of last resort (critically important antibiotics (CIAs)) human medicines in animals. Since 2009 there has been a reduction in usage of antibiotics in animals by 58% (it should be noted that usage levels were one of the highest in Europe in 2009) and it was stated that the pig sector, in spite of this decrease in antibiotic usage is still profitable. When questioned directly as to how they managed this reduction without affecting farm profitability, the response was that there was increased veterinary involvement to improve the health status of the pigs – the interventions did take a number of years to get this result however. Healthier pigs resulted in improved profitability and the eradication of some previously endemic diseases.

Review of Trade and Agricultural Directorate work of Antimicrobial use – Dr Michael Ryan

This work started in 2013-2014 and is at an early stage, however results to date show that China, U.S., Brazil and India are the top 4 users of antibiotics in the world, and this picture is unlikely to change by 2030. The work has predicted that there would be productivity losses in the range of 1-3% in relation to poultry, pigs and cattle if there was reduction targets set for usage of AM, however the conclusion that there would be a relatively small impact is not disaggregated between OECD countries and developing countries. The preliminary work shows that the growth in production globally will be largest in poultry, followed by pigs and relatively stable in relation to beef production. Most of the increase in production growth will be in developing countries with a concomitant increase in antibiotic usage and development and spread of antimicrobial resistance.

World Organisation for Animal Health (OIE) – Dr. Elisabeth Erlacher

The Tripartite meeting and agreement to an intersectoral 'One Health' approach was adopted in 2011, and the World Organisation for Animal Health (OIE) wants all of its members to work towards a Global Action Plan. This plan must have a procedure for collecting quality standardised data. There are no controls on antibiotic use in humans in over 100 countries, and counterfeit medicines make up more than 50% of circulating antibiotics. There is also a lack of veterinary oversight in many countries, with at least 15 (9%) OIE members having no medicines legislation.

The OIE has updated all standards and guidelines in relation to AM usage, and the OIE has requested the establishment of a global database on the use of antibiotics in animals, with a collection of baseline information and different reporting options. The OIE is proposing the collection of quantitative data with regard to usage by class, species and antibiotic type. A new ad hoc Group has been set up by the OIE to offer guidance in relation to collecting harmonised data and a phase 1 questionnaire will sent to members in October 2015, with the first meeting of the ad hoc group to be in Janaury 2016 which will give feedback to OIE World Assembly in 2016.

The challenges foreseen by the OIE with regard to controlling AM use are:

(i) Support for developing countries

(ii) Quality veterinary services

(iii) Controls on imported produce with use of more risk assessment and banning of non- priority practices

(iv) Awareness raising

(v) Animal Health and welfare must be sustained

(vi) Food security and food safety secured

(vii) No universal optimal solution

OIE concluded that there needs to be international solidarity to help developing countries, with more technical information and economic assessments as well as more public-private partnerships and research.

Update on Food and Agricultural Organisation's (FAO) activities related to AMR and AM usage in food and agriculture – Dr Henk Jan Smel

The mission of the Food and Agricultural Organisation (FAO) was highlighted as being to eliminate hunger, to fight poverty (rural poverty specifically) and to protect the earth. The FAO supports the World Health Organisation (WHO) with regard to the Global Action Plan for AMR and proposed that it is the WHO that should be the global director of all AMR strategies. The FAO stated that by 2050 there will be a 70% rise in demand for animal protein in sub Saharan Africa and food security is much more important than AMR to these populations.

In terms of reducing usage of antibiotics, the FAO was of the opinion that there was too much focus on regulation of usage without sufficient emphasis on the economic implications of same. Therefore tailored strategies need to take into account the following:

(i) Economic choices

(ii) Biosecurity/biosafety

(iii) Local circumstances

(iv) Socio-anthropologic specificities

(v) Gender issues

(vi) Small holdings

(vii) Intensifications

(viii) Existing governance

US perspective on reducing Antibiotic usage – Dr Stacey Sneeringer

An economic report due to be published in November 2015 found that US farmers use antibiotics to treat disease, control disease, prevent disease and increase productivity. A reduction in AM usage would have potential farm–level economic costs, with reduced animal productivity which would lead to increased input costs e.g. feed and increased veterinary costs (more disease treatment). However better biosecurity would decrease AM usage. An indirect effect of reduced antimicrobial usage would be more variability of the product, and reduced economy of scale. Market level effects would be less output, with increased price at market and less competitive product in the global market.

