EUROPEAN COMMISSION

Brussels, 18.11.2009

COM (2009) ZZZ

Staff working paper of the services of the Commission

on antimicrobial resistance

SANCO/6876/2009r6

Commission européenne, B-1049 Bruxelles / Europese Commissie, B-1049 Brussel - Belgium. Telephone: (32-2) 299 11 11.

TABLE OF CONTENTS

1. INTRODUCTION

Antimicrobials[1] are essential as drugs for human and animal health and welfare, and as disinfectants, antiseptics and hygiene products. Antimicrobial resistance (AMR) is a health concern that is related to both human and non-human antimicrobial usage. On 10 June 2008, the Employment, Social Policy, Health and Consumers Affairs Council adopted Conclusions on AMR[2] calling among other things upon the Commission to promote mutual cooperation between all Directorates General and concerned Agencies and to facilitate cooperation between Member States on all aspects of AMR. Reference is made to human and veterinary medicine, residues in the environment and the possible contribution of biocides to the occurrence of AMR. The management and the prevention of AMR has become more difficult during the past decades by the decreasing pace of introduction on the market of new classes of antimicrobial medicinal products.

The purpose of this document is:

- to provide an overview of ongoing EU activities related to AMR;
- to initiate a holistic reflection and discussion on AMR, to identify possible areas for further action and the types of possible actions.

Therefore, this working paper has to be considered as a basis for consultation and discussion with the experts of the Member States, the European scientific bodies and European stakeholders. It does not represent an official position of the Commission and the ideas it contains do not prejudge the form and content of any future Commission proposal.

This document is accompanied by an annex (SANCO/6877/2009) containing all the references mentioned in this working paper.

2. PROBLEM DEFINITION

Data collected by the European Antimicrobial Resistance Surveillance System (EARSS) indicate that AMR, resulting in treatments losing their efficacy, is an important, largely unresolved issue in public health. Each year 25,000 patients die in the EU from an infection caused by resistant micro-organisms with extra healthcare costs and productivity losses of at least 1.5bn € per year[3]. It remains a challenge to be tackled at the different levels of the health care system throughout the EU and at international level. A number of separate initiatives have been taken in the past regarding the monitoring, risk assessment and management of AMR in human and veterinary medicine, food safety and environmental contamination. However, as noted by the Council Conclusions, coordination between these activities should be promoted although harmonisation of Member states activities are based on different legal grounds and therefore risks inconsistent developments.

In line with international standards on risk management, the results of measures taken have to be evaluated. The monitoring of the prevalence of resistant agents - preferably harmonised- allows assessing the efficacy of measures taken so far, which are mainly based on recommendations for prudent use. The Commission

provided such recommendations in 1999 for veterinary medicine[4] and in 2002 for human medicine[5]. Monitoring results continue to show the presence of resistant zoonotic agents in food-producing animals[6] and the increasing occurrence of micro-organisms resistant to antimicrobials in hospitals, such as methicillin-resistant *Staphylococcus Aureus* (MRSA)[7].

3. MONITORING ACTIVITIES

3.1. Human medicine

AMR has been identified as a special health issue requiring epidemiological surveillance within the EU[8, 9].

The Commission has funded several European projects that provided valuable and comparable data on the burden of disease and resistance across Europe and generated awareness and understanding among policy-makers and communities at large including the monitoring of the use of antimicrobials in human medicine [10, 11, 12, 13, 14].

The European Antimicrobial Resistance Surveillance System (EARSS) is the dedicated network for the surveillance of AMR in Europe. Co-financed by the European Centre for Disease Prevention and Control (ECDC), EARSS collects routinely antimicrobial susceptibility data and provides spatial trend analyses.

ECDC established a group of national AMR focal points from Member States and EFTA-EEA countries in order to strengthen collaboration on this matter and publishes an annual report on AMR. In addition, ECDC is implementing a specific programme on AMR and healthcare-associated infections (HCAI) to develop a reference point for data, information and scientific advice on AMR and HCAI. At national level, following EU recommendations, almost all EU countries have already established or strengthened a surveillance system for AMR in the community and in hospitals. However, some countries still experience difficulties with respect to data access, quality of data, budget and information technology support.

