

APPENDIX II

**REVISION OF THE
CODE OF PRACTICE TO MINIMIZE AND CONTAIN FOODBORNE ANTIMICROBIAL RESISTANCE
(CXC 61-2005)
(For adoption by CAC at Step 8)**

1. Introduction

1. Antimicrobial resistance (AMR) poses an important, complex, and priority global public health challenge. Along 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 animal production (terrestrial and aquatic), plant/crop production and food/feed processing, packaging, storage, transport, and wholesale and retail distribution should form a key part of multi-sectoral national action plans to address risks of foodborne AMR.

2. This Code of Practice addresses the responsible and prudent use of antimicrobial agents by participants in the food chain, including, but not limited to, the role of competent authorities, the pharmaceutical industry, veterinarians, and plant/crop health professionals, and food producers and processors. It provides guidance on measures and practices at primary production, and during processing, storage, transport, wholesale and retail 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.

3. In keeping with the Codex mandate this Code of Practice addresses antimicrobial use along the food chain. It is recognized that the use of antimicrobial agents along the food chain may result in exposure to antimicrobial resistant bacteria or their determinants in the food production environment. As part of a One Health approach 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 food production environment of antimicrobials and their metabolites from food production related activities, and to minimize the risks associated with the selection and dissemination of resistant microorganisms and resistance determinants in the food production environment.

4. 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 Resistance 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), the *Code of Practice on Good Animal Feeding* (CXC 54-2004), and the *Guidelines for the Design and Implementation of National Regulatory Food Safety Assurance Program associated with the Use of Veterinary Drugs in Food Producing Animals* (CXG 71-2009) are particularly relevant for use of agricultural chemicals on plants/crops, animal feed, and veterinary drugs, respectively.

5. This Code of Practice provides risk management advice, including the responsible and prudent use of antimicrobial agents that can be applied proportionately to the 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 country and determining how best to reduce risk and protect public health.

6. The *Principles and Guidelines for the Conduct of Microbiological Risk Management* (CXG 63-2007) contains guidance for developing and implementing risk management measures. Setting priorities and identifying risk management measures should take into account the following:

- *WHO Guidance on Integrated Surveillance of Antimicrobial Resistance in Foodborne Bacteria, application of a One Health Approach*;
- *WHO List of Critically Important Antimicrobials for Human Medicine*, specifically the Annex with the complete list of antimicrobials for human use, categorized as critically important, highly important and important;
- Relevant chapters of the *OIE Terrestrial and Aquatic Animal Health Codes* and the *OIE List of Antimicrobial Agents of Veterinary Importance*; and
- National lists of important antimicrobials for humans and animals where they exist.

7. Where available, national and local guidelines to prevent, minimize and contain foodborne AMR 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.

8. 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 progressive implementation may be used by some countries to properly apply elements in this document proportionate to the foodborne AMR risk and should not be used to generate unjustified barriers to trade.

2. Scope

9. This Code of Practice provides risk management guidance to address the risk to human health of the development and transmission of antimicrobial resistant microorganisms or resistance determinants through food. It provides risk-based guidance on relevant measures and practices 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 animal production (terrestrial and aquatic) plant/crop production, and references other best management practices, as appropriate.

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

11. Most of the recommendations in this Code of Practice focus on antibacterials, however some recommendations may also be applicable to antiviral, antiparasitic, antiprotozoal, and antifungal agents, where there is scientific evidence of foodborne AMR risk to human health.

12. 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/crops¹ and recombinant DNA microorganisms²; non-genetically modified microorganisms (for example, starter cultures) intentionally added to food with a technological purpose; certain food ingredients, which could potentially carry antimicrobial resistance determinants, such as probiotics³; and biocides. In addition, AMR from non-food animals, non-food plants/crops, or non-food routes are also outside the scope of this document.

