CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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***AD HOC* CODEX INTERGOVERNMENTAL TASK FORCE ON ANTIMICROBIAL RESISTANCE**

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INFORMATION ON THE WORK BY FAO, WHO AND OIE ON ANTIMICROBIAL RESISTANCE

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS (FAO)

1. The use of antimicrobial drugs for treatment of animal diseases has benefits for animal health and therefore contributes to supporting the livelihoods and the economies of many countries. However, the use of antimicrobials for treatment and prophylaxis in food production animals, if not properly controlled, can result in the emergence and spread of antimicrobial resistant pathogens. The risk of antimicrobial resistance can be particularly high in countries where national policies and regulations, and systems for monitoring and surveillance of usage of antimicrobials and resistance are weak or inadequate.

2. FAO is looking at this issue in an integrated way as part of its results-based budgeting and work planning process. This approach is based on the setting of strategic objectives that provide a focus for action; the definition of expected results that contribute to attaining these objectives; and the alignment of programs and resources behind the objectives. Activities related to the containment of antimicrobial resistance associated with the use of antimicrobials in food animals are part of Strategic Objective D: *"Improved quality and safety along the production chain"* and Strategic Objective B *"Reduce animal disease and associated human health risks"*, and the relevant activities are mostly delivered through a multidisciplinary unit result *"Improved national/regional policies and capacities for assessment and management of priority food contamination risks along the production to consumption continuum"*.

3. Under this framework, FAO activities related to antimicrobial resistance include for example the implementation of a series of interlinked activities in the East Africa region that aim to improve food safety in different value chains. The poultry value chain in Kenya has been selected for a pilot study that will contribute to strengthening of national/regional policies, capacities and systems for management of microbiological contamination and antimicrobial resistance risks. Poultry production is important to the country and the wider East Africa region because of its contribution to improved livelihoods, household nutrition, food security and economic development. The safety of poultry products is therefore crucial for the protection of human health and to ensure that market opportunities are optimized.

4. The project is focussed on the prevention and control of microbiological contamination and antimicrobial resistance through the application of good management, husbandry, handling and hygiene practices along the poultry value chain. The levels and prevalence of pathogenic (*Salmonella* spp. and *Campylobacter* spp.) and antimicrobial resistant bacteria in poultry products will be assessed at different stages from primary production to consumption, contamination risk factors will be determined and the critical stages at which prevention and control measures can be most effectively applied will be identified. The project is being implemented in collaboration with the WHO in the framework of a related WHO-AGISAR[1] project.

5. Under the FAO pilot project, support will be provided to national governments/institutions and the East Africa Community, at a regional level, to develop and implement national/regional strategies and policies to improve food safety in the poultry sector in general; and to specifically address microbiological

[1] WHO 'Advisory Group on Integrated Surveillance of Antimicrobial Resistance'

contamination, and antimicrobial resistance risks, including improved systems for antimicrobials usage, and antimicrobial resistance monitoring and surveillance. Guidelines on management, husbandry, handling and hygiene practices in primary production, processing and distribution of poultry will be developed and disseminated in the region, and subsequently to other developing countries.

6. In the area of fisheries FAO organized an Expert Workshop on Improving Biosecurity through Prudent and Responsible Use of Veterinary Medicines in Aquatic Food Production in Bangkok Thailand from 15 – 18 December 2009. The meeting was hosted by the Aquatic Animal Health Research Institute of Thailand's Department of Fisheries and was attended by thirty nine experts from fourteen countries. Major concerns identified during the expert workshop include: a) authorization system of veterinary medicines and related issues; b) technical assistance (e.g. capacity, environmental and human impact evaluation capacity, trading compliance); and c) harmonization of international standards. The papers discussed at the meeting as well as the outcomes of the international survey on the use of veterinary medicines in aquaculture and the current status on the use of veterinary medicines in Chinese, Philippine, Thai and Vietnamese aquaculture conducted by FAO will be also part of the report. This will be used as background document to support the preparation of the FAO Code of Conduct for Responsible Fisheries (CCRF) Technical Guidelines on Prudent and Responsible Use of Veterinary Medicines in Aquaculture.