In order to address these shortcomings and based on the experiences gained, reflections can be made to further improve the surveillance system for AMR and for use of antimicrobials and to enable and/or improve access by decision makers, professionals and public to data and information on AMR and use of antimicrobials.

Antimicrobials and antimicrobial resistant agents may be spread to the environment by human or animal excretion or after sanitation operations based on antimicrobial use. The impact of theseAMR dimensions on the environment should be assessed.

3.2. Food safety and veterinary medicine

3.2.1. AMR monitoring in zoonotic infections

The monitoring of the occurrence of AMR in food-borne zoonotic agents is mandatory in a representative number of isolates of *Salmonella* spp,

Campylobacter jejuni and *Campylobacter coli* from cattle, pigs and poultry and food derived from those species[15]. Harmonisation between Member States and consistency with human isolates is guaranteed[16, 17, 18].

An EU wide baseline survey on the prevalence of MRSA in breeding pigs has been conducted in 2008. Furthermore, the European Food Safety Authority (EFSA) has published a guidance document for harmonized monitoring and reporting of AMR in commensals from animals[19].

EFSA analyses and reports results from Member States on AMR monitoring every year and publishes a summary in collaboration with ECDC[20]. At the end of 2009 or beginning of 2010, three additional EFSA reports are expected on AMR monitoring in *Salmonella* isolates in poultry and pigs, on *Campylobacter* isolates in broilers and on MRSA isolates in pigs. Harmonised monitoring for MRSA in intensively reared animals and AMR of *Campylobacter* spp. in poultry could be continued or repeated to evaluated trends. Specific surveys could be carried out also for AMR in commensals[21] and the emerging extended spectrum beta-lactamase (ESBL) resistance.

A Community Reference Laboratory for AMR was nominated[22] to guarantee a high quality of AMR testing by national reference laboratories.

3.2.2. AMR monitoring and impact on animal diseases

Good knowledge on the occurrence of AMR agents and their impact on animal health, welfare and production is lacking. Gathering of data on the occurrence of AMR in animal pathogens and its impact on animal health, welfare and production could be useful.

3.2.3. Monitoring of use of antimicrobials in veterinary medicine

The Commission gave the European Medicines Agency (EMEA) a mandate to take the lead in collecting data on the sales and use of antimicrobials in animals. The EMEA expects to produce an analysis of 2009 data and to implement a coordinated data collection from 2010 onwards. The data on sales and use of antimicrobials in animals could allow an assessment against the monitoring results of the occurrence of AMR on zoonotic and animal disease agents.

3.3. Biocides

In the case of biocidal products, Member States must prescribe that the holder of an authorisation shall immediately notify the competent authority of information on the development of resistance[23]. This is expected to help develop the evidence base to assess the risk of development of AMR on the long-term. Guidance on how to monitor the development of resistance in environmental conditions of use of biocides is still missing before monitoring programmes for AMR in all areas of biocide usage could be implemented.

4. RISK ASSESSMENT

A multidisciplinary approach involving microbiologists, epidemiologists and risk assessors from all the application areas is needed and must be coupled to the willingness to provide the appropriate approach for the generation of data for microbial risk assessment. This provides risk managers with robust scientific information on which they can base their policies.

4.1. Human medicine

Microbial risk assessment can be used to evaluate the level of exposure and the subsequent risk to human health due to a specific organism or a particular type of resistance. This technique is increasingly applied to human health to monitor patterns of certain type of AMR.

Microbial risk assessments highly depend on data. If available, the emergence of resistance in any organism could be investigated. The EARSS is the main source of data. However, laboratories participate on a voluntary basis and there may be large regional differences in the prevalence of AMR within countries. Only isolates from blood and spinal fluid samples are included in the EARSS surveillance. Although susceptibility testing is expected to be standardised, methodology may still vary. Data collection for microbial risk assessments and harmonisation of methodologies could thus be improved.