3. Definitions

The relevant definitions presented in the Codex Procedural Manual, *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*, *General Principles of Food Hygiene* (CXC 1-1969), *Principles and Guidelines for the Conduct of Microbiological Risk Assessment* (CXG 30-1999) and *Guidelines on Integrated Monitoring and Surveillance of Foodborne Antimicrobial Resistance* are applicable to this document.

The following definitions are included to establish a common understanding of the terms used in this document:

Antibacterial: A substance that acts against bacteria.

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.

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.

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

¹ 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).

² 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).

³ 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).

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, feed), harvest/slaughter, packing, processing, storage, transport, and distribution to the point of consumption.

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

Food production environment: The immediate vicinity of the food chain where there is relevant evidence that it could contribute to foodborne AMR.

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 an 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, taking into account the *WHO List of Critically Important Antimicrobials for Human Medicine*, including the classes described in the Annex of the “*List of Medically Important Antimicrobials, categorized as Critically Important, Highly Important, and Important*”, or equivalent criteria established in a national list, where available. It does not include ionophores or other agents determined not to be a foodborne AMR risk consistent with the *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*.

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

Pharmacovigilance: The collection and analysis of data on how products perform in the field after authorization and any interventions to ensure that they continue to be safe and effective. These data can include information on adverse effects to humans, animals, plants or the environment; or lack of efficacy.

Plants/crops: A plant or crop that is cultivated or harvested as food or feed.

Plant/crop health professional: An individual with professional or technical training, knowledge and experience in plant/crop health and protection practices.

Prevention of disease/prophylaxis: Administration or application of antimicrobial agents to an individual or a group of plants/crops or 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 or applied.

Veterinary medical use⁴ ⁵/phytosanitary use⁶ (food-producing animals or plants/crops): Administration or application of antimicrobial agents for the treatment, control/metaphylaxis or prevention/prophylaxis of disease.

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

4. General principles to minimize and contain foodborne antimicrobial resistance

Principles on AMR Risk Management (generally)

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

Principle 2: Considering that this document is to provide risk management guidance to address foodborne AMR risks to human health, for animal health and plant health aspects, relevant OIE and IPPC standards should be considered.

Principle 3: 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 humans, animal, and plant health of recommended risk management measures.

⁴ See also OIE Terrestrial Animal Health Code, specifically the chapter on Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals.

⁵ Also recognized as therapeutic use in some jurisdictions/organizations.

⁶ See also IPPC International Standard for Phytosanitary Measures, Glossary of Phytosanitary Terms.

Principle 4: The *WHO List of Critically Important Antimicrobials for Human Medicine*, the *OIE List of Antimicrobial Agents 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: On a continuous and progressive 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.

Principle on preventing infections and reducing the need for antimicrobials

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

Principles on the responsible and prudent use of antimicrobials (generally)

Principle 7: The decision to use antimicrobial agents should be based on sound clinical judgement, experience, and treatment efficacy. Where feasible and appropriate the results of bacterial cultures and integrated resistance surveillance and monitoring should also be considered.

Principle 8: Medically important antimicrobials should be prescribed, administered, or applied only by, or under the direction of, veterinarians, plant/crop health professionals, or other suitably trained persons authorized in accordance with national legislation.

Principle 9: Antimicrobial agents should be used as legally authorized and following all applicable label directions; except where specific legal exemptions apply.

Principle 10: The choice of which antimicrobial agent to use should take into consideration relevant professional guidelines, where available, results of antimicrobial 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 11: 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.

Principles on the use of antimicrobials in specific circumstances

Principle 12: Responsible and prudent use of antimicrobial agents does not include the use for growth promotion of antimicrobial agents that are considered medically important. Antimicrobial agents that are not considered medically important should not be used for growth promotion unless potential risks to human health have been evaluated through procedures consistent with the *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*.

Principle 13: Medically important antimicrobial agents should only be used for veterinary medical/phytosanitary use (treatment, control/metaphylaxis or prevention/prophylaxis of disease).

