CODEX ALIMENTARIUS COMMISSION

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Food and Agriculture Organization of the United Nations

World Health Organization

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

Agenda Item 5 **CX/AMR 18/6/5**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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

Sixth Session
Busan, Republic of Korea, 10-14 December 2018

PROPOSED DRAFT REVISION OF THE CODE OF PRACTICE TO MINIMIZE AND CONTAIN FOODBORNE ANTIMICROBIAL RESISTANCE (CXC 61-2005)

(Prepared by the Electronic Working Group
led by the United States of America and co-chaired by China, Chile, Kenya, United Kingdom)

Codex members and observers wishing to submit comments at Step 3 on this document should do so as instructed in CL 2018/74-AMR available on the Codex webpage/Circular Letters: http://www.fao.org/fao-who-codexalimentarius/resources/circular-letters/en/.

Introduction

1. The 5th Session of the Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance (TFAMR05, 2017) agreed to establish an electronic working group (EWG) to further revise the Code of practice to minimize and contain AMR (COP) for comments by Codex members and observers and consideration at TFAMR06. The EWG would be chaired by the United States of America and co-chaired by China, Chile, Kenya, United Kingdom and would work in English and Spanish. The terms of reference (TORs) of the EWG would be as described in Appendix II of REP17/AMR.

2. In addition, at the request of the 40th Session of the Codex Alimentarius Commission (CAC40, 2017), the FAO/WHO Expert Meeting on Foodborne Antimicrobial Resistance: Role of the Environment, Crops and Biocides took place in June 2018. The purpose of the expert meeting was to provide scientific advice to inform the work of the Task Force in the aforesaid areas. In July 2018, FAO and WHO published the summary report of the expert meeting on their respective websites. The final report is expected to be available in October 2018.

3. The co-chairs revised the COP based on comments[1] from Codex members and observers submitted to TFAMR05, the discussions[2] that took place at that session, the TOR[3] of the EWG, comments submitted by Codex members and observers during the two rounds of comments within the EWG, and recent developments in AMR since TFAMR05 including the FAO/WHO expert meeting[4] in collaboration with OIE. The revised COP as contained in Appendix I is presented for further comments by Codex members and observers and consideration by TFAMR06.

Conduct of the EWG

4. The EWG conducted two rounds of discussion (March and July 2018). The first round requested comments on the structure of the COP (including a revised introduction and scope), the second round requested comments on the entire text of the COP.

5. The first round of discussion considered alternate proposals for the structure of the document reflecting general aspects to be further developed (including a revised introduction and scope). Codex members and observers commented on the proposed structure and if they agreed with the general aspects to be covered for each of the sections.

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1 CX/AMR 17/5/5-Add.1, Conference room documents presented at TFAMR05 i.e. CRDs 2, 3 and 4.
2 REP18/AMR, paras. 9-28
3 REP18/AMR, paras. 27-28 , Appendix II
4 http://www.fao.org/food/food-safety-quality/scientific-advice/other-scientific-advice/en/
http://www.who.int/foodsafety/areas_work/antimicrobial-resistance/SciAdvTFAMR/en/

6. The proposed revised structure was available in English and Spanish on the platform for over a four-week period. The EWG received comments from a total of 26 participants, 22 members, 1 member organization, and 3 observers.

7. The second round of discussion considered the COP with (i) the revised proposed structure based on the first the round of discussion (including a revised introduction and scope) and (ii) the revised text. CX/AMR 17/5/5 was taken as the basis to incorporate the changes.

8. The proposed revised document was available in English and Spanish on the platform for over an eight-week period. The EWG received comments from a total of 30 participants, 22 members, 1 member organization, and 7 observers.

9. In summary, the EWG worked from March 2018 to September 2018 and received 53 sets of comments from 30 members, 1 member organization, and 7 observers. Appendix II contains the list of participants.

10. Following below is a summary of comments, main points of discussion, and revisions made during the two rounds of the EWG.

Summary of comments by Codex members and observers and main points of discussion in the EWG on the revision of the Code of practice to minimize and contain antimicrobial resistance (CXC 61 - 2005) (i.e. revised COP)

Proposed New Structure – Round 1

11. No specific comments on the new structure but on various sections of the COP as follows:

- The new structure is acceptable (with a range of replies from 'adequate' to 'fully support').
- No restructuring at this stage. Base the revision on the version of the document in CXAMR 17/5/5 and, following this, a new structure can be considered. Amend the document as agreed at TFAMR05 without restructuring now.
- Section of Responsibilities of Consumers:
  - Remove the section.
  - Question the need for the section and suggest reference to the WHO Five Keys to Safer Food Manual.
  - Include the WHO Five Keys and redraft the section to focus on communication strategies.
  - Include companion animals.

12. The second half of the document (after Section 4. General Principles) was adapted by creating three sections: 5. Responsible use of antimicrobial agents; 6. Practices during production, processing, storage, transport, retail and distribution of food; and 7. Communication to consumers. The relevant content under section 5 was moved with minimal revision taking into consideration comments from Codex members that preferred to retain the content from CX/AMR 17/5/5. The sections on Responsibilities of Consumers and Advocacy and Communication were re-drafted into a new Section 7.

13. The Introduction and Scope were revised to better reflect the context and scope of the COP. The following definitions were added: "animal feed", "crops", and "food chain". The following definitions were revised: "control of disease/metaphylaxis"; "one health"; "prevention of disease/prophylaxis"; and "treatment of disease". The term "plant" was replaced with "crop" throughout the document for consistency. General Principles were not modified; however, a strikethrough from 17/5/5/ was inadvertently omitted in Principle 6. Specific references to OIE chapters were removed based on a general reference to the OIE Terrestrial and Aquatic Health Codes at the beginning of the document. Text redundant with the OIE Codes was removed.

14. The document as revised above constituted the basis for Round 2.

Proposed new, revised text – Round 2

15. The following revisions and observations were made. Smaller revisions for clarity and consistency were also made but are not described in detail in this report.

Section 1. Introduction

- Clarified references in this section and throughout the document with respect to food chain, foodborne AMR microorganisms and resistance determinants, responsible and prudent use, agriculture (crops), and antimicrobial agents.
- Replaced "good practices" with "best management practices"; "animal husbandry" with "animal production; "crops" with "plants/crops"; and "crop health professional" with "plant/crop advisor or consultant" in this section and throughout the document.

- Noted that the Guidelines for risk analysis of foodborne antimicrobial resistance (CXG 77-2011) use only the term “crops”, but that other Codex documents also refer to “plants”. Definitions for the term “plants”, “crops” or “plants/crops” may need to be considered in the larger context of the Codex Alimentarius.
- Introduced two new paragraphs i.e. 2bis and 3bis.

Section 2. Scope

- Clarified references to foodborne AMR microorganisms and resistance determinants.
- Clarified references in this section and throughout the document with respect to food-producing animals.
- Did not include references to “companion animals”, “animal health”, and “non-food routes of exposure” as they appeared to be outside the mandate of the Codex Alimentarius.
- Replaced the term “animal feed” in this section with a reference to the Code of practice on good animal feeding (CXC 54-2004). It was noted that in this Code the term “food” means food for humans or animals, therefore it was suggested that the reference to “food” includes “animal feed”. It was also noted that in the section on definitions the definition of “animal feed” could be deleted by referring to the Codex definition of “food”.