4.2. Food safety and veterinary medicine

4.2.1. Zoonotic infections

A number of scientific opinions have been adopted by various EU scientific bodies such as EFSA and EMEA, elaborating an assessment of some important risks from food-borne AMR zoonotic agents and MRSA[4, 24, 25, 26, 27, 28, 29, 30, 31]. However, some micro-organisms, e.g. commensals and their role in further transmitting AMR genes to pathogenic ones, have not been covered by these opinions.

4.2.2. Animal diseases

A number of scientific papers assessing some important risks in the area of animal diseases have been published. International recommendations exist for analysing the risks to animal health from antimicrobial resistant micro-organisms[32]. Therefore, a risk assessment on AMR in animal health arising from the use of antimicrobials in the EU could be carried out, in particular with reference to prophylactic activities and /or mass therapy in intensive farming.Biocides

The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) recently concluded that in the face of the large increase of biocide use in many fields (personal care, hygiene, consumer products etc.) and the continuous increase in AMR, there is a serious lack of data and methodologies to clearly identify the risks arising from the use of biocides[33]. The generation of quantitative data on biocide exposure, the development of standard protocols for the evaluation of AMR induced by a biocide and environmental studies focussing on the identification and characterisation of AMR following use of biocides could be useful.

4.3. Comprehensive overview report focussing on zoonotic infections

In order to get a comprehensive overview on AMR focussed on zoonotic infections, the Commission requested EFSA, EMEA, ECDC and SCENIHR to provide a common scientific report based on the information currently available on:

- the public health problems linked to AMR, according to the source (use of antimicrobials in humans, in animals and in other applications);
- animal species/zoonotic agent/antimicrobial combinations considered of high concern; and
- areas where innovation and research should be encouraged.

The report was adopted by the three agencies and the scientific committee at the end of October 2009.

5. RISK MANAGEMENT

5.1. Human medicine

Commission policy with regard to AMR due to use of antimicrobials in human medicine is laid down in the Community Strategy against AMR[34]. Council Recommendations on the prudent use of antimicrobials and healthcare associated infection (HCAI) are components of this strategy.

5.1.1. Follow-up of Council Recommendation on prudent use[5]

Member States were asked to put in place specific strategies to contain AMR by establishing or strengthening surveillance systems on AMR and the use of antimicrobials, implementing control and preventive measures, promoting education and training of public health workers and inform the general public.

A first report on the implementation of this Recommendation[35] has been published and a second report is being prepared. Eighteen Member States have a national strategy in place while six are preparing one. In general, progress was reported on all the aspects of the Recommendation.

5.1.2. Health care associated infections (HCAI)

In order to address the spread of resistant micro-organisms in health care settings, the Council adopted in June 2009 on a proposal from the Commission, a Recommendation aiming at ensuring that Member States have the proper and adequate strategies to improve patient safety in their healthcare systems, including specific proposals to prevent and control HCAI[36]. It proposes to:

- give priority to the implementation of control measures and precautions.
- organise prevention and control programmes in healthcare institutions and ensure proper organisational and structural.
- establish / strengthen active surveillance systems on HCAI, pathogens, risk factors as well as process and structure indicators measuring compliance.

- foster education, training, research and information exchange.

ECDC is helping the Commission to foster the development of further guidance on HCAI, promote training and assist Member States to develop training.

Reflections are welcomed to consider the following issues:

- Adoption of strategy and action plans, and establishment of intersectorial coordinating mechanisms in all Member States;

- Strengthening of the surveillance system and bringing the information to the use of policy makers, professionals and public;

- Monitoring the implementation of the Recommendation and the impact of national measures;

- Improving education of healthcare professionals;

- inform and involve the general public;

- Enhancing the exchange of best practices.

