CODEX ALIMENTARIUS COMMISSION E

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World Health Organization

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Agenda Item 4 **CX/AMR 17/5/5**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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

Fifth Session

PROPOSED DRAFT REVISION OF THE *CODE OF PRACTICE TO MINIMIZE AND CONTAIN ANTIMICROBIAL RESISTANCE* (CAC/RCP 61-2005)

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

Codex members and Observers wishing to submit comments at Step 3 on the proposed draft revision of the *Code of Practice to Minimise and Contain Antimicrobial Resistance* (Appendix I to this document) should do so as instructed in CL 2017/83-AMR available on the Codex webpage/Circular Letters 2017: http://www.fao.org/fao-who-codexalimentarius/circular-letters/en/.

Report of the Electronic Working Group (EWG) on the Revision of the *Code of Practice to Minimize and Contain Antimicrobial Resistance* (CAC/RCP 61-2005)

1. The 40th Session of the CAC (CAC40) approved new work for the TFAMR and established two EWGs, working in English and Spanish and open to all Codex members and observers, to develop: a proposed draft revision of the *Code of Practice to Minimize and Contain Antimicrobial Resistance* (CAC/RCP 61-2005) (chaired by the United States of America and co-chaired by China, Kenya and the United Kingdom); and a proposed draft guidance on integrated surveillance of antimicrobial resistance (chaired by the Netherlands and co-chaired by Chile, China and New Zealand).

2. An EWG, open to all Members and Observers, was held from 26 July through 31 August 2017. Requests to participate in the EWG on the proposed draft revision of the *Code of Practice to Minimize and Contain Antimicrobial Resistance* (CAC/RCP 61-2005) were received from 44 Codex Members, 1 Codex Member Organisation and 18 Codex Observers. The list of Members and Observers is attached as Appendix II.

3. Through a participatory process in the Codex Forum, the working group reviewed and proposed revisions to the *Code of Practice to Minimize and Contain Antimicrobial Resistance* (CAC/RCP 61-2005). Participants were asked to comment on the overall structure and organization of the document taking into account the Report of the Physical Working Group on Antimicrobial Resistance (AMR) held 26 November to 2 December 2016 (CX/CAC 17/40/12 Add.2) and in particular Project Document/1 as adopted and approved for new work at CAC40.

4. The EWG took note that the purpose of the proposed new work is to revise the *Code of Practice to Minimize and Contain Antimicrobial Resistance* by broadening its scope, and developing risk-based guidance on the management of foodborne antimicrobial resistance that addresses the entire food chain, in line with the mandate of Codex. The objective is to minimize the risk to public health from the development and spread of foodborne antimicrobial resistance. The guidance should be scientifically supported and also take into account new developments, including the current and future revisions of lists of critically important antimicrobials, and the work of FAO, WHO and OIE in this area.

5. The EWG further took note that the scope of the revision should address the risk to human health associated with the presence in food and animal feed, and the transmission through food and animal feed, of AMR microorganisms or determinants. It should provide guidance on relevant measures along the food chain to minimize the development and spread of foodborne antimicrobial resistance, including guidance on the responsible and prudent use of antimicrobial agents in agriculture and aquaculture.

6. Following are key points of potential areas of consensus.

- Cross-reference where possible to other international texts. There is general consensus on cross-referencing relevant texts developed by OIE, WHO and other Codex texts. However, the extent of application of these texts and impact on trade in food will be a matter to be considered later.
- Strengthened text around the importance of reducing the need to use antimicrobials, such as improved biosecurity, husbandry measures, non-antimicrobial disease prevention measures etc.
- Expanding the detail and clarity of text regarding actions recommended by the broader range of stakeholders; most supported including consumers in this expanded cast list.
- Specifying within the text that antimicrobials should only be available from veterinarians or trained personnel.
- A need for the Code of Practice to be sufficiently pragmatic that all Codex countries can make use of it, taking into account the wide range of national situations of Codex countries.
- There is general need to harmonise definitions and only provide definition of terms used in the document.
- The document should also be aligned to the format of the *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance* (CAC/GL 77-2011).
- There is need to include the role of other stakeholders not captured in the current text (RCP61).

7. The EWG also identified several key areas lacking consensus that may benefit from additional comment and/or scientific advice. These areas may benefit from further comment and consideration at TFAMR5.

8. Following are key points describing areas lacking consensus that may benefit from additional comment and/or scientific advice.