Section 3. Definitions

- Confirmed definitions to be cited in one or more places.
- Did not include definitions not found in the current version of the document.
- Amended definitions using Codex or OIE definitions where possible and re-alphabetized them as needed.
- Did not modify definitions aligned with Codex and/or OIE documents, except as noted below.
    - Modified the definitions for “control of disease/metaphylaxis”, “growth promotion”, “prevention of disease/prophylaxis”, “treatment of disease” based on revisions to the OIE Terrestrial Animal Health Code at the 2018 OIE General Assembly.
    - Added definitions for “adverse health effect”, “extra- or off-label use”, “food-producing animal”, “Co-resistance” from CXG 77 as the terms are used in the proposed revised COP.
    - Modified the definition for “medically important antimicrobials” to provide greater specificity and context.
    - Added a definition for “pharmaceutical industry” based on the introduction of the term into the proposed revised COP.
    - Amended the definition for “plants/crops”.
    - Added a definition for “plant/crop advisor and consultant” based on the introduction of the term into the proposed revised COP.
    - Deleted the definition for “animal feed”.
    - It could be helpful to define “advertising” to differentiate between “direct-to-consumer advertising” vs. “labeling or educational materials to animal and crop professions”.
    - The definitions should be aligned between the three relevant Codex documents i.e. CXC 61, CXG 77 and the Guidelines on integrated monitoring and surveillance of foodborne AMR (under development – see Agenda Item 6).

Section 4. General Principles

- Tried to reconcile suggestions for revision to allow further consideration of the proposed Principles.
- Additional general principles that duplicate guidance found in other sections of the document or appeared to be more applicable to specific sections of the document were not incorporated or were addressed through revisions in the relevant sections.
- Concepts for general principles without providing specific text should be further developed to facilitate consideration by TFAMR06.
- Consider re-ordering the general principles at a later stage. Retain the existing numbering may avoid confusion while the document is undergoing revision.
- Revised some principles and left others unchanged due to (i) consensus on the current text (with minor revisions) or (ii) extensive comments submitted as summarized below:
    - *General Principle 1*: There appears to be good consensus based on relatively few comments received. There is a question on whether the term “applicable” should be deleted.

- *General Principle 2*: There appears to be good support for activities that prevent disease and thereby reduce the need for use of antimicrobial agents. However, one activity i.e. “alternatives to antimicrobial agents” received a number of comments. Key points of discussion were: deletion of the principle as adequate legislation on alternatives to antimicrobial agents may not exist in many countries and inclusion could inadvertent encourage inappropriate uses; concerns over the safety and effectiveness of such products and suggestions for edits; retention of the footnote with the inclusion of more examples or deletion of the footnote due to concerns over the examples.

  Based on the above, the text was revised and deletion of the footnote is proposed.

- *General Principles 3, 4*: There appears to be good consensus based on relatively few comments received. Small revisions were made to the text.

- *General Principle 5*: May need further consideration by TFAMR06 due to the extensive comments submitted. Therefore, no revisions were made to the text. Key points of discussion were: streamline the text e.g. to say “(medically important) antimicrobials should not be used for growth promotion (in food-producing animals)”; remove or retain (and possibly revise) the description of “risk analysis”; an improved definition of “medically important antimicrobials” would provide specificity and clarity to the text which may facilitate consensus on the fundamental concept.

- *General Principle 6*: Revise this Principle or move it to Section 5. Responsible Use of Antimicrobial Agents and/or combine it with Principle 7. The text was revised for further consideration by TFAMR06.

- *General Principle 7*: The text was revised based on proposals to revise the principle; move the principle to section 5 on responsible use of antimicrobial agents and/or combine this principle with Principle 6.

- *General Principles 8-10, 12-14, 16*: There appears to be good consensus based on relatively few comments received. Small revisions were made to the text to address these comments.

- *General Principle 11*: Concerns were expressed that the stepwise approach could be used to implement trade barriers. Suggestions were made for additional text to clarify this point. This proposal should be further discussed at TFAMR06.

- *General Principle 15*: The approach is not well understood in the international context and should be re-stated or deleted; additional “R’s” could be included.

Section 5. Responsible Use of Antimicrobial Agents

- The sections were edited to improve clarity and consistency and to eliminate redundancy.
- There were opposite views to reference VICH documents in the COP i.e. there are several VICH documents that could apply to the COP or VICH is not a multilateral organization and whether a reference to VICH should be included in the COP. As a compromise solution, a general reference to VICH was kept, and the footnote to a specific text was deleted.
- The term “drugs” was replaced with “antimicrobial agents” for consistency, including with the OIE Code. The term “competent authority” was replaced with “regulatory authority”; and the term “treatment” was replaced with “administration” in this section and throughout the document.
- Following comments that the research bullets in each section could be tailored to the relevant actor, no changes were made at this time considering the capacity of different actors to undertake research.
- Specific chapter and section references to the OIE Terrestrial and Aquatic Animal Health Codes were mostly replaced by an overarching reference early in the document. Some references to relevant chapters in the section on surveillance programs were retained.
- There were comments that a separate section for the responsible use of antimicrobials on plants/ crops could be developed to contain the relevant practices for crops, it was decided not to take this approach because it was perceived that many concepts were relevant for both animals and plants/crops and that differences could be adequately taken into account with paragraphs that described only animals or crops, as appropriate. A separate section for plants/crops might also need to repeat the structure of the various responsible actors.

- There were questions on whether the concept of “maximum permissible levels” is feasible for all aspects suggested in the sentence (paragraph 19). It was decided to delete this phrase.
- Two additional paragraphs 22bis and 22ter on pharmacovigilance were added.
- There were concerns on and suggestions to revise paragraph 24 on distribution of antimicrobial agents with respect to “targeted checks”. The second half of the sentence was therefore revised.
- There were objections to the inclusion of the term “compulsory” in paragraph 31 noting that effective procedures may not always be compulsory. The term “compulsory” was deleted.
- There were concerns about the sentence in paragraph 34 that states “Promotional campaigns involving economic or material benefits for prescribers or suppliers of antimicrobials should be prohibited.” The concern was that the measure was overly broad and needed further clarity. No changes were made at this stage, but a comment was noted about the need to distinguish different types of advertising and promotion.
- The text in paragraphs 44, 45 and 46 were revised and consolidated following comments that these paragraphs were redundant.
- There were comments that paragraphs 44, 45, and 46 were redundant. The text was revised and consolidated.
- There were questions on whether the phrase “to ensure that residue levels in or on the food do not present a risk for the consumer” in paragraph 58, was strictly within the mandate of TFAMR. The phrase was revised to read “to ensure that residue levels in or on the food do not present a foodborne AMR risk for the consumer”.

Section 6. Practices during production, processing, storage, transport, retail and distribution of food

- Did not include text related to the use of probiotics based on the presence of existing guidance i.e. The food safety assessment on the use of probiotics in foods is addressed in a Report of a Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Foods (FAO/WHO, 2002). In addition, probiotics were considered to be out of the scope of CXG 77 and a similar approach is proposed for the revision of the COP.
- Did not include text related to biocides based on the summary report of the FAO/WHO Expert Meeting on Foodborne Antimicrobial Resistance: Role of the Environment, Crops and Biocides took place in June 2018.
- Included text on control of technological treatments in the industry (60bis) and control of post-production contamination (60ter) for further consideration by TFAMR06.