5.2. Food safety and veterinary medicine

5.2.1. Prudent use initiatives

In 2005, the European Platform RUMA was established by different stakeholders to promote the responsible use of medicines, including antimicrobials, in animals. The Heads of Medicines Agencies adopted a strategic plan[37] on antimicrobial uses, supporting the Strategy on Antimicrobials of the Committee for Medicinal Products for Veterinary Use (CVMP)[38]. Recently the Commission initiated a so-called referral procedure[39] for all veterinary medicinal products containing quinolones or fluoroquinolones for all food-producing species. Its aim is to promote the prudent use of these classes of antimicrobials in veterinary medicines across the EU.

Reflections are welcomed on the strengthening the network of stakeholders involved in the prudent use of antimicrobials.

5.2.2. Veterinary medicines

A veterinary medicinal product may only be placed on the market in the Community when a marketing authorisation has been issued by the competent authority of a Member State[40] or by the Commission[41]. For this purpose, applicants are requested to address the issue of AMR and propose measures to limit its development from the intended use.

Furthermore, the CVMP has adopted numerous reflection papers and recommendations on the use and authorisation of antimicrobials.

Based on the comprehensive overview report (see paragraph 4.4) the need to take additional measures should be reflected on in order to enhance public health protection in the context of AMR

5.2.3. Feed additives

The safety assessment of feed additives carried out by EFSA prior to their pre-marketing authorisation includes the consideration of the potential AMR aspects.

A complete ban on the addition of antibiotics as growth promoters to feed applies from 1 January 2006[42]. The EC has also issued a Report on the use of coccidiostats and histomonostats as feed additives[43].

5.2.4. Medicated feed

Medicated feeds can only be produced in authorised premises, subject to specific official controls, and its use is restricted as it is supplied only to animals under prescription by a veterinarian[44].

5.2.5. Zoonoses control

The use of antimicrobial veterinary products as a specific method to control *Salmonella* is prohibited in poultry populations[45]. Targets for reduction of *Salmonella* have been laid down in several poultry populations[46] and *Salmonella* food safety criteria (absence in 25 g) apply to different foodstuffs[47]. These control measures for *Salmonella* in general are expected to result in a reduction of *Salmonella* in general and also the *Salmonella* strains resistant to antimicrobials.

Control programmes for certain food-borne zoonoses are lacking because cost-efficient mitigation options are still missing (e.g. *Salmonella* in pigs, *Campylobacter* in poultry). Control of resistant strains of such pathogen might be considered as a risk-based first step towards the control of the pathogen if efficient control options are available.

Reflections are welcomed to consider the following issues:

- Recommendation on the prudent use of antimicrobials in veterinary medicine and tools to improve it;
- Based on the outcome of the comprehensive overview report (see 4.4) and subject to specific case-by-case evaluation, targeted interventions e.g.
    - Rules on the absence of resistant zoonotic agents in food;
    - Targets for the reduction of resistant zoonotic agents at primary production with specific measures to achieve these targets;
    - To have restrictions on the use of antimicrobials if the use would pose a direct or indirect risk for animal or human health.

5.2.6. Link with animal health and welfare

Eradication and control programmes implemented for several animal diseases in the last 20 years have lead to a significant improvement of the animal health status of the farmed animals in the EU. In general the upgraded health and welfare status,

and the availability of better vaccines could result in a reduction of the use of antimicrobials. An improved monitoring of the use (see 3.2.3) is needed to demonstrate a possible significant effect. Reflections are welcomed to encourage further reduction of the need of using certain antimicrobials by improving the animal health status.

5.2.7. Plant protection products

The authorisation of antibiotics as plant protection products has been gradually banned in the EU and has ceased completely today[48, 49] even if they do not find any application as human or veterinary medicine[50].

Member States may authorise in exceptional and well controlled and monitored circumstances for a short period substances not complying with the legal requirement[51].

5.3. Biocides

The Review Programme of the Biocides Directive[52] currently evaluates active substances used in biocidal products[53] for their risks to human health and the environment. It would benefit from standard protocols for the evaluation of AMR induced by biocides as recommended by SCENIHR (see 4.3). A follow-up mandate has been submitted to SCENIHR asking to elaborate the recommendations from its Opinion, in particular related to the development of harmonised protocols for the evaluation of AMR induced by biocides. This research strategy could be the basis to launch Framework (FP)7 projects from 2010 onwards, in particular for the development of harmonised protocols.