- Approach to the format of the document: most contributors took a fairly ad hoc approach, but some clearly stated that since the remit was to revise rather than re-write the CoP, existing text should stand and be added to unless good reason for amending.
- There were many contributions and different approaches to definitions of treatment/metaphylaxis/control/prophylaxis/prevention.
- Likewise, there were different reactions to use of the term ‘medically important antimicrobials’. Comments took note of the WHO’s new position, but how MIAs and non-MIAs are dealt with regard to the scope of the Code of Practice looks still to be a matter which needs further exploration, whether for use overall, or how they relate to the use of antimicrobial growth promoters.
- Several Members brought up the text agreed by the G20 Agriculture Ministers on the approach to antimicrobial growth promoters as something which could be considered by the group as text is developed.
- A number of contributions referred to the Codex mandate and urged the group not to overstep its remit.
- The use of antimicrobials in crop agriculture is only mentioned in a few comments, though it is an area which likely requires scientific advice from FAO/WHO in order to enable the task force to outline risk management measures.

9. The Chairs of the EWG took note of the approach of several Member Countries and Organisations to preface their comments with a succinct list of key priorities and topic areas. This approach was thought to be valuable taking into consideration the extensive nature of comments on the text of the document. A succinct list of priorities or topic areas may be a valuable aid in arriving at further areas of consensus, identifying topics that require scientific advice, developing risk-based guidance, and appropriately addressing the entire food chain.

10. The EWG identified several areas of potential consensus and incorporated new and revised text in square brackets for further comment and potential adoption at TFAMR5. Similarly, the EWG identified potential consensus around existing text that could be deleted. It was suggested that some portions of existing text could be replaced with new information, language, references, or tools while other portions could be deleted by referencing other relevant standards. Importantly, the EWG noted that certain key concepts in the existing text continue to have value and should be retained. All text proposed for replacement or deletion is accordingly noted by ~~strikethrough~~ for further comment and consideration at TFAMR5. The proposed draft Revision of the *Code of Practice to Minimize and Contain Antimicrobial Resistance* is contained in Appendix I. A summary of all comments received in their original language is available with the EWG Chair.

11. The following are key points contained in the General Comments and after that are key points by topic heading in the draft document highlighting areas of discussion and the approach taken by the Chairs to revise the draft document based on comments of Members and Observers.

General Comments

12. Several Members and Observers provided general comments. In most cases, the comments highlighted overarching concepts that applied to their comments throughout the draft document. In some cases, the comments raised new ideas.

13. The Chairs, to the extent possible, identified areas of consensus and made suggested revisions to the draft document accordingly. The Chairs also added new concepts and ideas as text in square brackets for further consideration by the TFAMR under relevant sections in the draft document. Following are points raised among the general comments, including those that the Chairs believe may warrant further discussion to identify consensus.

- Many Members and Observers supported the One Health concept and suggested ways to adapt the text to address the ways human health is connected to that of animals, plants and the environment.
- Several Members and Observers emphasized that infection prevention and control and biosecurity measures are critical in the management of infectious diseases as they reduce the need for antimicrobials and consequently the opportunity for microorganisms to develop and spread resistance.
- Many Members and Observers supported the proposal to reference OIE Terrestrial Animal Health Code Chapter 6.9 and Aquatic Animal Health Code Chapter 6.2 to avoid duplication and the potential for ambiguity as the chapters are updated and revised. Members and Observers identified certain sections of text to be retained and sometimes provided condensed summaries of key concepts to retain.
- One Member suggested that separate Codes of Practices could be developed for different sectors, for example animals and crops, while another Member suggested that separate sections within the Code of Practice could be developed to address animals and crops.
- Several Members and Observers suggested additional actors that could be considered for inclusion in the Code of Practice, for example: feed and food business operators, veterinary faculties and agricultural schools, veterinary professional associations, industry stakeholder associations, farmers associations, laboratories, animal nutritionists, aquaculture producers, food processing industry, importers, apiculturists, and animal handlers. Some Members suggested a new section on Responsibilities of animal feed manufacturers and noted Chapter 6.9.8 of the OIE Terrestrial Animal Health Code with the same heading. Further discussion on whether to reference the OIE Chapter 6.9.8 or develop a new section could be beneficial.

Table of Contents

14. In the draft document it was noted that the Table of Contents would be revised following the content of the final document. One Member commented on the Table of Contents suggesting alternate headings - some of which revised the current headings and others which were new. The Member suggested new text and provided suggestions for deletion of text with reference to the OIE Terrestrial and Aquatic Animal Health Codes in different sections that followed.

