CODEX ALIMENTARIUS COMMISSION



Food and Agriculture Organization of the United Nations



Viale delle Terme di Caracalla, 00153 Rome, Italy - Tel: (+39) 06 57051 - E-mail: codex@fao.org - www.codexalimentarius.org

#### Agenda Item 3(b)

CX/AMR 17/5/4 November 2017

# JOINT FAO/WHO FOOD STANDARDS PROGRAMME

# AD HOC CODEX INTERGOVERNMENTAL TASK FORCE ON ANTIMICROBIAL RESISTANCE

**Fifth Session** 

## INFORMATION ON THE WORK OF OTHER RELEVANT INTERNATIONAL ACTIVITIES ON ANTIMICROBIAL RESISTANCE

# (Information of FAO and WHO)

## Food and Agriculture Organization of the United Nations (FAO)

1. FAO is dedicated to strengthening the global commitment to address the threat posed by AMR with a strong emphasis on enhancing action at a local level through regional and country activities. The adoption of the FAO Resolution on AMR, in support of the Global Action Plan on AMR, and the subsequent development of the FAO Action Plan on AMR<sup>1</sup> to support the food and agriculture to address AMR is the basis for the enhanced programme of work on AMR by the organization. As part of this, FAO, in collaboration with OIE and WHO, are implementing an intensive programme of tripartite activities in line with "The Tripartite's Commitment: Providing multi-sectoral, collaborative leadership in addressing health challenges<sup>2</sup>" published in October 2017 and reaffirming the organizations commitment to combat antimicrobial resistance at human-animal-ecosystems interface. An overview of tripartite activities was provided in in CX/CAC 17/40/14Add1<sup>3</sup> and a further update will be provided to the Task force.

2. This paper provides an overview of FAOs activities under the four pillars of its action plan – awareness, evidence, governance and good practice. The objective of the work is to strengthen and support the engagement of the food and agriculture sectors in efforts to address AMR, from the development of multistakeholder One Health National Action Plans (NAPs) through to their subsequent implementation. FAO is currently directly working with the food and agriculture sector in countries in Africa, Asia, Latin America and Eastern Europe and Central Asia to address AMR.

## Awareness raising and development of National Action Plans

3. Limited awareness and understanding among all stakeholders in the food and agriculture sector remains a critical barrier to a fully coordinated and effective One Health approach to addressing the threat of AMR. It remains essential to raise awareness among these stakeholders to increase the understanding of the relevance of AMR to them and the potential role that they can play in remedying the situation. In order to do so, a range of stakeholder events at national and regional level are being implemented, supported by the development of informational products tailored to the local situation. AMR is also being introduced into the agenda of meetings and events on related areas. For example, FAO has worked closely with ASEAN and SAARC to highlight the issue of AMR and the two regional organizations have subsequently convened Special Sessions on AMR. The ASEAN meeting (July 2017) developed a call to action on ASEAN cooperation on AMR as well as identified specific regional interventions to move respective national action plans forward. Similarly, FAO engagement in regional meetings in Latin America has facilitated in raising the profile of the issue.

<sup>3</sup> Available at: <u>http://www.fao.org/fao-who-codexalimentarius/sh-</u>

<sup>&</sup>lt;sup>1</sup> The FAO Action Plan and Resolution on AMR are available at <u>http://www.fao.org/3/a-i5996e.pdf</u>

<sup>&</sup>lt;sup>2</sup> The Tripartite's Commitment: Providing multi-sectoral, collaborative leadership in addressing health challenges is available at: <u>http://who.int/zoonoses/tripartite\_oct2017.pdf?ua=1</u>

proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-701-40%252FWD%252Fcac40\_14e.pdf

4. A library of informational products (videos, infographics, posters etc.) have been developed to support awareness raising on AMR and is available on the FAO webpage<sup>4</sup> and YouTube<sup>5</sup>. This is being complimented by communication strategies on AMR at global and regional level to ensure that pertinent information is reaching the relevant stakeholders. For example, a region-wide communication and advocacy strategy for AMR in Asia has been developed and a strategic framework for awareness and advocacy is under preparation in Latin America. Support is also being provided to countries to develop their national communication strategies.