Evaluation of the use of certain biocides and their impact on AMR in the context of the disposal of culled animals in animal disease-outbreaks should also be considered.

6. COMMUNICATION

AMR is a complex issue with links to public health, control/eradication of zoonoses, animal health and welfare, feeding, antimicrobial authorisation policy, research activities and environmental policy. People working in each of these areas may not always be aware on the actions already taken to control AMR or need to be informed on the difficulties encountered in one area due to less attention to AMR in another area. Therefore an intensive communication is needed between:

- Risk managers at national and Community level dealing with these different policy areas;

- The Commission and EU agencies/authorities (ECDC, EFSA, EMEA) and private European stakeholders organisations;

Discussion with international organizations in this field and in particular OIE, Codex and FAO, are also essential.

Furthermore, ECDC has established an European Antibiotic Awareness Day (EAAD) to increase public awareness about antibiotic resistance. The EAAD takes place each year on 18 November to raise awareness on how to use antimicrobials in a responsible way.

Reflections are welcomed to consider the following issues:

- Improving the education of the general public;
- Improving awareness, education and training of health professionals in human and veterinary medicine;
- Best use of the European Antibiotic Awareness Day;
- Communication and exchanges of views has to be intensified in particular with parties outside the Commission, this document being the starting point;
- Use of harmonised terminology e.g. breakpoint/cut-off values.

7. GLOBAL LINK: INVOLVEMENT IN INTERNATIONAL ACTIVITIES

7.1. Human medicine

The expansion in global trade and travel has increased the speed of AMR spread. The Community has therefore established links with numerous international organizations, including the WHO. The WHO launched the WHO Global Strategy for Containment of Antimicrobial Resistance which recognizes that antimicrobial resistance is a global problem that has to be addressed in all countries. The main recommendations are to establish national task forces to coordinate interventions aimed at strengthening surveillance of use and resistance, to improve access to appropriate antimicrobials, to reduce the disease burden and spread of infection, to enforce regulation and legislation related to containing AMR and to develop appropriate new drugs and vaccines. Several follow-up meetings took place[54] resulting in World Health Assembly resolutions[55] calling the WHO Member States to continue to pledge their commitment, including adequate resources, to promote the rational use of medicines.

7.2. Food safety and veterinary medicine

Since 1997, WHO, the Food and Agriculture Organisation of the United Nations (FAO) and the Office International des Epizooties (OIE) have organized a number of expert consultations to address the issues related to the antimicrobial use at the different steps of the food-chain, the emergence of resistant pathogens and the associated public health problems. The Codex Alimentarius Commission has established an *ad hoc* Intergovernmental Task Force on AMR. The aim is to develop science based guidance taking full account of the work and standards of other relevant international organizations, such as FAO, WHO and OIE. The guidance should provide a structured risk analysis framework on the risks associated with AMR in the food chain and the transmission through food of AMR linked to the non-human use of antimicrobials.

The Commission and the EU Members States are fully involved in order to ensure consistency between this future international guidance and the Community policy

in this area. The potential impact of AMR on international trade of food and animals should be carefully monitored.

8. INNOVATION AND RESEARCH ACTIVITIES ON AMR

8.1. Research under FP 6 and FP7 projects

Research to combat AMR has been given a high priority within the EU Framework Programmes and has received more than € 200 million of EU support over the last ten years.