Principle 14: Medically important antimicrobials should only be administered or applied for prevention/prophylaxis where professional oversight has identified well-defined and exceptional circumstances, appropriate dose and duration, based on clinical and epidemiological knowledge, consistent with the label, and in line with national legislation. Countries could use additional risk management measures for medically important antimicrobials considered highest priority critically important as described in the *WHO List of Critically Important Antimicrobials for Human Medicine*, the *OIE List of Antimicrobial Agents of Veterinary Importance*, or national lists, where available, including restrictions proportionate to risk and supported by scientific evidence.

Principle 15: When used for the control of disease/metaphylaxis, medically important antimicrobial agents should only be used on the basis of epidemiological and clinical knowledge and a diagnosis of a specific disease and follow appropriate professional oversight, dose, and duration.

Principle on surveillance of antimicrobial resistance and use

Principle 16: 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 antimicrobial agents in humans, food-producing animals, and plants/crops and transmission of pathogens and resistance genes between humans, food-producing animals, plants/crops, 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*.

5. Responsible and prudent use of antimicrobial agents

13. The *OIE Terrestrial and Aquatic Animal Health Codes* and the *OIE List of Antimicrobial Agents of Veterinary Importance* contain detailed information with respect to the control of veterinary medicines for use in food-producing animals and aquaculture.

14. For more information on the data requirements for authorization of antimicrobial agents for food-producing animals see relevant national guidelines or internationally harmonized guidelines.

5.1 Responsibilities of the competent authorities

15. The competent 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 health professionals, 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. It is the responsibility of competent authorities to develop up-to-date guidelines on data requirements for evaluation of antimicrobial agent applications, as well as ensuring that antimicrobial agents used in the food chain are used in accordance with national legislation.

16. 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 to minimize and contain 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.

17. National action plans may include recommendations to relevant professional organisations to develop species or sector-specific guidelines.

18. In order to promote responsible and prudent use of antimicrobial agents, it is important to encourage the development, availability, and use of validated, rapid, reliable diagnostic tools, where available, to support veterinarians and plant/crop health professionals in diagnosing the disease and selecting the most appropriate antimicrobial, if any, to be administered/applied.

19. The competent authorities should determine appropriate labelling, including the conditions that will minimize the development of foodborne AMR while still maintaining efficacy and safety.

Quality control of antimicrobial agents

20. Competent authorities should ensure that quality controls are carried out in accordance with national or international guidance and in compliance with the provisions of good manufacturing practices.

Assessment of efficacy

21. Assessment of efficacy is important to assure adequate response to the administration of antimicrobial agents. As part of the marketing authorization process, the assessment should include the efficacy with optimal dosages and durations, supported by clinical trials, microbiological data (including antimicrobial susceptibility testing), pharmacokinetic (PK) data, and pharmacodynamic (PD) data.

Assessment of the potential antimicrobial agents to select for resistant microorganisms

22. The competent authorities should assess the potential of medically important antimicrobial agents used along the food chain to select for foodborne AMR taking into account the *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*, the *WHO List of Critically Important Antimicrobials for Human Medicine*, the *OIE List of Antimicrobial Agents of Veterinary Importance*, or national lists, where available.

Assessment of the impact on the food production environment

23. In accordance with their national guidelines, competent authorities should consider results of foodborne AMR risk assessment of sources that contribute to the food production environment, e.g. reuse of waste water for irrigation, and use of manure, and other waste-based fertilizers for soil fertilization. When a foodborne AMR risk is determined through the *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance* the need for monitoring and proportionate risk management measures should be considered.

Establishment of a summary of characteristics for each antimicrobial product

24. Competent authorities should establish a Summary of Product Characteristics or similar document for each authorized antimicrobial product. The information in these documents can be utilized in labelling and as a package insert. Such information may include:

- brand/chemical/drug name;
- product description;
- indications for use;
- dosage forms/strengths/application rates;
- duration of treatment or application interval;
- contraindications; warnings;
- adverse reactions/phytotoxicity/incompatibilities;
- product interactions and uses in specific populations for each authorized antimicrobial product, when available;
- withdrawal periods or pre-harvest intervals; and
- storage conditions.