7. During 2010, FAO held a National Workshop in Songzi, China under the TCP/CPR/3203(D) Improvement of aquaculture food safety in Hubei Province. The workshop highlighted the need for implementation of Good Aquaculture Practices (GAqP) to minimize the use of chemotherapeutic agents in aquaculture. The project has chosen 10 demonstration ponds in Songzi area of Hubei Provice. Based on data collected from the project site, location-specific GAqP was drafted and the recommendations are currently being implemented in the demonstration ponds at the project site.

WORLD HEALTH ORGANIZATION (WHO)

8. The widespread use of antimicrobials for therapeutic purposes but also as growth promoters in livestock production has intensified the risk for the emergence and spread of resistant microorganisms. This raises particular concern since the same classes of antimicrobials are used both in humans and animals. Moreover few new antibiotics are being developed to replace those becoming ineffective through resistance. Food is generally considered to be the most important vector for spread of resistance between humans and animals.

9. Concerned about the extensive use of antibiotics in food-animal production , which may accelerate the development of resistant zoonotic bacteria in animals that may be further transmitted to humans via the food chain rendering treatment ineffective, the World Health Assembly adopted in 1998 a resolution (WHA51.17) on antimicrobial resistance. The WHA resolution urged Member states to encourage the reduced and rationale use of antimicrobials in food-animal production. This resolution was followed by the development later of WHO Global principles for the containment of antimicrobial resistance in animals intended for food.

10. The Publication of the Global Principles was followed by about 15 WHO expert consultations (some held jointly with FAO and OIE) to first assess the public health risk associated with the use of antimicrobials in animal husbandry (including aquaculture and propose management options to address the identified risks. This consultative process has clearly demonstrated that antimicrobial use in food animals can select for antimicrobial bacteria in the animal gut and subsequently these resistant bacteria or their resistant determinants can be transferred to humans via the food chain; and has resulted in three important outcomes

- The development of a WHO list of Critically Important Antimicrobials;
- The establishment of an Ad Hoc Intergovernmental Codex Task Force on Antimicrobial Resistance;
- The establishment of a WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance.

The WHO list of Critically Important Antimicrobials for Human Health

11. There are many serious infections in people (including enteric infections) where there are few or no alternate antimicrobials that can be used if antimicrobial resistance develops. These antimicrobial classes can be classified under various names such as "critically important", "essential", "reserve" or "last resort".

12. Antimicrobial classes could be classified as critically important when the drug is in a class that is the only available therapy or one of a limited number of drugs available to treat serious human disease or enteric pathogens that cause foodborne disease. The main bacteria that will need to be considered are those that are currently known to be likely transferred from food production animals to man as either zoonotic pathogens or commensal bacteria (i.e. *E.coli*, *Salmonella* spp., *Campylobacter* spp. and *Enterococcus* spp.). However, this classification also should take into account other bacteria that could be potentially transferred via foods as commensal bacteria (e.g. *Pseudomonas aeruginosa*).

13. WHO organized a working group consultation in Canberra in 2005 with the scope to develop a list of critically important antimicrobial agents in human medicine, The WHO classification in 2005 was the first important attempt to classify antimicrobial agents based on their importance in human medicine. The list was subsequently re-examined and updated during two meetings held in Copenhagen in 2007 (2nd Edition) and in 2009 (3rd edition). All reports including the updated versions of the WHO list of Critically important antimicrobials for Human Medicine are available at HTTP://WWW.WHO.INT/FOODBORNE_DISEASE/RESISTANCE/CIA/EN/INDEX.HTML

Management Options for Critically Important Antimicrobials for Human Medicine

14. The development of this list is part of a more comprehensive approach to the public health issue of antimicrobial resistance in both animals and humans. It was emphasized that there should be a sense of urgency to the development of such risk management strategies, particularly for quinolones and 3rd / 4th generation cephalosporins. In addition to management options for all antimicrobials, specific options include the following:

- Do not use these drugs at all;
- Use only in individual animals based on culture results and lack of alternative agents;
- Use only in individual animals;
- Use in groups of animals after risk assessment demonstrates acceptable level of safety.