Section 7. Communication to Consumers

- Made minor revisions to this section.

Points for further comments and discussion at TFAMR06

16. In addition to comments on the entire revised COP as contained in Appendix I, the following points may benefit from further comments and discussion at TFAMR06 in order to arrive at consensus on the related aspects of the document. Specific requests for consideration by TFAMR06 are indicated in the relevant bullets.

- *Definition of plants/crops*. Several comments indicate a need to consider the most appropriate term with respect to food of plant origin for human consumption. Some comments favor the use of “crops” in order to distinguish non-food plant substances (e.g. ornamental shrubs, fiber (cotton), etc.). Other comments favor the use of “plants/plant products” or “food of plant origin” to identify substances that would be consumed by humans. Other comments suggest that “fresh fruits and vegetables” may be more appropriate as these products are most likely to be consumed by humans without a kill step (i.e. cooking).

  Some sections of the text refer to “agriculture (crops)” to refer to the growing of crops/plants. A consistent definition could provide clarity in these sections. For the revision of the COP, the use of “plants/crops” was selected together with a specific definition to address this request.

  It is noted that CXG 77 use only the term “crops”, but that other Codex documents also refer to “plants”. Defining the term “plants”, “crops” or “plants/crops” may need to be considered in the larger context of Codex Alimentarius.

- *Plant/crop health professional*. A key risk management measure described in the document is administration or application of medically important antimicrobials under the supervision of qualified professionals. For animals, this generally means a veterinarian or a professional similarly authorized by national legislation. Different terms for professionals engaged in the diagnosis, prevention, and treatment of crop/plant diseases in lieu of "crop health professional" including "crop advisor and consultants" were offered. It was decided to replace "crop health professional" with the term "plant/crop advisor or consultant", however specific application of this term to concepts in the document needs to be carefully considered by TFAMR06.
- *Antimicrobials vs. antibacterials*. Recognizing the term antimicrobials includes antibacterial, antiviral, antifungal, and antiparasitic agents, there were suggestions that the document should focus or be limited to guidance on antibacterial agents. Alternatively, there were suggestions that CXC 61 should address all antimicrobials and so the references to antibacterial, antibiotic, and antibiotic resistance should be changed to antimicrobials, as appropriate, and the definitions for the former terms deleted. TFAMR06 should consider whether references to antibacterials/antibiotics/antibiotic resistance should be changed to antimicrobial agents/antimicrobials/antimicrobial resistance and if paragraph 6 is sufficient or should be further revised.
- *Medically important antimicrobials*. Recognizing the need to differentiate antimicrobials that are important for therapeutic use in humans (and therefore may require additional risk management measures) from those substances with antimicrobial properties that are not relevant for human medicine, there were varying views on which references in the document are relevant for medically important antimicrobials and which references are relevant for all antimicrobials. The definition was revised to increase clarity around this distinction.
- *General principles*. Varying opinions with suggestions ranging from deletion, modification, movement to other sections, and addition of new principles. TFAMR06 will need to carefully consider the relevance, wording, and order of each principle. In particular, TFAMR06 should address particular issues associated with the general principles highlighted in this report, in particular principles 2 and 5.
- *Stepwise approach*. Concerns about application of a stepwise approach and the potential for such an approach to be used to implement trade barriers. TFAMR06 should consider whether revisions to the proposed revised text are sufficient to address this concern.
- *Surveillance and monitoring programs*. Replacement of the section on surveillance programs with a reference to the Guidelines for integrated monitoring and surveillance (under development, see Agenda Item 6). TFAMR06 should consider whether guidance on surveillance and monitoring programs should continue to reside in the COP given the development of new, separate guidelines.
- *Alternatives to antimicrobials*. While alternatives to antimicrobials may be useful to reduce the need for antimicrobial agents, there is a need to ensure that such products have been determined to be safe and effective. In addition, there may be a need for evidence to support that the combination of such products with antimicrobial agents does not lead to decreased efficacy of the antimicrobial agent, unintended lengthening of the course of the disease, or an increase in resistant microorganisms. On a related point, the absence of regulatory frameworks in some countries for the evaluation of alternatives to antimicrobials and promotion of their use in the absence of adequate evaluation could be counterproductive. Finally, there may be a need to clarify alternative (substances) vs. alternative (practices) when describing the role of "alternative to antimicrobials" in the COP.
- *Practices during production, processing, storage, transport, retail and distribution of food*. Few comments were received on this section. TFAMR06 should consider whether this section should be further developed or whether it could become a sub-section.

APPENDIX I

**PROPOSED DRAFT REVISED CODE OF PRACTICE
TO MINIMIZE AND CONTAIN FOODBORNE ANTIMICROBIAL RESISTANCE
(CXC 61-2005)**

1. Introduction

1. Antimicrobial resistance (AMR) poses a complex, global public health challenge. Within the food chain, there is a need to address the risks associated with development, selection and dissemination of foodborne resistant microorganisms and resistance determinants. Responsible and prudent use of antimicrobial agents in all sectors following a One Health Approach and strategies for best management practices in plant/crop production animal production (terrestrial and aquatic) and food processing should form a key part of multi-sectoral national action plans to address risks of foodborne antimicrobial resistance.

2. This Code of Practice addresses the responsible and prudent use of antimicrobial agents by participants in the food chain, including the role of regulatory authorities, pharmaceutical industry, animal health professionals and plant/crop advisors or consultants, and food producers and processors. It provides guidance on measures and practices at primary production, and during processing, storage, transport, retail and distribution of food to prevent, minimize and contain foodborne antimicrobial resistance in the food supply. It also identifies knowledge gaps and provides guidance on communication strategies to consumers.

2bis. In keeping with the Codex mandate this Code of Practice focuses on antimicrobial use in the food chain. It is recognized that the use of antimicrobial agents in the food chain may result in exposure in the environment. As part of a One Health strategy to minimize and contain antimicrobial resistance, only authorized products should be used and best practices in the food production sector should be followed to minimize the occurrence/persistence in the environment of antimicrobials and their metabolites from anthropogenic sources, and to minimize the risks associated with the selection and dissemination of resistant microorganisms and resistance determinants in the environment.

3. This Code of Practice is an integral part of risk analysis focusing on risk management options and should be read in conjunction with other Codex texts including the *Guidelines on integrated monitoring and surveillance of foodborne antimicrobial resistanc*e and the *Guidelines for risk analysis of foodborne antimicrobial resistance* (CXG 77-2011). In addition, the *Code of hygienic practice for fresh fruits and vegetables* (CXC 53-2003) and the *Code of practice on good animal feeding* (CXC 54-2004) are particularly relevant for use of agricultural chemicals on plants/crops and animal feed, respectively.

3bis. This Code of Practice provides risk management advice, including the responsible and judicious use of antimicrobial agents that can be applied proportionate to risks identified through the risk analysis process described in the *Guidelines for risk analysis of foodborne antimicrobial resistance*. Risk managers are responsible for prioritizing and assessing foodborne AMR risks appropriate to the region and determining how best to reduce risk to introduce levels of protection appropriate for circumstances.