Monitoring and surveillance programs

25. Competent authorities should establish systems for the monitoring and surveillance of foodborne antimicrobial resistance and antimicrobial use (AMU) following the Codex Guidelines on Integrated Monitoring and Surveillance of Foodborne Antimicrobial Resistance and OIE standards for monitoring of antimicrobial resistance and use in animals.

26. Competent authorities should have in place a pharmacovigilance program for the monitoring and reporting of suspected adverse reactions to veterinary antimicrobial agents, including lack of the expected efficacy that could be related to foodborne antimicrobial resistance. The information collected through the pharmacovigilance program can contribute to a comprehensive strategy to minimize antimicrobial resistance along the food chain.

27. In cases where the assessment of data collected from pharmacovigilance and from other post-authorization surveillance including, if available, targeted surveillance of antimicrobial resistance in veterinary or plant/crop pathogens, suggests that the conditions of use of the given antimicrobial agent marketing authorization should be reviewed, competent authorities shall endeavour to achieve this re-evaluation.

Distribution of antimicrobial products

28. Competent authorities should make sure antimicrobial products are distributed through licensed/authorized distribution systems in accordance with national legislation.

29. Competent authorities should prevent illegal medicines and unapproved formulations from entering distribution systems.

Control of advertising

30. Competent authorities should ensure that advertising and promotion of antimicrobial products is done in accordance with national legislation or policies.

31. Advertising and promotion of antimicrobial agents should be done in a manner consistent with specific regulatory recommendations for the product.

Training on foodborne antimicrobial resistance and the responsible use of antimicrobial agents

32. Training should be supported, to the extent possible, by the competent authorities on topics related to minimizing antimicrobial resistance and encouraging the responsible use of antimicrobial agents. Training may take the form of communication and outreach and should be relevant to veterinarians and plant/crop health professionals, manufacturers and marketing authorization holders, wholesale and retail distributors, food animal and plant/crop producers, and other participants along the food chain as appropriate. Training and communication may broadly address other public health-related activities.

33. Relevant information may include, but is not limited to:

- information on disease prevention and management strategies to reduce the need to use antimicrobial agents;
- relevant information to enable the veterinarians and plant/crop health professionals to use or prescribe antimicrobial agents responsibly and prudently;
- the need to adhere to responsible and prudent use principles and using antimicrobial agents in production settings in agreement with the provisions of the marketing authorizations and professional advice;
- utilizing the *WHO List of Critically Important Antimicrobials for Human Medicine*; the *OIE List of Antimicrobial Agents of Veterinary Importance*, and national lists where they exist;
- information on appropriate storage conditions for antimicrobial agents before and during use and the safe disposal of unused and out of date antimicrobials;
- understanding relevant risk analysis of antimicrobial agent products and how to use that information;
- national action plans, if available, and international strategies to fight and control antimicrobial resistance;
- good antimicrobial use practices, antimicrobial prescription writing and establishment of withdrawal period;
- training in new methodologies for molecular analysis of resistance; understanding methods and results of susceptibility testing of antimicrobials and molecular analysis;
- the ability of antimicrobial agents to select for resistant microorganisms or resistance determinants that may contribute to animal, plant/crop, or human health problems;
- understanding the process of identifying, evaluating, implementing, and monitoring the effectiveness of risk management options; and
- the collection and reporting of AMR and AMU monitoring and surveillance data.