15. These options are listed in the order that will minimize selective pressure and are therefore least likely to contribute to the development and spread of resistant bacteria in animals treated with these agents.

16. Contingency plans could be developed to control or eradicate *Salmonella* and other zoonotic pathogenic bacteria resistant to two or more “critically important” antimicrobials when they appear in food production animals or in the food supply.

17. Options include:

- Recall associated foods;
- Restrict movement of infected or colonized animals;
- Processing that guarantees removal of all resistant bacteria;
- Destroy food items;
- Destroy groups of animals infected or colonized.

18. These options are listed in the reverse order that will minimize the spread and persistence of these multi-resistant bacteria and thus safeguard public and animal health.

The WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance

19. The WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (WHO-AGISAR HTTP://WWW.WHO.INT/FOODBORNE_DISEASE/RESISTANCE/AGISAR/EN/INDEX.HTML) was established in December 2008 to support WHO's effort to minimize the public health impact of antimicrobial resistance associated with the use of antimicrobials in food animals. In particular, the Advisory Group will assist WHO on matters related to the integrated surveillance of antimicrobial resistance and the containment of food-related antimicrobial resistance. The terms of reference of WHO-AGISAR are as follows:

- Develop harmonized schemes (including appropriate sampling) for monitoring antimicrobial resistance in zoonotic and enteric bacteria.

- Support WHO capacity-building activities in Member countries for antimicrobial resistance monitoring (AMR training modules for Global Foodborne Infections Network training courses and workshops (GFN HTTP://WWW.WHO.INT/GFN/TRAINING/EN/INDEX.HTML;
- Promote information sharing on AMR;
- Provide expert advice to WHO on containment of antimicrobial resistance with a particular focus on Human Critically Important Antimicrobials;
- Support and advise WHO on the selection of sentinel sites and the design of pilot projects for conducting integrated surveillance of antimicrobial resistance;
- Support WHO capacity-building activities in Member countries for antimicrobial usage monitoring.

20. The WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance comprises over 20 internationally-renowned experts in a broad range of disciplines relevant to antimicrobial resistance, appointed following a web-published call for advisers, and a transparent selection process. WHO-AGISAR holds regular telephone conferences and annual face-to-face meetings. The first meeting of AGISAR was held in Copenhagen, Denmark. The second meeting of AGISAR was held in Guelph, Canada on 5-7 June 2010. The four AGISAR subcommittees (antimicrobial usage monitoring, antimicrobial resistance monitoring, capacity building and data management) are in the process of developing practical tools/guidelines/protocols to support WHO Member Countries in their efforts to implement a national program for integrated surveillance of antimicrobial resistance.

The way forward

21. WHO will work closely with partners at international, regional and national levels to ensure the implementation of the Global principles for the containment of antimicrobial resistance in animals intended for food, in particular the ban of antimicrobial growth promoters, the rationale prescription and use of veterinary drugs and the restriction of use in animals of Human Critically Important Antimicrobials in animal husbandry, in particular quinolones and 3rd and 4th generation cephalosporins..

22. WHO will work with FAO, OIE as well as powerful stakeholders, including industry, to achieve real reduction of use of certain classes of antimicrobials in animals and the phasing out of the use of antimicrobials as growth promoters in animals intended for food.

23. The WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) will enhance the capacity of Member countries (through training courses and sentinel studies), particularly developing countries to conduct surveillance of antimicrobial use and resistance, to implement intervention strategies to contain antimicrobial resistance and to implement risk assessment approaches to support selection of risk management options

24. AGISAR will provide guidance to the WHO on a framework for the development of an international network to promote and enhance collaboration on harmonization and data sharing.

25. As follow up of the activities of the Codex *Ad Hoc* Intergovernmental Codex Task Force on Antimicrobial Resistance, WHO will provide to its Member Countries support and guidance for implementation of the guidelines on risk analysis of antimicrobial resistance

WORLD ORGANISATION FOR ANIMAL HEALTH (OIE)

26. Since veterinary products are key elements that enable early detection, efficient prevention and control of animal diseases, the World Organisation for Animal Health (OIE) has developed a coherent strategy for its activities in the area of veterinary drugs, vaccines and diagnostics.