4. The *Principles and guidelines for the conduct of microbiological risk management* (CXG 63-2007) contains guidance for developing and implementing risk management measures. *WHO guidance on integrated surveillance of antimicrobial resistance in foodborne bacteria, application of a One Health Approach* and *critically important antimicrobials for human medicine* and relevant chapters of the *OIE terrestrial and aquatic animal health codes* and the *List of antimicrobials of veterinary importance* should also be referenced for setting priorities and identifying risk management measures.

5. Where available, national and local guidelines to prevent, minimize and contain foodborne antimicrobial resistance should be taken into consideration. Best management practices and guidelines on the responsible and prudent use of antimicrobials developed by governmental and professional organizations should also be considered.

6. Recognizing there are mechanisms of co-resistance or co-selection in a range of antimicrobial agents, most of the recommendations in this Code of Practice will focus on antibacterials, however some recommendations may also be applicable to antiviral, antiparasitic, antiprotozoal, and antifungal agents.

2. Scope

7. This Code of Practice provides risk management guidance to address the risk to human health associated with the presence in food[1] and the transmission through food of antimicrobial resistant microorganisms or resistance determinants. It provides risk-based guidance on relevant measures along the food chain to minimize and contain the development and spread of foodborne antimicrobial resistance, including guidance on the responsible and prudent use of antimicrobial agents in plant/crop production and animal production (terrestrial and aquatic) and references to other best management practices as appropriate. It also provides risk-based guidance on practices during production, processing, storage, transport, retail and distribution of food to minimize and contain the development and spread of foodborne antimicrobial resistance. Its objectives are to minimize the potential adverse impact on human health from foodborne AMR resulting from the use of antimicrobial agents in the food chain.

8. This document includes guidance for all interested parties involved in the authorization, manufacture, sale and supply, prescription and use of antimicrobial agents along the food chain together with those involved in the handling, preparation, food processing, distribution and consumption of food who have a role to play in optimizing the use of antimicrobial agents and/or who have a role with limiting the development and spread of foodborne antimicrobial resistant microorganisms and resistance determinants.

9. As there are existing Codex or internationally recognized guidelines, the following areas related to antimicrobial agents or AMR are outside the scope of this document: residues of antimicrobial agents in food; AMR marker genes in recombinant-DNA plants/crops and recombinant DNA microorganisms[2]; non-genetically modified microorganisms (for example, starter cultures) intentionally added to food with a technological purpose[3]; and certain food ingredients, which could potentially carry antimicrobial resistance determinants, such as probiotics[4]. In addition, AMR from non-food animals or non-food routes are also outside the scope of this document.

3. Definitions

Antibacterial: A substance that acts against bacteria.

Antibiotic: A naturally derived substance from a biological source that acts against microorganisms, specifically bacteria.

Antibiotic resistance: The ability of a microorganism, specifically bacteria, to multiply or persist in the presence of an increased level of an antibiotic relative to the susceptible counterpart of the same species.

Adverse health effect: An undesirable or unwanted outcome in humans. In this document, this refers to the human infections caused by AMR microorganisms and determinants in food or acquired from food of animal/crop origin as well as increased frequency of infections and treatment failures, loss of treatment options, and increased severity of infections manifested by prolonged duration of disease, increased hospitalization and mortality[5].

Antimicrobial agent: Any substance of natural, semi-synthetic, or synthetic origin that at *in vivo* concentrations kills or inhibits the growth of microorganisms by interacting with a specific target. The term antimicrobial is a collective for antiviral, antibacterial, antifungal, antiparasitic, and antiprotozoal agents.

Antimicrobial resistance (AMR): The ability of a microorganism to multiply or persist in the presence of an increased level of an antimicrobial agent relative to the susceptible counterpart of the same species.

Antimicrobial resistance determinant: The genetic element(s) encoding for the ability of microorganisms to withstand the effects of an antimicrobial agent. They are located either chromosomally or extra-chromosomally and may be associated with mobile genetic elements such as plasmids, integrons or transposons, thereby enabling horizontal transmission from resistant to susceptible strains.

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1 As described in the *Code of practice on good animal feeding* (CXC 54-2004), food means food for man or animals.

2 The food safety assessment on the use of antimicrobial resistance marker genes in recombinant-DNA plants is addressed in the *Guidelines for the conduct of food safety assessment of foods derived from recombinant-DNA plants* (CXG 45-2003).

3 The food safety assessment on the use of antimicrobial resistance marker genes in recombinant-DNA microorganisms is addressed in the *Guideline for the conduct of food safety assessment of foods produced using recombinant-DNA microorganisms* (CXG 46-2003).

4 The food safety assessment on the use of probiotics in foods is addressed in the Report of the *Joint FAO/WHO working group on drafting guidelines for the evaluation of probiotics in foods* (FAO/WHO, 2002).

5 *First Joint FAO/OIE/WHO expert workshop on non-human antimicrobial usage and antimicrobial resistance: scientific assessment* (December 2003).

Control of disease/metaphylaxis: Administration of antimicrobial agents to group of animals containing sick and healthy individuals (presumed to be infected), to minimize or resolve clinical signs and to prevent further spread of the disease.

Co-resistance: The ability of a microorganism to multiply or persist in the presence of different classes of antimicrobial agents due to possession of various resistance mechanisms.

Cross-resistance: The ability of a microorganism to multiply or persist in the presence of other members of a particular class of antimicrobial agents or across different classes due to a shared mechanism of resistance.

Extra- or off-label use: The use of an antimicrobial agent that is not in accordance with the approved product labelling.

Food chain: Production to consumption continuum including, primary production (food-producing animals, plants/crops), harvest/slaughter, packing, processing, storage, transport, and retail distribution to the point of consumption.

Food-producing animals: Animals raised for the purpose of providing food to humans.

Growth promotion: Administration of antimicrobial agents to only increase the rate of weight gain and/or the efficiency of feed utilization in animals. The term does not apply to the use of antimicrobials for the specific purpose of treating, controlling, or preventing infectious diseases.

Marketing authorization: Process of reviewing and assessing a dossier to support a antimicrobial agent to determine whether to permit its marketing (also called licensing, registration, approval, etc.), finalized by granting of a document also called marketing authorization (equivalent: product license).

Medically important antimicrobials: Antimicrobial agents important for therapeutic use in humans as described in the *WHO list of critically important antimicrobials* or national lists, where available. It does not include ionophores or other antimicrobial agents not used for human therapeutic use.

One Health Approach: A collaborative, multisectoral, and trans-disciplinary approach - working at the local, regional, national, and global levels - with the goal of achieving optimal health outcomes recognizing the interconnection between humans, animals, crops, and their shared environment.

Pharmaceutical industry: Manufacturers and marketing authorization holders of antimicrobial agents.

Pharmacovigilance: to be further developed.

Plants/crops: A cultivated plant that is grown as food or feed, especially a grain, fruit or vegetable, including all edible parts.

Plant/crop advisor and consultant: Plant/crop health professionals with knowledge and experience in crop production and protection practices.