Actions on AMR in livestock production - Japan

In Japan there is a Food Safety law in place which regulates the amount of antibiotics that can be administered in feed, at the different animal growth stages and in different animal species. Antibiotic prescribing has been decoupled from supply (prescribers of antibiotics cannot sell them). The Japanese Department of Agriculture has published Prudent Use Guidelines which focus on the following:

(i) Prevention of infection – management of feeding, sanitation & vaccination

(ii) Definitive diagnosis

(iii) Effective use of AM – sensitivity test

(iv) Sharing of information about AMR amongst relevant parties – vets, farmers

AMR in Japan is seen as is an issue for the following:

(a) Food security

(b) Public Health

(c) Consumer demands

French National Action plan – M. Patrick Dehaumont

The current French National Action plan (Ecoantibio – with Eco referring to economy) runs from 2012 -2016, with version 2 due in 2017. The plan set a quantitative objective to reduce AM usage by 25% in 5 years, with a qualitative objective to reduce usage of critically important antibiotics. The level of animal exposure to antibiotics was 17% lower in 2013 when compared to 1999, but the point was made that it was important to examine the indicator as tonnage can be too quantitative and not indicative of exposure.

In 2014 French Regulations were published with provisions for levels of antibiotic usage, including a reduction in the usage of flouroquinolones and third and fourth generation cephalosporins. There was also a new legal basis enacted making a clinical examination and antibiogram mandatory,

including a mandatory declaration in a national database for all antibiotics supplied. The veterinary code for all veterinarians includes an undertaking to this effect.

France urged every country to have an action plan for prudent use of antibiotics in veterinary medicine, with measurable objectives in terms of reducing usage. It was also proposed that there should be a limit on preventive use, with antibiotic use as a growth promoter being forbidden.

Panel Discussion on OECD's economic approach to contribute to addressing the increase in antimicrobial use and the development of resistance in the livestock sector

Mr. William Hall, Senior Policy Advisor, AMR review, UK

Dr Christina Greko, Sweden

Dr Gerard Moulin, France

Mr. James Anderson, European Federation of Pharmaceutical Industries & Associations, Belgium

Dr Piero Garzaro, Kaiser Permanente Healthcare, US

The OECD proposes next to look at the impact of reducing usage of Antimicrobials in animals and the issue of food security as well as the possible threat to food supply. Panelists felt there is already a global action plan in place and no need to discuss that further, rather governments need to mobilise all stakeholders. There is already guidance on what to do from the various organisations therefore no need for more documents. It is essential to have regulations in place to support the 'One Health' initiative but there are different starting points for countries and different approaches needed to ensure sustainable production. It was commented that growth promotion and routine use are one and the same, but that it is possible to move away from routine use by starting a system for continuous improvement with stakeholder engagement.

It is necessary to follow up regulations with data on usage, as having this data is an intervention in itself as it provides an opening for a very useful discussion with farmers and vets.

Farmers have a right to an income, which must be balanced with the interests of society. There is a cost in reducing antibiotic usage, which includes investment in more robust systems. Reduction in disease level will always reduce usage levels, and there needs to be a working model which engages people to work towards change.

It was mentioned that all human healthcare is publicly funded. As vets in practice are in the private sector perhaps a new business model could be considered for veterinary services. A model whereby the vet gets paid for advice rather than drug sales, and farmer has healthier animals that are more productive. However the question then arises as to who pays the vet, should for example the farmer pay, or should society reward best practice.

A study is required on the cost of risk management measures; including a study on the impact of these measures reviewing the initial level of disease and the cost of interventions (no information

available in the animal health sector, but OECD has done this in relation to human diseases). There also needs to be more information on the costs of various actions such as constructing a database. However there is also the case for good governance in the absence of specific data or evidence, as in some ways there are incentives to keeping the debate going, but leadership on addressing the challenge of AMR is also required.

In Sweden there was a significant reduction in AM usage. During this period of reduction there were a lot of disease issues which took time and investment to resolve. However, collaborative opinion in Sweden was that it is beneficial in the long term to reduce AM usage as it results in a better herd health status. It is important to establish an appropriate level of antimicrobial use, and not to be solely focused on reduction level targets.

It was acknowledged that there are huge data gaps in the area of AMR on the human side, and even more so in relation to livestock, but there will never be perfect data so policy decisions and actions are required now, given that potential societal costs are enormous when compared to productivity gains.

The discussion and workshop concluded with the OECD proposing to now examine the economic impact for the agri-sector of changing from one system of production, to another that involves more antimicrobial targeted use. The OECD will next endeavour to set up a farm level analysis network involving not just high income but also developing countries.