27. Within this strategy, OIE pays specific attention to the responsible and prudent use of antimicrobials, but also to the need for harmonised approaches for the approval and use of veterinary medicinal products recognising the key role of good governance on all matters related to veterinary medicinal products. The strengthening of the actions in this field started with the adoption of Resolution n° 25 on veterinary products at the 77th OIE General Session in May 2009.

28. At the OIE 78th OIE General Session in May 2010, the Fifth Strategic Plan (2011-2015) of the OIE was adopted by the Delegates of the 176 OIE Members, to improve animal health, veterinary public health

and animal welfare world-wide. The plan includes good governance of veterinary services, the reinforcement of veterinary services capacities and infrastructure, including veterinary legislation and more generally the linkages between animal health, food safety and food security. Veterinary medicinal products, including antimicrobials, are specifically mentioned and activities related to this area will be strengthened in the coming years.

OIE activities are based on several complementary approaches:

(a) **The development and regular updating of international standards and guidelines within the mandate of the OIE as the standard-setting body for animal health and zoonotic diseases, recognised by the World Trade Organization**

29. The OIE is currently working on the elaboration of guidelines on antimicrobial resistance related to aquaculture. An OIE *ad hoc* Group on the responsible use of antimicrobials aquatic animals was created and met for the first time in January 2010 in order to draft standards for the responsible production, distribution (including international trade) and use of antimicrobials in aquatic animals for inclusion in the *Aquatic Animal Health Code*.

30. The proposal to update the existing chapters in the OIE *Terrestrial Animal Health Code* and *Manual of Diagnostic Tests and Vaccines in Terrestrial Animals*, related to antimicrobial resistance dealing with terrestrial animals, was approved at the 78th OIE General Session and a first meeting of an *ad hoc* Group will be organised in November 2010 to start the process.

31. The outcome of the Codex Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance will be taken into account and WHO and FAO experts are invited to participate to this Group.

(b) **The provision of permanent support to Veterinary Services and laboratories to enable OIE Members to implement the published standards**

32. The evaluation of the performance of Veterinary Services, the OIE PVS tool, is based on a qualitative assessment of the performance and the compliance of Veterinary Services with the OIE international standards. 106 countries have already requested this independent evaluation (June 2010). The PVS Gap Analysis, allows countries to quantify their needs and the corresponding budget, based on the outputs of the initial PVS evaluation. In June 2010, 53 Countries have requested a Gap analysis mission.

33. The OIE Laboratory Twinning Programme, launched in 2006 creates opportunities for developing and in-transition countries to develop laboratory diagnostic methods and scientific knowledge based on the OIE Standards. The programme, now enlarged to Collaborating Centres, aims at mobilising the existing expertise of the whole network of the 227 OIE Reference Laboratories and Collaborating Centres to develop capacities in geographic areas that are currently underrepresented. More than 20 twinning projects are underway and 10 others in preparation and this activity will be further enhanced in areas related to veterinary medicinal products.

34. To facilitate scientific cooperation and allow future interactions between existing and future OIE collaborating Centres and reference Laboratories, OIE organised the Second Global Conference of OIE Reference Laboratories and Collaborating Centres, held in OIE Headquarters in June 2010 with the participation of FAO and WHO.

35. In addition to the existing Collaborating Centre on Veterinary Medicinal Products and Reference Laboratory on antimicrobial resistance, OIE's activities in the area of veterinary medicinal products will be further supported by a new Collaborating Centre on Diagnosis and Control of Animal Diseases and Related Veterinary Product Assessment in Asia, that was approved at the OIE 78th OIE General Session in May 2010.

(c) **The modernisation or update of national legislation, including marketing approval and control of veterinary products**

36. In the context of global challenges currently facing animal health and veterinary public health, veterinary legislation is a crucial infrastructure component for all countries. The OIE developed and will develop new tools to provide guidance for its Members, which provides a minimal framework to help them to update their national legislation in accordance with international standards. (HTTP://WWW.OIE.INT/ENG/OIE/ORGANISATION/A_GUIDELINES_VET%20LEG.PDF).