15. The Chairs did not include the new headings, but did include in square brackets text which introduced new concepts in line with the Main Aspects to be covered in Project Document 1 in the relevant sections of the document that followed. The Chairs decided to retain the current topic headings with small modifications because most Members and Observers provided new content and revisions under the topic headings proposed in the draft document. The TFAMR should revisit the topic headings at a later stage after evaluating the content of the Code of Practice.

Rationale: The final Table of Contents should reflect the content of the Code of Practice.

Introduction

16. Most Members and Observers agreed with the new text proposed for the Introduction and offered minor edits. Several Members and Observers encouraged the EWG to retain important concepts from the existing text.

17. The Chairs modified the new text in Paragraphs 1-3 keeping it in square brackets for further comments and potential adoption at the TFAMR5. The Chairs retained important content in Paragraphs 4-6 (previously numbered as Para 1, 2, 4). Formerly numbered Para 3 is proposed for deletion.

Note: For the purpose of this report new paragraph numbers are stated as **Paragraph xx** and former paragraph numbers are referred to as **Para xx.**

Rationale: The new text includes the objectives in Project Document 1. Important concepts, identified by Members and Observers, are retained. Para 3 describes the process for developing RCP61 which has been superseded by the mandate of TFAMR and is therefore proposed for deletion.

Aims and Objectives

18. Most Members and Observers agreed with the proposal to replace the Aims and Objectives with new sections on Scope and General Principles – following the structure of GL77. Several Members and Observers encouraged the EWG to retain important concepts, particularly those found in Para 7 and 8. Some Members and Observers provided new text and revised text and suggested text for deletion.

19. The Chairs marked the current text in the section (Para 5-8) for proposed deletion and modified the text in the new sections on Scope and General Principles to take into account many comments and proposals. The Chairs moved and revised certain text as follows.

Para 5: Concepts moved to Scope, Paragraph 7.

Para 6: Concepts moved to Introduction, Paragraphs 4-7 and Scope, Paragraph 7.

Para 7: Concepts moved to Introduction, Paragraph 6; Definitions, One Health; General Principle 10; new section Responsibilities of the Regulatory Authorities, Assessment of Environmental Impact, Paragraphs 20; and Responsibilities of the Regulatory Authorities, Development of Research; Paragraph 33.

Para 8, bullet 1: General Principle 12.

Para 8, bullet 2: General Principle 2.

Para 8, bullet 3: General Principle 13.

Para 8, bullet 4: General Principle 14.

Para 8, bullet 5: General Principle 5.

Para 8, bullet 6: Introduction, Paragraph 4 and Scope, Paragraph 7.

Rationale: Important concepts in the former section Aims and Objectives are retained. The text is revised taking into consideration the Objectives, Scope, and Main aspects to be covered in Project Document 1. Coherence with GL77 is improved by following a similar structure.

[Scope]

20. Most Members and Observers agreed with the proposal to develop a new section on Scope following the structure of GL77. Several Members and Observers encouraged the EWG to retain important concepts in the current Aims and Objectives. Some Members and Observers suggested new text, revised text, and minor edits.

21. The Chairs modified the section on Scope taking into consideration the different proposals by Members and Observers. Important concepts in the Aims and Objectives were moved into the new section on Scope. Some Members suggested additional actors in the food chain that could be included within the scope of this Code of Practice. Similarly, some Members suggested separate Codes of Practice could be developed for different sectors.

22. The Chairs, taking into consideration Project Document 1, made minor edits to Paragraph 7 and added Paragraph 8 from GL77 as new RCP61 Paragraph 8 to maintain coherence between the two documents. The TFAMR should consider whether additional actors could be added to the Code of Practice and the question of whether separate Codes of Practice should be developed for different sectors.

Rationale: Minor modifications to the Scope were made to improve clarity and coherence. The TFAMR should comment on the development of sections addressing additional actors in the food chain.

[Definitions]

23. Most Members and Observers concurred with the need to include definitions as part of the Code of Practice. Many Members and Observers agreed with the proposal to include definitions at the beginning of the Code of Practice, rather than at the end, following the structure of GL77. However, some Members pointed out that having definitions at the beginning of the document could be distracting. Most Members and Observers commented on the new definitions presented, while fewer commented directly on the existing definitions at the end of the document.

24. In particular, Members and Observers provided comments and questions on antibiotic resistance, therapeutic use, treatment, control, prevention, growth promotion, and medically important antimicrobials. The comments demonstrated a range of opinions and should be further discussed at the TFAMR. Key areas of comment included the following.