The programmes support studies on basic phenomena of resistance, on epidemiology and translational research merging basic genomics with clinical and public health research and on the use of antimicrobials in the farming sector and the consequences along the food chain. To promote the rational use of antibiotics, the European biotechnology industry is mobilized to develop point-of-care diagnostic tests for early identification of the disease-causing agents. In FP6 several European-wide projects were funded that focus on areas like the development of evidence based patient management guidelines for respiratory infections, the control of healthcare associated infections, and the identification of new targets for drug candidates as well as new natural products from antibiotic-producing organisms. In the animal sector, AMR has been addressed through research on alternatives to the use of antimicrobial growth promoters and breeding for disease resistance and in the "farm to fork" approach through assessment of the antimicrobial hazard. In FP7, a major effort has been made to address one of the most urgent medical needs, which are new drugs against severe Gram negative infections and on epidemiology of multi-drug resistant strains. In the latest call, the impact of antibiotic therapy on the human host was addressed in several selected proposals as well as clinical validation of diagnostic tests[56]. Related initiatives, such as European Technology Platforms or the Joint Technology Initiative on Innovative Medicines also consider the issue of AMR.

8.2. Innovation

The Commission has already taken steps to address the issue of availability of effective drugs, including antimicrobials, such as providing support to micro, small and medium sized enterprises to develop new medicines[57]. The Swedish Presidency has hosted on 16 and 17 September a conference with a focus on the discrepancy between AMR and the lack of new drugs foreseen in the pharmaceutical sector. The aim was to explore ways of creating incentives for the development of new drugs.

Further Research topics/initiatives on AMR and related issues could be considered where additional needs are identified.

9. CONCLUSIONS

AMR has been recognised as a serious threat to public health in the 1990's. Since then, the Commission has launched different initiatives in human medicine, veterinary medicine and food safety and has developed tools to monitor the effect of these actions. Progress has been made in certain areas but additional actions are still needed. Discussions in the appropriate fora are required to fill the identified

knowledge and data gaps and to improve the assessment and management of AMR.

EUROPEAN COMMISSION

Annex to the staff working paper of the services of the Commission on

antimicrobial resistance

SANCO/6877/2009r2

List of reference used in the staff working paper of the services of the Commission on antimicrobial resistance

1 For the purpose of this paper, an active substance of synthetic or natural origin which destroys bacteria, suppresses their growth or their ability to reproduce, excluding antivirals and antiparasites

2 Council Conclusions on Antimicrobial Resistance (AMR) adopted during the 2876th Employment, Social Policy, Health and Consumers Affairs Council meeting of 10 June 2008.

3 http://ecdc.europa.eu/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf

4 The opinion of the (former) Scientific Steering Committee of the Commission on AMR adopted on 28 May 1999. http://ec.europa.eu/food/fs/sc/ssc/out50_en.html.

5 Council Recommendation 2002/77/EC of 17 November 2001 on the prudent use of antimicrobial agents in human medicine (OJ L 34, 5.2.2002, p. 13)

6 Annual epidemiological report on communicable diseases in Europe 2008. Stockholm, European Centre for Disease Prevention and Control (ECDC).

7 Assessment of the Public Health significance of meticillin resistant *Staphylococcus aureus* (MRSA) in animals and foods, adopted by Scientific Opinion of the Panel on Biological Hazards of EFSA on 5 March 2009. http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902408708.htm.

8 Commission Decision 2000/96/EC of 22 December 1999 on the communicable diseases to be progressively covered by the Community network under decision No 2119/98/EC of the European Parliament and of the Council (OJ L 28, 3.2.2000, p.50).

9 Decision No 2119/98/EC of the European Parliament and of the Council of the 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community (OJ L 268, 3.10.1998, p.1).

10 European Antimicrobial Resistance Surveillance System (EARSS): since nine years this project has been collecting data from over 1300 hospitals in 31 countries in the European region, measuring the antibiotic resistance of important bacteria that cause infections in European citizens.

11 European Surveillance of Antimicrobial Consumption (ESAC): this project has set up a continuous, comprehensive and comparable database on antibiotic use in Europe.

12 European Committee on Antimicrobial Susceptibility Testing (EUCAST): a standing committee consisting of a body of experts that defines common reference methods which permit comparison of AMR data across Europe.

13 Burden of Disease & Resistance in European Nations (2007-2010) – BURDEN is project which aims to provide comparable information on burden of disease and resistance across Europe and to generate awareness and understanding among policy-makers and communities at large.