Knowledge gaps and research

34. To further elucidate the risk from foodborne AMR, the relevant authorities could encourage public and private research in the following areas and not limited to:

- improve the knowledge about the mechanisms of action, pharmacokinetics and pharmacodynamics of antimicrobial agents to optimize the dosage regimens for veterinary medical use/phytosanitary use and their efficacy;
- improve the knowledge about the mechanisms of transmission, selection, co-selection, emergence and dissemination of resistance determinants and resistant microorganisms along the food chain;
- develop practical models for applying the concept of risk analysis to assess the public health concern precipitated by the development of foodborne AMR;
- 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 foodborne AMR development and spread;
- assess the primary drivers leading to use of antimicrobials at the farm, sub-national, and national levels, and the effectiveness of different interventions to change behavior and reduce the need to use antimicrobial agents in food production;
- improve the knowledge on behavior change and on cost-effective interventions to reduce the need of antimicrobial agents;
- develop safe and effective alternatives to antimicrobial agents, new antimicrobial agents, rapid diagnostics, and vaccines; and
- improve knowledge on the role of the environment on the persistence of antimicrobial agents, and the emergence, transfer and persistence of foodborne antimicrobial resistance determinants and resistant microorganisms.

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

35. The competent authorities should develop effective procedures for the safe collection and disposal of unused, substandard and falsified drugs, illegally marketed, or out-of-date antimicrobial agents.

5.2 Responsibilities of Manufacturers and Marketing Authorization Holders**Marketing authorization of antimicrobial agents**

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

- to supply all the information requested by the national competent authority in order to establish objectively the quality, safety and efficacy of antimicrobial agents;
- 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; and
- to utilize manufacturing standards/practices and comply with national regulations in order to minimize contamination of the food production environment.

Marketing and export of antimicrobial agents

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

38. Only antimicrobial agents meeting the quality standards as specified in the legislation of the importing country should be exported.

39. The amount of antimicrobial agents marketed should be provided to the national competent authority when requested, and in addition, when feasible, information on estimated of types of use (e.g. treatment, control, prevention), route of administration and target species.

40. 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

41. It is the responsibility of manufacturers and marketing authorization holders to advertise antimicrobial agents in accordance with the provisions of paragraphs 30 and 31, and not to inappropriately advertise antimicrobial agents directly to producers.

42. Manufacturers and marketing authorization holders should not provide incentives that have a financial value to prescribers or suppliers for the purpose of increasing the use or sales of medically important antimicrobials.

Training

43. It is the responsibility of the marketing authorization holders to support training on topics related to foodborne antimicrobial resistance and the responsible use of antimicrobial agents as described in paragraph 32, as appropriate.

Research

44. It is the responsibility of the marketing authorization holders to supply required data to register antimicrobial agents including data regarding the safety and efficacy of products as appropriate.

45. Research on the development of new antimicrobials, safe and effective alternatives to the use of antimicrobials, rapid diagnostics and vaccines are encouraged.

5.3 Responsibilities of wholesale and retail distributors

46. Wholesalers and retailers distributing medically important antimicrobial agents should only do so on the prescription of a veterinarian or order from a plant/crop health professional or other suitably trained person authorized in accordance with national legislation. All distributed products should be appropriately labelled.

47. Distributors should keep records of medically important antimicrobials supplied according to the national regulations and may include, for example:

- date of supply;
- name of responsible veterinarian or plant/crop health professional or other suitably trained and authorized person;
- name of medicinal product, formulation, strength and package size;
- batch number;
- quantity supplied;
- expiration dates;
- manufacturer name and address; and
- target species.

48. Distributors should support training, as appropriate, on topics related to foodborne antimicrobial resistance and the responsible use of antimicrobial agents using information provided by the competent authorities, manufacturers and marketing authorization holders, veterinarians and plant/crop professionals and other relevant entities as described in paragraph 32, as appropriate.

5.4 Responsibilities of Veterinarians⁷ and Plant/Crop Health Professionals

49. Veterinarians and plant/crop health professionals should identify new or recurrent disease problems and develop strategies in conjunction with competent authority to prevent, control, or treat infectious disease at the national level. These may include, but are not limited to, biosecurity, improved production practices, proper animal nutrition and safe and effective alternatives to antimicrobial agents, including vaccination or integrated pest management practices where applicable/available.

50. Professional organizations should be encouraged to develop species or sector-specific guidelines on the responsible and prudent use of antimicrobial agents.