5. A particular focus of in country work is the development of National Action Plans (NAPs) on AMR, a starting point for which is the development of a national situation analysis. FAO is completing a short guidance to support inclusion of the relevant food and agriculture aspects in any situation analysis related to AMR. In addition FAO supports stakeholder engagement initiatives, policy development programmes, development of work plans, and strategies for monitoring and evaluation of the NAPs leading to the adoption of One Health NAPs by countries.

## Evidence and surveillance

6. To support the food and agriculture sectors in understanding their capacities in relation to AMR susceptibility testing and surveillance, FAO has developed a tool for the assessment of AMR laboratory capacity and surveillance (ATLASS). This tool has been successfully applied in in six countries with further assessments scheduled for later this year. The outcomes are used as the basis for national level discussions on the establishment of AMR surveillance programmes in the food and agriculture sector, with the objective of building on existing capacities to the extent possible to facilitate sustainability.

7. A number of country-level initiatives are underway in different regions to improve local knowledge of antimicrobial use (AMU) in agriculture. For example, in Asia, information on AMU in the livestock production system commenced with the development of a framework to track the flow of antimicrobials to and within production systems, by mapping of the livestock sector, the food production sector and defining the value chains for antimicrobials produced locally and internationally. In some countries this is also linked with efforts to explore the economic aspects of minimizing AMU in animal production. Approaches vary by country, but emphasis is focused on expansion and strengthening pre-existing mechanisms of on-farm data collection.

8. A regional workshop on AMR surveillance in the food and agriculture in south East Asia was convened in Bangkok, Thailand in December 2016 to support the establishment of feasible surveillance programmes for AMR in the animal sector in a sub-group of countries in Asia. Subsequent discussions at the policy as well as the technical level, have enabled further alignment of national programmes and the surveillance strategy guidelines are expected to be finalized at the end of November. A first regional workshop in East Africa was implemented last month to initiate a coordinated and regionally-relevant AMR surveillance plan.

9. Capacity development activities, including laboratory training, have been implemented in the Asian region for interested countries in preparation for implementation of their monitoring and surveillance programmes with similar activities being planned in other regions. To support this work and particularly those countries with little or no capacity to date, FAO has developed a guidance document on some of the practical aspects of initiating surveillance such as the types of samples to include and the laboratory methods to conduct susceptibility testing.

10. FAO has identified 10 Reference Centres around the world to specifically support the implementation of its work with the food and agriculture sectors in member countries related to AMR. Work plans are currently being developed for each Reference Centre to enable them to become operational in the course of 2018.

11. Increasing knowledge about the significance of contamination of the environment and foods with low concentrations of antimicrobial residues has prompted renewed interest in antimicrobial residues. Residue monitoring may prove to provide an indirect measure of antimicrobial use. Residue monitoring studies and training have been have been initiated in some countries.

## Governance

12. To establish efficient and effective governance mechanisms, access to up-to-date national legislation relevant for antimicrobial use (AMU) and antimicrobial resistance (AMR) plays a key role. FAO is supporting legislative review processes and development or revision of existing legislation at country-level to ensure that the relevant legal instruments are in place to facilitate actions. Lessons learned from these reviews are being documented and will form the basis of an overarching review and guidance document on the legislative aspects of addressing AMR in the food and agriculture sectors.

<sup>&</sup>lt;sup>4</sup> The FAO webpage on AMR is available at <u>http://www.fao.org/antimicrobial-resistance/en/</u>

<sup>&</sup>lt;sup>5</sup> Examples of FAO videos on AMR are available at <u>https://youtu.be/x2Ixa-CkZok</u>

13. FAO hosts FAOLEX, the largest collection of agriculture relevant legislative instruments and has begun the process of identifying existing records in FAOLEX that are relevant for AMU/AMR, and tagging them appropriately for easy identification and retrieval. To date this encompasses legislation governing veterinary medicines, feed, and maximum residue limits (MRLs) for veterinary medicines. Records will also include, among others, selected instruments in the areas of food safety, animal health, animal production, fisheries/aquaculture, feed, waste/hazardous waste/hazardous substances, environmental protection and water quality. The work is also facilitating a comparative legal analyses for a study on AMR legislation to support guidance in this area.