Prevention of disease/prophylaxis: Administration of antimicrobial agents to an individual or a group of animals at risk of acquiring a specific infection or in a specific situation where infectious disease is likely to occur if the antimicrobial agent is not administered.

Therapeutic use: Administration of antimicrobial agents for the treatment, control/metaphylaxis and prevention/prophylaxis of disease.

Treatment of disease: Administration of antimicrobial agents to an individual or group of animals showing clinical signs of infectious disease.

4. General principles to minimize and contain antimicrobial resistance

Principle 1: A One Health Approach should be considered, wherever possible and applicable, when identifying, evaluating, selecting, and implementing foodborne AMR risk management options.

Principle 2: Biosecurity, appropriate nutrition, vaccination, animal and plant/crop best management practices, and alternatives to antimicrobial agents[6] where appropriate, and that have been proven to be efficacious and safe, should be considered to reduce the need for use of antimicrobial agents.

Principle 3: Science-based species or sector-specific responsible and prudent antimicrobial use guidelines should be developed, implemented, and reviewed on a regular basis to maintain their effectiveness in minimizing the risk of foodborne antimicrobial resistance. Such guidelines could be included as a part of national action plans or stakeholder-led plans on antimicrobial resistance with development and dissemination shared among countries and organizations.

[6] ~~Could include ethnoveterinary and other approaches, e.g. herbal medicine, prebiotics, competitive exclusion bacteriophages, immunomodulators, organic acids and teat sealants~~.

Principle 4: The *WHO list of critically important antimicrobials*, the *OIE list of antimicrobials of veterinary importance*, or national lists, where available, should be considered when setting priorities for risk assessment and risk management to minimize and contain antimicrobial resistance. The lists should be regularly reviewed and updated as necessary when supported by scientific findings as new scientific data emerges on resistance patterns.

Principle 5: Responsible and prudent administration in food-producing animals does not include the use for growth promotion of antimicrobial agents that are considered medically important or are able to cause cross-resistance to other antimicrobial agents, or classes of antimicrobial agents, that are considered medically important, in the absence of a risk analysis. This risk analysis should:

- be undertaken by the appropriate national regulatory authority;
- be based on adequate scientific evidence; and
- include a publicly available summary.

Principle 6: Medically important antimicrobial agents should only be used for therapeutic purposes (treatment, control/metaphylaxis or prevention/prophylaxis of disease); or in certain circumstances for research and conservation.

Principle 7: Medically important antimicrobial agents should only be used in well-defined circumstances for the prevention/prophylaxis of a specific disease risk and follow appropriate professional oversight, dose, and duration.

Principle 8: Antimicrobial agents should be used as legally authorized and following all applicable label directions; except where specific legal exemptions apply.

Principle 9: Foodborne AMR risk management measures should be implemented in a way that is proportionate to the risk and reviewed on a regular basis as described in the *Guidelines for risk analysis of foodborne antimicrobial resistance*. Risk managers should consider potential unintended consequences to human and animal health of recommended risk management measures.

Principle 10: Monitoring and surveillance of the use of antimicrobial agents and the incidence or prevalence, and in particular trends, of foodborne antimicrobial resistant microorganisms and resistance determinants are among the critical factors to consider when developing risk management measures and evaluating the effectiveness of implemented risk management measures. Use of medically important antimicrobial agents in humans and food-producing animals, and transmission of pathogens and resistance genes between humans, food-producing animals, and the environment are additional factors to consider, through the foodborne AMR risk analysis process described in the *Guidelines for risk analysis of foodborne antimicrobial resistance*.

Principle 11: This document is designed to provide a framework, for the development of measures to mitigate the risk of foodborne AMR, that countries may implement, as part of their national strategy on AMR, in accordance with their capabilities, based on their national priorities and capacities, and within a reasonable period of time. A stepwise approach may be utilized by some countries to properly implement applicable elements in this document proportionate to the foodborne AMR risk and should not be used inappropriately to generate barriers to trade.

Principle 12: Medically important antimicrobials should be administered, prescribed, or applied only by, or under the direction of, veterinarians, plant/crop advisors or consultants or other suitably trained persons authorized in accordance with national legislation.

Principle 13: Administration of antimicrobial agents should take into consideration sampling and susceptibility testing of isolates from the production setting, where appropriate, and make adjustments to the antimicrobial agent selection based on clinical outcomes or when foodborne AMR risks become evident.

Principle 14: Administration of antimicrobial agents should be based on sound clinical judgement, experience, and treatment efficacy. Where feasible and appropriate the results of bacterial cultures and antimicrobial susceptibility testing and integrated resistance surveillance and monitoring can also be considered.

Principle 15: The reduce, replace and rethink (RRR) strategy on the use of antimicrobial agents in animals and on plants/crops should be actively promoted within all sectors.

Principle 16: On a continuous and stepwise implementation of risk management measures along the food chain to minimize the possible risks associated with foodborne AMR, priority should be given to the most relevant elements from a public health perspective.

5. Responsible and prudent use of antimicrobial agents

10. The *OIE terrestrial and aquatic animal health codes* contain detailed information with respect to the control of veterinary medicines for use in food-producing animals and aquaculture.

11. For more information on the data requirements for authorization of antimicrobial agents for food-producing animals see the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) guidelines.

Responsibilities of the regulatory authorities

12. The regulatory authorities, including the authority responsible for granting the marketing authorization for antimicrobials for use along the food chain, have a significant role in specifying the terms of the authorization and in providing appropriate information to the veterinarian and plant/crop advisors or consultants, or other suitably trained persons authorized in accordance with national legislation and producers through product labelling and/or by other means, in support of the responsible and prudent use of antimicrobial agents along the food chain.

13. It is the responsibility of regulatory authorities to develop up-to-date guidelines on data requirements for evaluation of antimicrobial agent applications. National governments in cooperation with animal, plant/crop, and public health professionals should adopt a One Health Approach to promote the responsible and prudent use of antimicrobial agents along the food chain as an element of a national strategy for the containment of antimicrobial resistance. Good animal production (terrestrial and aquatic) and best management practices for plant/crop production, vaccination and biosecurity policies and development of animal and plant/crop health programs at the farm level contribute to reduce the prevalence of animal and plant/crop disease requiring antimicrobial administration and can be incorporated into national strategies to complement activities in human health.

14. If dose ranges/application rates or different durations/re-application intervals of antimicrobial agent administration are indicated, the regulatory authorities should give guidance on the approved product labelling regarding the conditions that will minimize the development of foodborne AMR based on a risk assessment, while still maintaining efficacy and safety, when this information is available.

Quality control of antimicrobial agents

15. Regulatory authorities should ensure that quality controls are carried out in accordance with international guidance and in compliance with the provisions of good manufacturing practices.

Assessment of efficacy

16. Assessment of efficacy is important to assure adequate response to the administration of antimicrobial agents. As part of the marketing authorization process, it should include the efficacy with optimal dosages and durations, supported by clinical trials, microbiological data (including antimicrobial susceptibility testing) and pharmacokinetic data. It may also include assessment of through proper veterinary care, program evaluation and good pharmacovigilance practices.