14 eBug pack: development and dissemination of a School Antibiotic & Hygiene Education Pack based on a successful project in the UK. This project aims to increase awareness of the benefits of antibiotics as well as prudent use and improve hand and respiratory hygiene, thus reducing the spread of respiratory, gastrointestinal, and skin infections and decreasing the demand of antibiotics.

15 Directive 2003/99/EC of the European Parliament and of the Council of 17 November 2003 on the monitoring of zoonoses and zoonotic agents, amending Council Decision 90/424/EEC and repealing Council Directive 92/117/EEC (OJ L 325, 12.12.2003, p.31).

16 Commission Decision 2007/407/EC of 12 June 2007 on a harmonised monitoring of antimicrobial resistance in *Salmonella* in poultry and pigs (OJ L 153, 14.6.2007, p. 26).

17 Commission Decision 2007/516/EC of 19 July 2007 concerning a financial contribution from the Community towards a survey on the prevalence and antimicrobial resistance of *Campylobacter* spp. in) broiler flocks and on the prevalence of *Campylobacter* spp. and *Salmonella* spp. in broiler carcasses to be carried out in the Member States (OJ L 190, 21.7.2007, p. 25).

18 Commission Decision 2008/55/EC of 20 December 2007 concerning a financial contribution from the Community towards a survey on the prevalence Salmonella spp. and methicillin-resistant *Staphylococcus aureus* in herds of breeding pigs to be carried out in the Member States (OJ L 14, 17.1.2008, p. 10).

19 Report of the Task Force on Zoonoses Data Collection including guidance for harmonized monitoring and reporting of antimicrobial resistance in commensal *Escherichia coli* and *Enterococcus* spp. from food animals (The EFSA Journal (2008) 141: 1-44).

[2]0 The Community Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents, Antimicrobial Resistance and Foodborne outbreaks in the European Union in 2006, The EFSA Journal (2007), 130.

21 An organism that derives benefit from living in close physical association with another organism that derives neither benefit nor harm from its relationship with the commensal.

22 Commission Regulation (EC) No 776/2006 of 23 May 2006 amending Annex VII to Regulation (EC) No 882/2004 of the European Parliament and of the Council as regards Community reference laboratories (OJ L 136, 24.5.2006, p.3).

[2]3 Article 14(1) of Directive 98/8/EC of the European Parliament and of the Council on the placing on the market of biocidal products.

[2]4 Assessment of the Public Health significance of meticillin resistant *Staphylococcus aureus* (MRSA) in animals and foods, adopted by Scientific Opinion of the Panel on Biological Hazards of EFSA on 5 March 2009. http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902408708.htm.

[25] Reflection paper on MRSA in food producing and companion animals in the EU: epidemiology and control options for human and animal health, adopted by the CVMP of EMEA on 12 March 2009. http://www.emea.europa.eu/pdfs/vet/sagam/6829009en.pdf.

[26] The opinion of the EFSA BIOHAZ Panel on food-borne antimicrobial resistance as a biological hazard, adopted on 9 July 2008. http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902034881.htm.

[27] Revised reflection paper on the use of 3rd and 4th generation cephalosporins in food-producing animals in the EU: development of resistance and impact on human and animal health, adopted by the Committee for Veterinary Medicinal Products (CVMP) of EMEA on 11/3/2009. http://www.emea.europa.eu/pdfs/vet/sagam/8173006enfin.pdf.

28 Public statement on the use of (fluoro)quinolones in food-producing animals in the European Union: Development of resistance and impact on human and animal health adopted by the CVMP of EMEA on 15 February 2007. http://www.emea.europa.eu/pdfs/vet/srwp/18465106en.pdf.

[29] Reflection paper on the use of fluoroquinolones in food-producing animals in the EU: development of resistance and impact on human and animal health, adopted by the CVMP of EMEA in 2006. http://www.emea.europa.eu/pdfs/vet/srwp/18465105en.pdf.