# Good Practices.

14. Recognizing that progress on combating AMR will not be achieved without changing practices, this is a key focus for FAO activities on AMR. While globally driven, the need to adapt practices to the local context is viewed as critical for success. Changing practices begins with awareness and FAO have recently produced a video looking at the situation in four countries to highlight the challenges, feasibility and approaches to changing practices to reduce antimicrobial use<sup>6</sup>. At country level, this work begins with studies to review of existing knowledge, attitude, and practices (KAP) and such studies have already been undertaken or initiated a number of countries in Asia, where an enhanced KAP+ framework has been developed, which also takes account of potential interventions. This is supported by more centralised initiatives to review existing practices, examples of which follow below.

# Animal Feeding Practices

15. AMR has been on the agenda of the annual joint meeting of FAO and the International Federation of Feed Industries for the past three years. As a result of the progressive engagement with the animal feed the sector to address AMR, this issue is now a regular discussion item during the annual International Feed Regulators Meetings<sup>7</sup>. FAO has produced a video to highlight how the feed sector can contribute to decrease the use of antimicrobials "Voices from the feed sector on containing antimicrobials resistance<sup>8</sup>".

16. In light of the positive role changes in animal feed and nutrition can play in reducing AMU and the need for practical guidance for countries, FAO is developing "Animal nutrition strategies to reduce the use of antibiotics in animal production (swine, poultry and ruminants)". This publication, together with case studies, will be disseminated through a series of workshops and technical documents organized in collaboration with the feed industry, to support changing animal feeding practices.

17. Work is also underway on a document on `Eubiotics in animal nutrition' that will provide additional information on feed ingredients that can be used to ensure adequate growth of the animal without the use of antibiotics as growth promoters. FAO is engaged with a variety of stakeholders from the public and private sector to secure the safety of feed and therefore contribute to decrease need for antimicrobial treatments to animals and facilitates the Multi-Stakeholder Partnership for Feed Safety.

## Fisheries and aquaculture Practices

18. FAO is finalising the FAO Code of Conduct for Responsible Fisheries (CCRF) – Technical Guidelines on the Prudent and Responsible Use of Veterinary Medicines in Aquaculture. It provides information on the global challenges, the risk and benefits of antimicrobial use, salient issues concerning their use, and a number of recommendations to governments and to the private sector, including guidance for small-scale aquafarmers and to aquatic animal health professionals. FAO is also developing a publication on Responsible Management of Bacterial Diseases in Aquaculture as a key reference in the work on AMU and AMR in aquaculture. Direct support is also being provided to the fisheries sector in countries in Asia and Latin America and the Caribbean with particular emphasis on engaging this sector in National Action Plan development and implementation. Further details are available in a recent paper presented to delegates to the FAO Committee on Fisheries Sub-Committee on Aquaculture<sup>9</sup>.

https://www.youtube.com/watch?v= QfcLEHIWZA

<sup>&</sup>lt;sup>6</sup> An FAO video on food practices to address AMR is available at: <u>https://youtu.be/U0TQE\_XZRPo</u> <sup>7</sup> A short video description of the International Feed Regulators Meeting is available at

<sup>&</sup>lt;sup>8</sup> Voices from the feed sector on containing antimicrobials resistance is available at: <u>https://www.youtube.com/watch?v=\_8HIJiGzSTc</u>

<sup>&</sup>lt;sup>9</sup> Antimicrobial resistance in aquaculture is available at <u>http://www.fao.org/cofi/46073-015d659aed398efe120a5953620684aea.pdf</u>

#### Crop production

19. Given that some antimicrobials used in veterinary and human medicine are also used in horticulture production, FAO convened a meeting on 1-3 October 2017 to begin gathering evidence of AMR linked to antimicrobial use in horticulture. A review of the literature was undertaken in advance and is now been finalized based on inputs from the expert meeting. The meeting also considered data from some 30 countries provided in response to a call for data on antimicrobial use in plant production. Despite these efforts, a noticeable paucity of data in the area of AMR and horticulture was noted. This issue will be further addressed in ongoing work on AMR. Nevertheless the importance of good practice to minimize antimicrobial use and ensure appropriate use, when needed, were highlighted.