Assessment of the potential antimicrobial agents to select for resistant microorganisms

17. The regulatory authority should assess the potential of medically important antimicrobial agents to select for resistant microorganisms taking into account *Guidelines for risk analysis of foodborne antimicrobial resistance*, the *WHO list of critically important antimicrobials*, the *OIE list of antimicrobials of veterinary importance*, or national lists, where available.

Assessment of environmental impact

18. Regulatory authorities should assess the impact of proposed antimicrobial agent-use on the environment in accordance with national guidelines or recognized international guidelines.

19. Regulatory authorities should consider the environmental aspects on foodborne AMR e.g. pollution from pharmaceutical manufacture, impacts of reusing waste water for irrigation, and using manure and/or municipal wastes for soil fertilization. When foodborne AMR risk is determined through the *Guidelines for risk analysis of foodborne antimicrobial resistance* the need for monitoring and proportionate risk management measures can be considered.

Establishment of a summary of product characteristics for each antimicrobial agent

20. Regulatory authorities should establish a Summary of Product Characteristics or similar document. The information in the summary of product characteristics can be utilized in labelling and as a package insert.

Surveillance and monitoring programmes

21. Regulatory authorities should establish systems for the surveillance and monitoring of antimicrobial resistance and antimicrobial use following the *Guidelines on integrated monitoring and surveillance of foodborne antimicrobial resistance*, taking into consideration relevant sections of *Guidelines for risk analysis of foodborne antimicrobial resistance*; *WHO guidelines on integrated surveillance of antimicrobial resistance in foodborne bacteria, application of a One Health Approach*; and *OIE terrestrial animal health code* Chapter 6.7 Harmonization of national antimicrobial resistance surveillance and monitoring programmes and Chapter 6.8 Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals, the *OIE aquatic animal health code* Chapter 6.3 Monitoring of the quantities and usage patterns of antimicrobial agents used in aquatic animals and Chapter 6.4 Development and harmonization of national antimicrobial resistance surveillance and monitoring programmes for aquatic animals and section 8 of chapter 6.9.3 on post-marketing antimicrobial surveillance.

22. The surveillance and monitoring of antimicrobial resistant bacteria in different production sectors and in different food products and at different stages of the food chain, should be undertaken to understand the development and dissemination of antimicrobial resistance, provide relevant risk assessment data, and to assess the effectiveness of interventions. Surveillance and monitoring programmes may entail specific or continuous data collection, analysis and reporting that quantitatively monitors temporal trends in the occurrence and/or prevalence and distribution of resistance to antimicrobial agents; and also allow the identification of emerging or specific patterns of resistance. Surveillance and monitoring programmes should be prioritized based on the risk to public health, national priorities, should be practical and feasible, and may be implemented following a stepwise approach.

22bis. Regulatory authorities should have in place a pharmacovigilance program for the monitoring and reporting of adverse reactions to veterinary antimicrobial drugs, including lack of the expected efficacy related to microbial resistance. The information collected through the pharmacovigilance program should form part of the comprehensive strategy to minimize microbial resistance.

22ter. In cases, where the assessment of data collected from pharmacovigilance and from other post-authorization surveillance including, if available, targeted surveillance of antimicrobial resistance, suggests that the conditions of use of the given veterinary antimicrobial drug should be reviewed, regulatory authorities shall endeavor to achieve this re-evaluation.

Distribution of antimicrobial agents

23. Regulatory authorities, to the extent possible, should make sure antimicrobial agents are distributed through appropriate distribution systems in accordance with national legislation and medically important antimicrobials are distributed to appropriately credentialed/registered veterinarians, plant/crop advisors or consultants, or other suitably trained persons authorized in accordance with national legislation.

24. Distribution should be regularly controlled by the regulatory authorities, and monitoring of sales of antimicrobial agents could be undertaken and information could be analyzed with appropriate context to identify areas of concern and potential follow up.

Control of advertising

25. Regulatory authorities should assure that advertising of antimicrobial agents is done in accordance with national legislation.

26. Advertising of antimicrobial agents should be done in a manner consistent with prudent use guidelines and any other specific regulatory recommendations for the product.

27. All advertising of medically important antimicrobial agents should be controlled by the relevant authorities.

- The authorities should ensure that advertising of antimicrobial agents:
    - complies with the marketing authorization granted, in particular with the content of the summary of product characteristics; and
    - complies with each country's national legislation.

Training of users of antimicrobial agents

28. Training should involve all the relevant professional organizations, regulatory authorities, pharmaceutical industry, schools, research institutes, professional associations, trade associations and other approved users such as farmers and producers and should focus on:

- information on disease prevention and management strategies to reduce the need to use antimicrobial agents;
- relevant information to enable the veterinarian and plant/crop advisors or consultants to use or prescribe antimicrobial agents responsibly and prudently;
- training in new methodologies for molecular analysis of resistance;
- the ability of antimicrobial agents to select for resistant microorganisms that may contribute to animal, plant/crop, or human health problems; and
- the need to observe responsible and prudent use recommendations and using antimicrobial agents in production settings in agreement with the provisions of the marketing authorizations and professional advice.

Knowledge gaps and research

29. The relevant authorities should encourage public and private research to:

- improve the knowledge about the mechanisms of action, pharmacokinetics and pharmacodynamics of antimicrobial agents to optimize the dosage regimens and their efficacy;
- improve the knowledge about the mechanisms of transmission, selection, co-selection, emergence and dissemination of resistance determinants and AMR microorganisms through food;
- develop practical models for applying the concept of risk analysis to assess the public health concern precipitated by the development of resistance;
- further develop protocols to predict, during the authorization process, the impact of the proposed use of the antimicrobial agents on the rate and extent of resistance development; and
- develop and encourage good animal production and plant/crop production best management practices and alternative methods to prevent and treat infectious diseases that would reduce the need to use antimicrobial agents
- develop safe and effective alternatives to antimicrobial agents, new antimicrobial agents, rapid diagnostics, and vaccines
- determine the potential transfer to fresh produce and other plants/crops of resistant microorganisms and determinants from animal manures or other biological materials used as fertilizer or selected for during the use of production practices, and if there is subsequent transfer through food to consumers.
- improve the knowledge and the role of the environment on the transfer and persistence of antimicrobial agents.
- determine the potential transfer to animals of resistant microorganisms and determinants due to agricultural chemical use.

30. Research should be conducted, as resources permit, on antimicrobials, their metabolites, and risks of foodborne resistant microorganisms and resistance determinants in the primary production environment, and if feasible, factors affecting and the magnitude of resistance determinant transfer among microorganisms in the environment leading to foodborne AMR risk.

Collection and destruction of unused or out-of-date antimicrobial agents

31. The relevant authorities should develop effective procedures for the safe collection and destruction of unused or out-of-date antimicrobial agents.

Responsibilities of Manufacturers and Marketing Authorization Holders

Marketing authorization of antimicrobial agents

32. It is the responsibility of the antimicrobial agent marketing authorization holders:

- to supply all the information requested by the national regulatory authority in order to establish objectively the quality, safety and efficacy of antimicrobial agents; and
- to ensure the quality of this information based on the implementation of procedures, tests and trials in compliance with the provisions of good manufacturing, good laboratory and good clinical practices.

Marketing and export of antimicrobial agents

33. Only officially licensed/authorized antimicrobial agents should be marketed, and then only through distribution systems in accordance with national legislation.