51. Antimicrobial agents should only be prescribed or administered when necessary, only as long as required, and in an appropriate manner:

- A prescription, order for application, or similar document for medically important antimicrobial agents should indicate the dose, the dosage intervals, route and 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, in accordance with national legislation. Prescriptions or orders should also indicate the owner and the location 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/or the direction of a veterinarian or consultation with a plant/crop health professional, and the conditions stipulated in the national legislation; and
- Protocols for monitoring use to allow for data collection or for quality assurance purposes should be considered as recommended in the Guidelines on Integrated Monitoring and Surveillance of Foodborne Antimicrobial Resistance.

52. For food-producing animals, the appropriate use of medically important antimicrobial agents in veterinary practice is a clinical decision that should be based on the experience of the prescribing veterinarian⁷ and epidemiological and clinical knowledge and, if available, based on adequate diagnostic procedures. When a group of food-producing animals, which may have been exposed to pathogens, they may need to be treated without recourse to a laboratory confirmed diagnosis based on antimicrobial susceptibility testing to prevent the development and spread of clinical disease.

53. For plant/crop production, the appropriate use of medically important antimicrobial agents to manage disease/pests should be based on the principles of integrated pest management (IPM), consultation with a plant/crop health professional, historical and epidemiological knowledge of the disease/pest situation, and monitoring of the current disease/pest status. Only authorized products should be used following label directions. Alternatives to medically important antimicrobials should be considered when available and their safety and effectiveness has been determined. Medically important antimicrobial agents should only be used to the extent necessary for a specific disease and follow appropriate professional oversight, dose, and duration.

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

⁷ Under some circumstances, this may refer to a suitably trained person authorized in accordance with national legislation, for example an Aquatic Animal Health Professional.

- The expected efficacy of the administration based on:
 - the expertise and 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 the 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 ideally be based on the results of microbiological susceptibility tests derived from relevant samples;
 - the appropriate route of administration;
 - results of initial administration;
 - previous published scientific information on the treatment of the specific disease and available scientific knowledge on antimicrobial use and resistance;
 - evidence-based therapeutic guidelines, such as species or sector-specific guidelines on the responsible and prudent use of antimicrobial agents, if available; and
 - the likely course of the disease.
- The need to minimize the adverse health effect from the development of antimicrobial 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 whenever possible;
 - optimized dosing regimens;
 - the route of administration;
 - 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; and
 - the importance of the antimicrobial agents to human and veterinary medicine.
- If the label conditions allow for flexibility, the veterinarian or plant/crop health professional 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

55. 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 use of approved or appropriate withdrawal periods. It is the veterinarian's responsibility to define the conditions of use including the dosage regimen, the route of administration, and the duration of the administration and the withdrawal period.

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

57. Medically important antimicrobials should not be used off-label for plants/crops, except off-label use for emerging disease control, in accordance with national legislation.

Record keeping and recording

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

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

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

60. Veterinarians and plant/crop health professionals should also periodically review farm records on the use of antimicrobial agents to ensure compliance with their directions.

61. Veterinarians and plant/crop health professionals may have a role to play assisting the competent authorities in monitoring and surveillance programs related to AMU and AMR as appropriate.

Training

62. Professional or other organizations should support the development and/or delivery of training on issues related to antimicrobial resistance and the responsible use of antimicrobial agents as described in paragraph 32, as appropriate.

5.5 Responsibilities of food animal and plant/crop producers

63. Producers are responsible for implementing health programs on their farms to prevent and manage disease outbreaks with assistance of veterinarians, plant/crop health professionals, 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 reducing the need to use antimicrobials agents to minimize risk of foodborne AMR.