20. FAO is working on the development of tools and instruments to support regulation and use of antimicrobial chemicals (e.g. pesticides) in the agriculture sector and support implementation of the international Code of Conduct on Pesticide Management.<sup>10</sup>. FAO also promotes integrated pesticide management (IPM) as the preferred approach to crop production and has regional programmes ongoing in Asia, the Near East and Africa. This approach aims to minimize pesticide use including use of antimicrobials in crop production and more information on IPM and its role in pesticide risk reduction is available online.<sup>11</sup>

#### Food processing and biocide use

21. In light of the importance of biocides (disinfectants, sanitizers) in achieving and maintaining microbiological food safety and in response to requests for information on biocide use, FAO convened a technical meeting on AMR and biocides in food production and processing on 18-19 October 2017 to review the available information on this issue and discuss follow-up actions. Noting the limited data on the issue and also the important role of biocides in food safety it was agreed that there was a need for greater awareness on good practices in relation to sanitation and disinfection to ensure this valuable resource are used optimally and effectively. Key aspects of such guidance was developed in the course of the meeting and this will be further developed in the coming months.

#### Food production and agriculture environment

22. FAO is collecting and synthesizing knowledge on the role of agriculture in contaminating the environment with antimicrobial (AM) residues and AMR bacteria as well as assessing the threats that AMR bacteria and residues in the environment pose for food contamination and safety. A meeting about soil and water contamination with AMR and AM residues was held on Oct 30-Nov 1, 2017 at FAO Headquarters in Rome. Experts from North and South America, Europe, Asia, and Africa identified current gaps in knowledge critical for the control of environmental AMR and proposed future studies. Although recognized as an important source of environmental loading with AMR bacteria, the attributable contribution of agriculture to the problem, compared to pharmaceutical, hospital and municipal waste water treatment and sludge, remains unknown. Nevertheless, environmental protection mitigation strategies that can be implemented immediately, even before additional data becomes available, were proposed. The summary review of the current situation is now in being finalized. In addition a systematic review of AMR in water and the environment is also underway in Latin America.

23. On 2-4 May 2018, FAO will host the Global Symposium on Soil Pollution (GSOP18) in Rome, Italy. This symposium will cover a number of themes that address AMR in the environment including: 1) pollution in fields, 2) impact on human health, 3) remediation of soil pollution, 4) policy development, and 5) thresholds of pollution in agriculture Recognizing antimicrobial residues and antimicrobial resistant organisms (above the normal flora) as soil pollutants, AMR will be one of the cross-cutting theses of the symposium.

24. FAO would like to express its sincere appreciation to those countries support the organization to implement its Action Plan on AMR, namely the United Kingdom, the United States of America, the Russian Federation, France and Sweden.

## WORLD HELATH ORGANIZATION (WHO)

## Integrated surveillance on antimicrobial resistance in foodborne bacteria

25. WHO established the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (WHO AGISAR)<sup>12</sup> in 2008. AGISAR supports the efforts of WHO and its Member States to minimize the public health impact of antimicrobial resistance (AMR) associated with the use of antimicrobials in food producing animals.

<sup>&</sup>lt;sup>10</sup> The tools and guidelines available can be found at: <u>http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/en/</u>

<sup>&</sup>lt;sup>11</sup> More information on IPM available at: <u>http://www.fao.org/agriculture/crops/core-themes/theme/pests/ipm/en/</u>

<sup>&</sup>lt;sup>12</sup> For more information on AGISAR see: <u>http://who.int/foodsafety/areas\_work/antimicrobial-resistance/agisar/en/</u>

26. In 2013, after a consultative process of four years, WHO published the first version of the "Integrated Surveillance of Antimicrobial Resistance: Guidance from a WHO Advisory Group" (the AGISAR guidance 2013).<sup>13</sup> The AGISAR guidance 2013 has been revised in 2017 in support of the implementation of the global action plan on AMR, in collaboration with FAO and OIE.<sup>14</sup> Similar to the AGISAR guidance 2013, the revised guidance describes a step-by-step approach to designing a programme of integrated surveillance of antimicrobial resistance in foodborne bacteria and includes recommended standardized and validated antimicrobial susceptibility testing methods, harmonized interpretive criteria, and approaches to the collection and reporting of antimicrobial consumption and use data.