- Only antimicrobial agents meeting the quality standards of the importing country should be exported from a country in which the products were produced;
- The information necessary to evaluate the amount of antimicrobial agents marketed should be provided to the national regulatory authority.

34. Package size and the concentration and composition of antimicrobial formulations should be adapted as far as possible to the approved indications of use in order to avoid improper dosing, overuse and leftovers.

Advertising

35. It is the responsibility of the marketing authorization holders to only advertise antimicrobial agents in accordance with the provisions of paragraphs 25-27 on the Responsibilities of the Regulatory Authorities, Control of Advertising and to not advertise medically important antimicrobials to producers.

36. Advertising should only be targeted to persons permitted to prescribe or supply antimicrobial agents. Promotional campaigns involving economic or material benefits for prescribers or suppliers of antimicrobials should be discouraged.

Training

37. It is the responsibility of the marketing authorization holders to participate in the training of users of antimicrobial agents as defined in paragraph 28.

Research

38. It is the responsibility of the marketing authorization holders to support the development of research as defined in paragraph 29, as appropriate.

39. Research on the development of new antimicrobials, safe and effective alternatives to the use of antimicrobials, rapid diagnostics and vaccines should be performed.

Responsibilities of wholesale and retail distributors

40. Wholesalers and retailers distributing medically important antimicrobial agents should only do so on the prescription of a veterinarian or other suitably trained person authorized in accordance with national legislation and all products should be appropriately labelled.

41. Distributors should encourage compliance with the national guidelines on the responsible use of medically important antimicrobial agents and should keep records of all antimicrobials supplied according to the national regulations including, for example:

- date of supply
- name of prescribing veterinarian or other suitably trained and authorized person
- name of user
- name of medicinal product, formulation, strength and package size
- batch number
- quantity supplied
- expiration dates

42. Distributors should support the training of users of antimicrobial agents as defined in paragraph 28.

Responsibilities of Veterinarians[7] and Plant/Crop Advisors or Consultants

43. Veterinarians and plant/crop advisors or consultants should identify new or recurrent disease problems and develop alternative strategies to prevent or treat infectious disease. These may include, but are not limited to, biosecurity, improved production practices, and safe and effective alternatives to antimicrobial agents, including vaccination where applicable/available.

45. Professional organizations should develop species or sector-specific guidelines on the responsible and prudent use of antimicrobial agents. National action plans may include recommendations to develop species or sector-specific guidelines.

47. Antimicrobial agents should only be used when necessary, as only as long as necessary, and in an appropriate manner:

[7] Under some circumstances, this may refer to a suitably trained person authorized in accordance with national legislation.

- A prescription or order for application for medically important antimicrobial agents should indicate the dose, the dosage intervals, the duration of the administration, the withdrawal period, when appropriate, and the amount of antimicrobial agent to be delivered depending on the dosage and the characteristics of the individual or population to be treated;
- The quantity of the antimicrobial provided to the end-user should be limited only for the administration concerned. Prescriptions should also indicate the owner and the identification of the food-producing animals or plants/crops to which the antimicrobials are to be administered;
- All medically important antimicrobial agents should be prescribed or applied and used according to label directions and the conditions stipulated in the national legislation.
- Protocols for monitoring use to allow for data collection or for quality assurance purposes should be considered.

48. For food-producing animals, the appropriate use of medically important antimicrobial agents in practice is a clinical decision that should be based on the experience and local expertise of the prescribing veterinarian, and the accurate diagnosis, based on adequate diagnostic procedures. There will be occasions when a group of food-producing animals, which may have been exposed to pathogens, may need to be treated without recourse to an accurate diagnosis and antimicrobial susceptibility testing to prevent the development and spread of clinical disease and for reasons of animal welfare.

49. To be further developed: a paragraph describing the diagnosis and treatment of plants.

50. Determination of the choice of an antimicrobial agent should be based on:

- The expected efficacy of the administration based on:
    - the experience of the veterinarian, plant/crop health professional or suitably trained and authorized person;
    - the spectrum of the antimicrobial activity towards the pathogens involved;
    - the history of the production unit particularly in regard to the antimicrobial susceptibility profiles of the pathogens involved. Whenever possible, the antimicrobial susceptibility profiles should be established before the commencement of the administration. If this is not possible, it is desirable for samples to be taken before start of the administration to allow, if necessary, for adjustment of therapy based on susceptibility testing. Should a first antimicrobial administration fail or should the disease recur, the use of a second antimicrobial agent should be based on the results of microbiological susceptibility tests;
    - the appropriate route of administration;
    - results of initial administration;
    - previous published scientific information on the treatment of the specific disease;
    - the likely course of the disease.
- The need to minimize the adverse health effect from the development of microbial resistance based on:
    - the choice of the activity spectrum of the antimicrobial agent. Narrow-spectrum antimicrobials should be selected whenever possible/appropriate;
    - the targeting of specific microorganism;
    - known or predictable susceptibilities using antimicrobial susceptibility testing;
    - optimized dosing regimens;
    - the use of fixed combinations of antimicrobial agents (i.e. only combinations contained in authorized veterinary medicinal products) which are effective against the target pathogens;
    - the importance of the antimicrobial agents to human and veterinary medicine; and,
    - the route of administration
- If the label conditions allow for flexibility, the veterinarian or plant/crop advisor or consultant should consider a dosage regimen that is long enough to allow an effective treatment, but is short enough to limit the selection of resistance in foodborne and/or commensal microorganisms.

Off-label use

51. For food-producing animals, the off-label use of a veterinary antimicrobial agent may be permitted in appropriate circumstances and should comply with the national legislation including the appropriate and/or approved withdrawal periods to be used. It is the veterinarian's responsibility to define the conditions of use including the therapeutic regimen, the route of administration, and the duration of the administration and the withdrawal period. Off-label use of medically important antimicrobial agents should not be permitted for growth promotion.

52. Human health risk related to foodborne antimicrobial resistance should be an important factor when considering the off-label use of veterinary antimicrobial agents.

53. Medically important antimicrobials should not be used off-label for plants/crops.

Record keeping and recording

54. For food-producing animals and plants/crops, records on antimicrobial agent administration should be kept in conformity with national legislation or best management practice guidelines.

In particular, for investigation of antimicrobial resistance, veterinarians and plant/crop advisors or consultants or suitably trained persons authorized in accordance with national legislation should:

- record the antimicrobial susceptibility testing results;
- record the antimicrobial used, the dosage regimen and the duration; investigate adverse reactions to antimicrobial agents, including lack of expected efficacy, and report it, as appropriate, to the regulatory authorities (through a pharmacovigilance system, if available).

55. Veterinarians and plant/crop advisors or consultants should also periodically review farm records on the use of antimicrobial agents to ensure compliance with their directions.

Training

56. Professional organizations should participate in the development and/or delivery of training of users of antimicrobial agents as defined in paragraph 28.

Responsibilities of food producers

57. Producers are responsible for implementing health programmes on their farms to prevent and manage disease outbreaks. They should call on the assistance of veterinarians, plant/crop advisors or consultants, or other suitably trained persons authorized in accordance with national legislation. All participants involved in primary production of food have an important role to play in preventing disease and ensuring the responsible and prudent use of antimicrobial agents to minimize risk of foodborne AMR.