64. Producers of food animals and plants/crops have the following responsibilities:

- to use antimicrobial agents only when necessary, under the supervision of a veterinarian or plant/crop health professional 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 health professional, 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 health professional 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 and dying animals, dispose of dead animals, diseased plants/crops promptly under approved condition by competent authorities;
- to comply with the storage conditions of antimicrobial agents according to the approved product labelling;
- to comply with the recommended withdrawal periods or pre-harvest intervals;
- 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 health professional, or other suitably trained person authorized in accordance with national legislation in charge of the production unit of recurrent disease problems or suspected lack of efficacy of antimicrobial applications;
- to maintain or have their veterinarian, plant/crop health professional, or other suitably trained individual 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, for example, the following:
 - copy of the prescription, order for application or other documentation, when available;
 - name of the antimicrobial agent/active substance and batch number;
 - name of supplier;
 - date of administration; species and number of animals or plants/crops;
 - identification of the production unit to which the antimicrobial agent was administered;
 - disease treated, prevented, or controlled;

- relevant information on animals or plants/crops treated (number, age, weight);
 - quantity/dose and duration of the antimicrobial agent administered;
 - withdrawal periods or pre-harvest intervals;
 - result of treatment, in consultation with the veterinarian or plant/crop health professional; and
 - name of the prescribing veterinarian, plant/crop health professional 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 infection prevention and control measures as appropriate and as provided in the *OIE Terrestrial and Aquatic Animal Health Codes*;
 - to participate in training on issues related to antimicrobial resistance and the responsible use of antimicrobial agents as described in paragraph 32, as appropriate; and
 - to assist the relevant authorities in surveillance programs related to antimicrobial use and antimicrobial resistance, as appropriate.

65. The responsible and prudent use of antimicrobial agents should be supported by continuous efforts in disease prevention to minimize infection during production. Efforts should aim to improve health, thereby reducing the need for antimicrobial agents. This can be achieved by, for example, improving hygiene, biosecurity, 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.

66. Disease prevention through the use of vaccines, and other measures that have been clinically proven to be safe and efficacious for supporting animal health, such as adequate nutrition can be considered and applied when appropriate and available.

67. Prevention and reduction of the incidence and severity of plant pests and diseases should be implemented by applying good agricultural practices, such as crop rotation, accurate and timely diagnosis and monitoring of diseases, use of disease resistant crop varieties, exclusionary practices that prevent introduction of pathogens into a crop, careful site selection integrated pest management strategies and biological controls when appropriate and available.

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

68. Concerted efforts of all stakeholders along the food chain are required to minimize and contain foodborne illness, including illness related to foodborne AMR. While this Code focuses on responsible and prudent use of antimicrobial agents in primary production at the farm level, the later phase of the food chain also plays an important role in preventing foodborne AMR infection and illness.

69. The food processing industry and food retailers should refer to the *Principles and Guidelines for the Conduct of Microbiological Risk Management*).

70. Food should be produced and handled in such a way as to minimize the introduction, presence and growth of microorganisms, which apart from having the potential to cause spoilage and foodborne illnesses can also disseminate foodborne AMR. Slaughterhouses and processing plants should follow good manufacturing practices and the Hazard Analysis and Critical Control Points (HACCP) principles. The *General Principles of Food Hygiene* is a useful reference in this respect.

71. Food business operators should provide training on good hygienic practices, including those for minimizing cross-contamination. The *WHO Five Keys to Safer Food* contains useful information for food handlers to minimize the transmission of foodborne illness, including resistant infections.

7. Consumer practices and communication to consumers

72. Government, food industry and other stakeholders along the food chain should inform and educate consumers on the risks of foodborne illness, including infections with resistant microorganisms and ways to minimize the risk of infection.

73. Some aspects to consider when communicating to consumers are:

- identifying all the stakeholders and having a common message;
- providing information that is science-based, clear, accessible, and targeted to a non-scientific audience; and
- considering local characteristics that affect how risks are perceived (e.g. religious belief, traditions).

74. Various manuals from international organizations, such as the FAO, WHO and OIE can be used as tools to assist in awareness raising for consumers on how to minimize foodborne bacteria in their food.

75. For more information on risk communication refer to *WHO Integrated Surveillance of Antimicrobial Resistance in Foodborne Bacteria, Application of a One Health Approach* and *FAO/WHO Risk Communication applied to Food Safety Handbook* and *the Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*.