27. WHO AGISAR is currently developing a global protocol on surveillance of extended spectrum betalactamase (ESBL) producing Escherichia coli using a "One Health" approach ("Tricycle ESBL E. coli surveillance project"). Tricycle ESBL E.coli surveillance project is intended to monitor the prevalence of ESBL E.coli in humans, the food chain and the environment. Four countries have been trained to pilot the protocol during a period of one year, including Ghana, Pakistan, Indonesia and Malaysia. The pilot phase of the project will start in the late November 2017.

28. The Tricycle ESBL E. coli surveillance project also includes the protocol development of measuring certain antimicrobial residues in sewage as a proxy for human use of antimicrobials. This strategy will be of special interest to countries where sales data and prescription data is difficult to get.

29. WHO AGISAR's national capacity building projects are also underway to strengthen the integrated surveillance of AMR in 16 countries.<sup>15</sup> "The global workshop to strengthen the integrated surveillance of antimicrobial resistance by taking a One Health approach" took place in Sapporo, Japan in September 2017 by convening all of the principal investigators of the capacity building projects, and the network was established to continue a cross-national dialogue.

30. Recognizing the need to foster the establishment of national antimicrobial resistance surveillance systems, WHO has developed the Global Antimicrobial Resistance Surveillance System (GLASS)<sup>16</sup>. The aim of the WHO GLASS is to provide a platform to report and analyse standardized, comparable and validated data on antimicrobial resistance in order to: (i) inform decision-making; (ii) drive local, national and regional action; and (iii) provide the evidence base for action and advocacy. The early implementation phase of WHO GLASS focuses on the assessment and reporting of resistance of selected priority human bacterial pathogens to selected priority antimicrobials. These priority antimicrobial-pathogen (drug-bug) combinations include the following foodborne bacteria: fluoroquinolone-resistant Salmonella spp., third-generation cephalosporin-resistant Salmonella spp., and carbapenem-resistant Salmonella spp.. It is planned that WHO GLASS will include data from the integrated surveillance across the human-animal ecosystems interface (a scaled Tricycle project).

31. Currently, 47 countries are enrolled in WHO GLASS and nine others are going through the enrolment procedures. The first GLASS report is planned to be published in January 2018 with information about the development process and data received from participating countries. It is planned that the WHO GLASS will expand a scope of data in future.

32. WHO is currently commissioning a systematic review of current evidence addressing the potential impacts on human health from antimicrobial agents in the environment. This review is expected to answer the following main questions:

- What the pathways exist for the release of antimicrobials into the environment;
- What antimicrobials are of most concern with regard to the selection and development of antimicrobial resistance within the environment; and
- What the fate and persistence of antimicrobials is in the environment.

Following evaluation of available evidence, prioritized research needs will be proposed, as well as potential resolutions.

<sup>&</sup>lt;sup>13</sup> Available at: <u>http://apps.who.int/iris/bitstream/10665/91778/1/9789241506311\_eng.pdf?ua=1</u>

<sup>&</sup>lt;sup>14</sup> Details of the revised integrated surveillance guidance will be provided on

http://who.int/foodsafety/areas\_work/antimicrobial-resistance/agisar/en/

<sup>&</sup>lt;sup>15</sup> Countries supported by WHO include: Albania, Argentina, Bhutan, Chad, Ecuador, Ethiopia, Islamic Republic of Iran, Japan, occupied Palestinian territory, Philippines, South Africa, Suriname, Tanzania, Thailand, Zambia and Zimbabwe.
<sup>16</sup> <u>http://www.who.int/antimicrobial-resistance/global-action-plan/surveillance/glass/en/</u>

33. In 2016 WHO developed a methodology for monitoring national antimicrobial consumption (AMC).<sup>17</sup> Since then, WHO supported the implementation of a national monitoring system in 20 LMIC countries through trainings and follow-up workshops. Countries are submitting data to the global AMC surveillance program, will be linked to the WHO GLASS, and will be published in 2018. WHO will continue to conduct trainings on the WHO methodology and support countries in implementing national surveillance system to monitor AMC.