58. Producers have the following responsibilities:

- to use antimicrobial agents only when necessary, under the supervision of a veterinarian or plant/crop advisor or consultant when required, and not as a replacement for good management and farm hygiene practices, or other disease prevention methods;
- to implement a health plan in cooperation with the veterinarian, plant/crop advisors or consultants, or other suitably trained person authorized in accordance with national legislation that outlines measures to prevent disease;
- to use antimicrobial agents in the species, for the uses and at the doses on the approved labels and in accordance with the prescription, product label instructions or the advice of a veterinarian, plant/crop advisors or consultants or other suitably trained person authorized in accordance with national legislation familiar with the food-producing animals or the plant/crop production site;
- to isolate sick animals and dispose of dead or dying animals or plants/crops promptly under conditions approved by relevant authorities;
- to comply with the storage conditions of antimicrobial agents according to the approved product labelling;
- to address infection prevention and control measures regarding contacts between people, veterinarians, plant/crop advisor or consultants, breeders, owners, children and the food-producing animals or plants/crops treated;
- to comply with the recommended withdrawal periods or pre-harvest intervals to ensure that residue levels in or on the food do not present a foodborne AMR risk for the consumer;

- to not use out-of-date antimicrobial agents and to dispose of all unused or out-of-date antimicrobial agents in accordance with the provisions on the product labels and national legislation;
- to inform the veterinarian, plant/crop advisor or consultant, or other suitably trained person authorized in accordance with national legislation in charge of the production unit of recurrent disease problems or failures of antimicrobial applications;
- to maintain all clinical and laboratory records of microbiological diagnosis and susceptibility testing. These data should be made available to the professional in charge of the administration in order to optimize the use of antimicrobial agents.
- to keep adequate records of all antimicrobial agents used, including the following:
    - name of the antimicrobial agent/active substance and batch number;
    - name of supplier;
    - date of administration; species and number of animals;
    - identification of the production unit (animal age, numbers, weights) to which the antimicrobial agent was administered;
    - disease treated, prevented, or controlled;
    - number of animals treated;
    - daily dose and number of treatment days;
    - quantity and duration of the antimicrobial agent administered;
    - withdrawal periods;
    - result of treatment;
    - name of the prescribing veterinarian, plant/crop advisor or consultant or other suitably trained person authorized in accordance with national legislation.
- To ensure sound management of wastes and other materials to minimize dissemination of excreted antimicrobial agents, resistant microorganisms and resistance determinants into the environment where they may contaminate food;
- To address on-farm biosecurity measures and take basic infection prevention and control measures as appropriate and as provided in the *OIE terrestrial and aquatic animal health code*;
- To assist the relevant authorities in surveillance programs related to antimicrobial use and antimicrobial resistance, as appropriate.

59. The responsible and prudent use of antimicrobial agents should be supported by continuous efforts in disease prevention to minimise infection during production and decrease exposure to antimicrobial agents. Efforts should aim to improve health, thereby reducing the need for antibiotics. This can be achieved by improving hygiene, biosecurity and health management on farms, improving animal and plant/crop genetics, and implementing national or international good animal production (terrestrial and aquatic), and plant/crop production practices. Disease prevention through the use of vaccines, integrated pest management, and other measures that have been clinically proven to be safe and efficacious, such as probiotics (beneficial bacteria found in various foods), prebiotics (non-digestible foods that help probiotic bacteria grow and flourish) or competitive exclusion products (intestinal bacterial flora that limit the colonization of some bacterial pathogens) may be considered and applied wherever appropriate and available. Disease prevention through the use of vaccines and other appropriate measures aimed at supporting animal health (such as adequate nutrition and whenever available feed additives such as prebiotics, probiotics) should be considered.

60. Concerted efforts of all stakeholders within the entire food chain are required to minimize and contain foodborne antimicrobial resistance. While such efforts mainly focus on responsible and prudent use of antimicrobial agents in primary production at the farm level, the later phase of the food chain also plays a significant role in preventing transmission and spread of resistant bacteria and resistance determinants.

Food processing industry, food retailers and consumers should take necessary action in accordance with the *Principles and guidelines for the conduct of microbiological risk management*.

6. Practices during production, processing, storage, transport, retail and distribution of food

60bis. Control of technological treatments in the industry: Technological treatments of food preservation based on the application of one or more bacteriostatic factors to prevent microbial growth (sub-lethal treatments) can increase the phenotypes of resistant bacteria, contrary to conventional bactericidal treatments. Modern conservation systems cause some bacteria to be only stressed and can increase resistance through phenotypic and / or genotypic adaptations. This adaptation is sometimes associated with an increase in resistance to different antibiotics.

60ter. Control of post-production contamination: Post-production contamination should not be underestimated. It can occur in the different stages of the production and consumption chain, in which food handlers have an important responsibility to avoid contamination of food with microorganisms that can be carriers of resistance genes. Food contamination usually occurs at times of increased handling, in meat during slaughter or processing. In ready-to-eat foods, the real risk is presumed cross-contamination, directly between raw and processed foods or indirectly through contaminated hands, surfaces or utensils and vectors.

7. Communication to consumers

61. Government, food industry and other stakeholders along the food chain should inform and educate consumers on the risks of foodborne AMR and ways to minimize the risk of infection.

Some aspects to consider when communicating to consumers are:

- Identifying all the stakeholders and having a common message;
- Providing information that is clear, accessible, and targeted to a non-scientific audience;
- Considering local characteristics that affect how risks are perceived (e.g. religious belief, traditions);
- Understanding the audience and testing messages to ensure they are culturally and demographically appropriate.

62. For more information on risk communication refer to *WHO integrated surveillance of antimicrobial resistance in foodborne bacteria* and *FAO/WHO risk communication applied to food safety handbook* and *the Guidelines for risk analysis of foodborne antimicrobial resistance.*

63. The best way for consumers to prevent foodborne AMR is through proper food handling. The *WHO Five Keys to Safer Food Manual* can be used to teach consumers how to minimize foodborne bacteria in their food.

APPENDIX II

LIST OF PARTICIPANTS

- **Chair**: United States of America
- **Vice-Chairs**: Chile, China, Kenya and the United Kingdom

Codex Members

1. Argentina
2. Australia
3. Brazil
4. Canada
5. China
6. Colombia
7. Costa Rica
8. Cuba
9. Denmark
10. Ecuador
11. Egypt
12. Germany
13. Japan
14. Kazakhstan
15. Malaysia
16. Mexico
17. Netherlands
18. New Zealand
19. Nicaragua
20. Nigeria
21. Norway
22. Peru
23. Poland
24. Republic of Korea
25. Russian Federation
26. South Africa
27. Sweden
28. Thailand
29. United Kingdom
30. United States of America

Codex Member Organization

31. European Union

Codex Observers

32. International Association for Consumer Food Organizations (IACFO)
33. International Feed Industry Federation (IFIF)
34. International Dairy Federation (IDF)
35. International Meat Secretariat (IMS)
36. Consumers International (CI)
37. HealthforAnimals
38. Organisation Mondiale De La Sante Animale (OIE)