37. The OIE also continues to actively help countries to build and implement effective legislation to assure the quality, safety and efficiency of veterinary medicinal products and will organise a First OIE Global Conference on Veterinary Legislation, on the theme 'Modernising Veterinary Legislation for Good Governance" to be held in Djerba Tunisia on 7-9 December 2010.

38. As an associated Member of the VICH (International Co-operation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products), OIE is actively promoting the need for harmonisation in the approval and registration process for veterinary medicinal products.

39. To prepare the VICH IV Public Conference "VICH impact and future expectations", a questionnaire had been developed by OIE/VICH in order to get a general view on the worldwide situation of public policy and its implementation dealing with veterinary products. The questionnaire also helped to evaluated how the VICH initiative could be used by all the OIE Members as a tool to develop and improve international and regional cooperation in the establishment and enforcement of legislation dealing with veterinary medicinal products.

40. During the conference that took place from 24 to 25 June 2010 at OIE Headquarters in Paris, the results of the questionnaire were presented and the proposal for a future strategy on extending the appreciation of VICH activities towards non-VICH countries and regions was discussed. OIE will continue to actively provide its support to the VICH process, with a wider understanding of VICH standards as part of capacity building and harmonisation in the area of veterinary medicines regulation.

(d) **Communication**

41. Since its last meeting of the Codex Task Force on Antimicrobial Resistance, the OIE has undertaken a number of initiatives specifically directed to veterinary medicinal products to enhance awareness on the need for responsible and prudent use of veterinary drugs.

42. OIE has organised two regional conferences specifically dedicated to veterinary medicinal products, entitled "Towards the harmonisation and improvement of registration, distribution and quality control".

43. The first one was organised in Africa in March 2008 in Dakar (Senegal) and the second one took place in the Middle East in Damascus (Syria) in December 2009.

44. Since, to further enhance awareness and strengthen the link between OIE and its 176 Members, the OIE has started to organise regional training workshops for OIE National Focal Points on veterinary products who were designated by the OIE Delegates. Their tasks, conducted under the authority of the OIE Delegate, include communication and establishment of networks with authorities and experts on veterinary products; the monitoring of legislation and the control of veterinary products, and also the consultation and preparation of comments on draft texts of standards, guidelines and recommendations related to veterinary products and proposed by the OIE.

45. The first training workshop will take place in Europe, (July 2010, Serbia), followed by a workshop in the Americas, (September 2010, Colombia), in Africa (November 2010, South Africa) and in Asia-Pacific (June 2011, Cambodia). The WHO has been invited to participate in theses future training activities.

46. These events are aiming at improving the governance related to veterinary medicinal products covering all steps, production, distribution and use.

(e) **Collaboration with relevant international organisations**

47. The OIE continues to emphasize the need to reinforce the relationship with the Codex Alimentarius Commission (CAC). In the capacity of an observer organisation, the OIE contributes to the work of several Codex Committees related to veterinary medicinal products;

48. Considering that antimicrobial resistance is a global, multidisciplinary issue, the OIE is permanently renewing and strengthening collaboration with WHO and FAO, and Member countries. This close cooperation, which is actively being developed, will help to obtain the benefits of synergies amongst the different organisations.

49. A first meeting of the OIE/FAO/WHO Consultative *ad hoc* Group on Collaborative Activities on Antimicrobial Resistance was held on 30 September and 1 October 2009 in OIE Headquarters in Paris (France) with the aim of finding common areas for cooperation and maintaining good communication

between FAO, OIE and WHO in this field. After mapping out the areas where antimicrobial resistance may arise, the *ad hoc* Group identified five main areas of activities currently addressed by the three organisations:

i) Guidelines, standards and harmonisation;

ii) Legislation, inspection/control;

iii) Data collection and surveillance;

iv) Capacity building; and

v) Communication.

50. As a concrete outcome WHO and FAO experts have been invited to participate in a new *ad hoc* Group on antimicrobial resistance and the WHO has been invited to take part in the future training of OIE focal points on veterinary products that will be organised in different Regions in the next 12 months.