- Whether 'One Health' definitions could be derived that have shared understanding across sectors (humans, animals, crops).
- When the Code of Practice should use the term antimicrobial resistance or antibiotic resistance.
- How to best distinguish therapeutic uses (i.e. related to infectious disease) from production uses (i.e. growth promotion).
- How to apply the relatively new term, medically important antimicrobial, to distinguish classes of antimicrobials important for therapeutic use in human medicine from antimicrobial classes that are not used in human medicine.

25. Two Members reminded the EWG that definitions should be relevant to the text of the chapter and should be aligned with other definitions in Codex, in particular GL77.

26. The Chairs made modifications to the definitions in the draft document based on comments by Members and Observers maintaining them in square brackets for further discussion.

Rationale: Definitions should facilitate the use of the chapter. Definitions should be updated and revised based on current scientific knowledge taking into account advancement in antimicrobial resistance risk analysis. Definitions in Codex texts and other relevant texts under the World Trade Organization Sanitary and Phytosanitary Agreement (i.e. OIE Terrestrial and Aquatic Animal Health Codes, International Plant Protection Convention), WHO and FAO should be taken into consideration.

[General Principles to Minimize and Contain Antimicrobial Resistance]

27. Most Members and Observers supported the proposal to develop General Principles to promote coherence with GL77 and to highlight important elements to minimize and contain antimicrobial resistance. Several Members and Observers provided suggested revisions and new General Principles.

28. The Chairs modified the General Principles taking into account comments and added General Principles where new concepts were proposed or moved from other areas of the text.

Rationale: Revisions to the General Principles provide clarity and more detail. Additional General Principles help address a more broad scope and may include valuable concepts.

Responsibilities of the Regulatory Authorities

29. Many Members and Observers supported the proposal to reference OIE Terrestrial Animal Health Code Chapter 6.9 and Aquatic Animal Health Code Chapter 6.2 to avoid duplication and the potential for ambiguity as the chapters are updated and revised. Members and Observers identified certain sections of text to be retained and sometimes provided condensed summaries of key concepts to retain.

30. The Chairs adopted summaries of key concepts and provided a reference to relevant sections of the OIE Aquatic and Terrestrial Animal Health Codes, Paragraphs. The Chairs identified some sections of text for potential deletion by the TFAMR, Para 10-11, 13-16, and 18-34, as being duplicative of the OIE Terrestrial Animal Health Code Chapter 6.9.3. The Chairs modified some text to make it applicable across sectors. The Chairs included additional paragraphs based on suggestions of new concepts by Members and Observers.

31. Most Members and Observers supported referencing the OIE Terrestrial and Aquatic Animal Health Codes for sections dealing with the registration of veterinary antimicrobials. Many members and Observers suggested retaining the section on surveillance programs and including a reference to the new proposed draft Codex guidelines on integrated surveillance of antimicrobial resistance along with reference to existing texts on surveillance found in the OIE Codes and WHO AGISAR. Several Members and Observers suggested the sections on pharmacovigilance could also reference the OIE Chapters and therefore be proposed for deletion, however there *were some* Members that seemed to indicate pharmacovigilance should be retained. Further discussion on the value of retaining pharmacovigilance could be beneficial.

Rationale: Streamlining the content of this section while retaining key concepts will avoid duplication and prevent ambiguity with the OIE Terrestrial and Aquatic Animal Health Codes. Modifying text to be applicable across sectors will broaden the scope of the guidance. Adding new concepts and detail will increase the value of the section.

Responsibilities of the Veterinary Pharmaceutical Industry/[Responsibilities of Manufacturers]

32. Several Members and Observers provided suggestions for minor editing of this section.

33. The Chairs modified some text to make it applicable across sectors and made small changes based on suggestions of Members and Observers.

Rationale: Modifying text to be applicable across sectors will broaden the scope of the guidance.

Responsibilities of Wholesale and Retail Distributors

34. Several Members and Observers provided suggestions for minor editing of this section.

35. The Chairs modified some text to make it applicable across sectors and made small changes based on suggestions of Members and Observers.

Rationale: Modifying text to be applicable across sectors will broaden the scope of the guidance.

Responsibilities of Veterinarians [and Plant Health Professionals]

36. Members and Observers supported the proposal to reference OIE Terrestrial Animal Health Code Chapter 6.9.6 and Aquatic Animal Health Code Chapter 6.2 to avoid duplication and the potential for ambiguity as the chapters are updated and revised. Members and Observers identified certain sections of text to be proposed for deletion.