34. Standardized methodologies to survey antimicrobial use in hospitals and in community settings are being developed, and will complement the surveillance of AMC. WHO will coordinate regional trainings on the methodology and facilitate data collection following the trainings.

35. WHO has recently initiated work on antimicrobial stewardship to improve antimicrobial prescribing and use. The Essential Medicines List<sup>18</sup> and categorization of antimicrobials into Access, Watch and Reserve will be one of the tools for stewardship activities. In November 2017, WHO headquarters convened experts to discuss antimicrobial stewardship at the local and national level and the activities that WHO can undertake in the coming years.

36. Other activities associated with antimicrobial consumption and use includes the Price and Availability Survey that enables collection of data on pricing and shortages of 12 classes of antimicrobials. The survey has been conducted in several LMICs during 2017 and the data is currently being analyzed.

37. WHO has published the priority pathogen list<sup>19</sup> and the review of the R&D pipeline for antibiotics.<sup>20</sup> WHO has identify a list of priority pathogens (PPL) for R&D with the highest priority to be given to Enterobacteriaceae, Acinetobacter and Pseudomonas. WHO plans to have annual review the R&D pipeline and to update the PPL in 3 to 5 years. WHO also supports the Global Antibiotic Research And Development Partnership (GARDP) in collaboration with DNDi. WHO is investigating in the field of rapid diagnostic tests for AMR.

## Use of medically important antimicrobials in the food chain

WHO list of Critically Important Antimicrobials for Human Medicine (WHO CIA list)

38. The development of the WHO list of Critically Important Antimicrobials for Human Medicine (WHO CIA List) was initiated almost 15 years ago following the recommendation of a 2004 expert workshop on 'Non-Human Antimicrobial Usage and Antimicrobial Resistance: Management Options', jointly convened by FAO, OIE and WHO.<sup>21</sup>

39. The WHO CIA List provides a ranking of Medically Important Antimicrobials to help prioritize risk management options regarding their use in non-human settings.

40. The list was recently updated in 2016 and the most important change in this 5th revision is the new classification of Polymyxins as "highest priority critically important antimicrobials" because of the identification of plasmid-mediated colistin resistance and potential transmission through the food chain.

41. The current list and the process/criteria used to establish the list were published in April 2017 and are available online along with its advocacy brochure.<sup>22</sup>

## WHO guidelines on use of medically important antimicrobials in food-producing animals

42. WHO published, "WHO guidelines on use of medically important antimicrobials in food-producing animals" in November 2017.<sup>23</sup> Building upon two decades of WHO work on containment of antimicrobial resistance (AMR) from the food chain, the aim of these guidelines is to help preserve the effectiveness of medically important antimicrobials, particularly those antimicrobials judged to be critically important for human medicine, in direct support of the global action plan on AMR.<sup>24</sup>

43. The formal guidelines were developed following stringent WHO process and procedures, overseen by the WHO Guideline Review Committee, which requires that formal recommendations are based on sound evidence and are therefore of the highest quality. The guidelines include recommendations based on evidence derived from WHO commissioned systematic and narrative literature reviews and best practice statements, addressing the use of antimicrobials in food-producing animals for different purposes.

<sup>&</sup>lt;sup>17</sup> <u>http://www.who.int/medicines/areas/rational\_use/WHO\_AMCsurveillance\_1.0.pdf?ua=1</u>

<sup>&</sup>lt;sup>18</sup> http://www.who.int/medicines/publications/essentialmedicines/en/

<sup>&</sup>lt;sup>19</sup> <u>http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/</u>

<sup>&</sup>lt;sup>20</sup> http://www.who.int/medicines/news/2017/IAU AntibacterialAgentsClinicalDevelopment webfinal 2017 09 19.pdf

<sup>&</sup>lt;sup>21</sup> Available at: <u>http://apps.who.int/iris/bitstream/10665/68701/1/WHO\_CDS\_CPE\_ZFK\_2004.8.pdf?ua=1</u>

<sup>22</sup> http://www.who.int/foodsafety/publications/antimicrobials-fifth/en/