[30] EMEA guidance on AMR and to the CVMP strategy on AMR. http://www.emea.europa.eu/htms/vet/vetguidelines/safety.htm under "antimicrobials".

[31] CVMP strategy on antimicrobials 2006-2010 http://www.emea.europa.eu/pdfs/vet/swp/35329705.pdf.

32 http://www.oie.int/eng/normes/mcode/en_chapitre_1.6.8.htm.

33 SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), Assessment of the Antibiotic Resistance Effects of Biocides, 19 January 2009.

[34] Communication from the Commission of 20 June 2001 on a Community strategy against antimicrobial resistance (COM(2001) 333 final, Volume I - not published in the Official Journal).

[35] COM(2005) 684 final.

36 Council Recommendation of 9 June 2009 on patient safety including the prevention and control of healthcare-associated infections (OJ L 1541, 3.7.2009, p. 1).

37 www.hma.eu/uploads/media/Stakeholders_Information_May2009_rev_3.pdf.

[38] The CVMP is responsible for preparing the opinions of the European Medicines Agency (EMEA) on purely scientific criteria concerning veterinary medicinal products. The CVMP may use the expertise of the Scientific Advisory Group on Antimicrobials for its tasks concerning antimicrobials.

[39] Article 35 of Directive 2001/82/EC (OJ L311, 28.11.2001, p.1).

40 Directive 2001/82/EC (OJ L 311, 28.11.2006, p. 1).

41 OJ L 136, 30.4.2004, p.1.

[4]2 Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition (OJ L 268, of 18.10.2003, p. 29.).

43 Report from the Commission to the Council and the European Parliament on the use of coccidiostats and histomonostats as feed additives (COM (2008) 233 final, 5 May 2008 (http://ec.europa.eu/food/food/animalnutrition/feedadditives/docs/Report-Coccs-233-2008-EN.pdf).

44 Directive 90/167/EEC laying down the conditions governing the preparation, placing on the market and use of medicated feedingstuffs in the Community (OJ L 211, 9.8.1990, p. 16).

[4]5 Commission Regulation (EC) NO 1177/2006 of 1 August 2006 implementing Regulation (EC) No 2160/2003 of the European Parliament and of the Council as regards requirements for the use of specific control methods in the framework of the national programmes for the control of Salmonella in poultry (OJ L 212, 2.8.2006, p.3).

[4]6 Regulation (EC) No 2160/2003 of the European Parliament and of the Council of 17 November 2003 on the control of *Salmonella* and other specified food-borne zoonotic agents (OJ L 325, 12.12.2003, p. 1).

47 Commission Regulation (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs (OJ L 338, 22.12.2003, p.1)

48 Commission Decision of 30 January 2004 concerning the non-inclusion of certain active substances in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing these substances (OJ L 37, 10.2.2004, p. 27).

49 Commission Decision of 31 March concerning the non-inclusion of cresylic acid, dichlorphen, imazamethabenz, kazugamycin and polyoxin in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing these substances (OJ L 97, 15.4.2005, p. 38).

[5]0 That were on the market before 14th May 2000.

[5]1 Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market (OJ L 230, 19.8.1991, p. 1).

52 Commission Regulation (EC) No 2076/2002 of 20 November 2002 extending the time period referred to in Article 8(2) of Council Directive 91/414/EEC and concerning the non-inclusion of certain active substances in Annex I to that Directive and the withdrawal of authorisations for plant protection products containing these substances (OJ L 319, 23.11.2002, p. 3).

53 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market (OJ L 150, 8.6.2002, p. 7).

54 2nd International Conference on Improving the Use of Medicines (2004); WHO's 15th Expert Committee for the Selection and use of Essential Medicines (2007).

55 Resolution WHA58.27 on Improving Antimicrobial Resistance. Resolution WHA60.16, on Rational Use of Medicines.

56 http://ec.europa.eu/research/health/infectious-diseases/antimicrobial-drug-resistance/projects_en.html .

57 See Commission Regulation (EC) No 2049/2005, (OJ L329, 16.12.2005, p.4.).