37. The Chairs identified some sections of text for potential deletion by the TFAMR, Para 48, 53. The Chairs modified some text to make it applicable across sectors. The Chairs included additional paragraphs based on suggestions of new concepts by Members and Observers.

Rationale: Streamlining the content of this section while retaining key concepts will avoid duplication and prevent ambiguity with the OIE Terrestrial and Aquatic Animal Health Codes. Modifying text to be applicable across sectors will broaden the scope of the guidance. Adding new concepts and detail will increase the value of the section.

Responsibilities of Producers

38. Members and Observers supported the proposal to reference OIE Terrestrial Animal Health Code Chapter 6.9.7 and Aquatic Animal Health Code Chapter 6.2 to avoid duplication and the potential for ambiguity as the chapters are updated and revised.

39. The Chairs modified some text to make it applicable across sectors. The Chairs included additional paragraphs based on suggestions of new concepts by Members and Observers.

Rationale: Modifying text to be applicable across sectors will broaden the scope of the guidance. Adding new concepts and detail will increase the value of the section.

[Responsibilities of Consumers]

40. Some Members and Observers provided new content for this area.

41. The Chairs added the new content in square brackets for further comment and consideration by the TFAMR making small revisions for consistency and clarity.

[Advocacy and Communication]

42. A Member proposed a new section on Advocacy and Communication.

43. The Chairs included the new section in square brackets with minor revisions to broaden the scope in line with the other sections.

Rationale: The proposed new section introduced a concept not currently contained in the draft document.

Conclusions

44. Some Members and Observers commented that concepts in the Conclusions should be retained, while others indicated they could be proposed for deletion.

45. The Chairs proposed Para 60 and 62 for potential deletion. The Chairs moved Para 61 to General Principle 11.

Rationale: Concepts in Para 60 and 62 are contained in the preceding text. The concept in Para 61 was not covered elsewhere and was considered to be important for overall implementation of the Code of Practice.

End Notes

46. Few Members and Observers commented on these references.

47. The Chairs proposed the references for deletion.

Rationale: While the references may still contain relevant material, they are likely to be among many other references that could be accessed as part of a library on antimicrobial resistance.

List of Abbreviations Used in This Code

48. Most Members and Observers concurred with the inclusion of abbreviations/acronyms in the Code of Practice. Many concurred with the proposal to move them to the beginning of the text following the structure of GL77.

49. The Chairs moved the section to the beginning of the document. The final list of abbreviations/acronyms should be reviewed after the final content of the text is developed.

Rationale: The use of abbreviations/acronyms can improve the efficiency of the text, however they should be clearly stated and used consistently.

Glossary of Definitions and Terms

50. Fewer Members and Observers commented on the definitions at the end of the text. Most agreed with the proposal to list them earlier in the text following the structure of GL77. The definition of growth promotion seemed to have more consensus than the other definitions. Some Members preferred to retain the current definitions.

51. The Chairs moved the definition of Growth Promotion to the preceding section on Definitions. The Chairs proposed for deletion the definitions of Veterinary Antimicrobial Drug noting a similar definition included above taken from GL77. The Chairs proposed for deletion the definitions of Disease Treatment/Therapeutic Use and Disease Prevention/Prophylactic Use noting that similar definitions are included above. Substantial comments were received on definitions and this is an area for further comments and discussion by the TFAMR.

Rationale: Definitions promote common understanding of concepts in the Code of Practice and promote coherence with other Codex texts and standards.

Conclusions

52. Members and Observers generally agreed the Code of Practice should be revised by broadening its scope, and developing risk-based guidance on the management of foodborne antimicrobial resistance that addresses the entire food chain, in line with the mandate of Codex.

53. Members and Observers generally agreed that the structure of the revised Code of Practice should follow that of GL77, including Introduction, Scope, Definitions, General Principles.

54. Members and Observers generally agreed portions of the existing text continued to have value and should be retained; while some sections relating primarily to specifics around a veterinary medicines dossier for food-producing animals could be deleted as they are duplicated in the OIE Aquatic and Terrestrial Animal Health Codes.

55. Members and Observers supported the addition of new text providing additional risk-based guidance and new sections describing the responsibilities or additional actors in the food supply chain.

Recommendations

56. The TFAMR should consider the adoption of new text and text proposed for deletion as contained in Proposed Draft Revision of the Code of Practice to Minimize and Contain Antimicrobial Resistance, Appendix I.