<sup>&</sup>lt;sup>23</sup> http://www.who.int/foodsafety/publications/cia\_guidelines/en/

<sup>&</sup>lt;sup>24</sup> http://apps.who.int/iris/bitstream/10665/193736/1/9789241509763\_eng.pdf?ua=1

44. The process to develop WHO guidelines are described in the WHO handbook for guideline development (second edition).<sup>25</sup> These included: (i) identification of priority questions and critical outcomes; (ii) retrieval of the evidence in a transparent manner using standard methods for systematic reviews; (iii) narrative literature reviews produced by topic-expert scientists; (iv) assessment and synthesis of the evidence; (v) use of this evidence for the formulation of recommendations; (vi) planning for dissemination, implementation, impact evaluation and future updating of the guidelines.

45. The process of the guideline development was managed by the WHO Steering Group, while the Guideline Development Group consisting of external experts was responsible for the drafting of these guidelines. Priority questions on the effects of limitations of use of medically important antimicrobials in food-producing animals on antimicrobial resistance in human and animal populations, including overall use and specifically for growth promotion, disease prevention, and treatment were agreed on by the WHO Steering Group.

46. These questions guided systematic reviews and narrative literature reviews and the evidence identified was summarized in evidence-to-recommendation tables to enable the GDG to use the appropriate evidence to formulate each recommendations.

47. The GRADE (grading of recommendations, assessment, development and evaluation) approach was used to appraise and use the evidence to develop recommendations.

48. Full reports from two systematic reviews and the supplemental review, and three literature reviews can be found in the Web Annex A to the guidelines online.<sup>26</sup>

- 49. There are four recommendations and two best practice statements as follows:
  - Medically important antimicrobials should not be used for growth promotion.
  - For prevention in the absence of disease, preference should be given to non-antibiotic options such as hygiene, biosecurity, vaccines, or probiotics. Exceptionally, under veterinary supervision antibiotics can be used starting with veterinary only drugs, then antibiotics in the WHO CIA List in the reverse order of their importance for human health.
  - For control and prevention of the dissemination established infection, and for treatment: antimicrobials classified as "important" and "highly important" should be used. In the absence of option in these categories, use of antimicrobials classified as critically in the reverse order of their importance can be considered under veterinary supervision.
  - Use of antimicrobials classified as Highest Priority Critically Important Antimicrobials, which are last resort to treat life threatening human infections, should be restricted in animals as they are in humans.
- 50. Two best practice statements are as follows:
  - New classes of antimicrobials developed for use in humans will be considered critically important for human medicine unless categorized otherwise by WHO.
  - Medically important antimicrobials that are not currently used in food production such as carbapenems should not be used in the future in food production including in food-producing animals or plants.

51. These guidelines apply universally, regardless of region, income and setting, however, the GDG acknowledged that implementation of these guidelines in low and middle-income countries may require special considerations.

52. These include assistance with animal health management to reduce the need for antimicrobials, including improvements in disease prevention strategies, housing and husbandry practices.

53. Furthermore, many countries may need technical and laboratory capacity building assistance for conducting the recommended bacterial culture and sensitivity testing. International organizations such as FAO and OIE may be able to assist in implementation of these guidelines. Finally, the Guideline Development Group emphasized the need for countries to conduct surveillance and monitoring of antimicrobial usage in food producing animals to monitor and evaluate the implementation of these guidelines.

<sup>&</sup>lt;sup>25</sup> http://apps.who.int/medicinedocs/documents/s22083en/s22083en.pdf

<sup>&</sup>lt;sup>26</sup> http://apps.who.int/iris/bitstream/10665/259241/1/WHO-NMH-FOS-FZD-17.2-eng.pdf?ua=1

#### Next steps

54. The revision of the WHO CIA List and recommendations on the use of medically important antimicrobials with a human health focus will be followed by the revision of the OIE list of Antimicrobial agents of Veterinary importance and recommendation on all antimicrobials including veterinary drugs not used in human medicine with animal health focus.

55. The outcome of these two first steps will inform joint tripartite FAO/OIE/OIE recommendations on use of all antimicrobial agents, including antimicrobials only used in veterinary medicine, in food producing animals, including aquaculture.