57. The TFAMR should consider the range of actors that could reasonably be included in the Code of Practice taking into account numerous participants in the food chain, as described in Paragraph 13 above.

58. The TFAMR should consider the Definitions presented to ensure they are relevant to the Code of Practice, aligned with other Codex texts, based on current scientific knowledge, and take into account advancement in antimicrobial resistance risk analysis.

59. The TFAMR should consider the General Principles to ensure they contain those principles related to the content of the chapter and avoid unnecessary duplication with other Codex texts or references.

60. To evaluate proposed new text and to further develop risk-based guidance for the Code of Practice, the TFAMR should consider updated scientific information on important factors influencing foodborne AMR, taking into consideration animals, crops, environment, and also manure, biocides, waste and packaging, production systems and practices (including animal husbandry of nomadic herds and ethno-veterinary use of plants), food processing, retail handling and consumption.

Appendix I

PROPOSED DRAFT REVISION OF THE *CODE OF PRACTICE TO MINIMIZE AND CONTAIN ANTIMICROBIAL RESISTANC*E (CAC/RCP 61-2005)

(for comments at Step 3 through CL 2017/83-AMR)

This document contains contributions from Codex Members and Observers, including potential areas of consensus, identified in the Electronic Working Group (EWG) held 26 July to 31 August 2017. New and revised text in [square brackets] is proposed for further comment and potential adoption at TFAMR5. Similarly, the working group identified potential consensus around existing text that could be deleted. All text proposed for replacement or deletion is accordingly noted by ~~strikethrough~~ for further comment and consideration at TFAMR5.

Table of Contents

[List of Acronyms Used in the Document]

ADI	Acceptable Daily Intake
AMR	Antimicrobial Resistance
AMU	Antimicrobial Use
CAC	Codex Alimentarius Commission
CAC/RCP	Codex Alimentarius Commission/Recommended Code of Practice
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Foods
FAO	Food and Agriculture Organization of the United Nations
MRL	Maximum Residue Limit
OIE	Office International des epizooties/International Office of Epizooties, World Organisation for Animal Health
VICH	International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products
VMP	Veterinary Medicinal Product
WHO	World Health Organization

Introduction

[1. Antimicrobial resistance poses a complex, global public health challenge. Within the food production to consumption continuum, there is a need to address the selection and dissemination of resistant microorganisms and resistance determinants. The development of strategies for good practices in agriculture (crops), aquaculture and animal husbandry including the responsible and prudent use of antimicrobials in all sectors following a One Health approach will form a key part of multi-sectoral national action plans to address risks of foodborne antimicrobial resistance.]

[2. 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 *Proposed Draft Guidelines on Integrated Surveillance (CAC/GL xx-xxxx)* and Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance CAC/GL 77-2011. In addition, the Codex Code of Hygienic Practice for Fresh Fruits and Vegetables (CAC/RCP 53-2003) and the Code of Practice on Good Animal Feeding (CAC/RCP 54-2004), and Principles and Guidelines for the Conduct of Microbiological Risk Management (CAC/GL 63-2007) are particularly relevant for use of agricultural chemicals on crops and animal feed, respectively. WHO guidelines on Integrated surveillance of antimicrobial resistance in foodborne bacteria, Application of a One Health Approach (2017) and Critically Important Antimicrobials for Human Medicine (2016) and relevant chapters of the OIE Terrestrial and Aquatic Animal Health Codes and the List of Antimicrobials of Veterinary Importance should also be referenced.]

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

~~1.~~ [4.] This document provides ~~additional~~ guidance ~~for~~ [on relevant measures along the food chain to minimize the development and spread of foodborne antimicrobial resistance, including guidance on] the responsible and prudent use of antimicrobials in [the] food [chain]~~-producing animals, and should be read in conjunction with the Recommended International Code of Practice for Control of the Use of Veterinary Drugs CAC/RCP 38-1993~~. It's objectives are [part of a One Health approach] to minimize the potential adverse impact on public [and animal] health resulting from the use of antimicrobial agents in [the] food [chain]~~-producing animals~~, in particular the development of antimicrobial resistance. It is also important to provide for the safe and effective use of ~~veterinary~~ antimicrobial [agents]~~drugs in veterinary medicine~~ by maintaining their efficacy. This document defines the respective responsibilities of authorities and ~~groups~~[relevant stakeholders] involved in the authorization, production, control, distribution and use of ~~veterinary~~ antimicrobials such as the national regulatory authorities, ~~the veterinary pharmaceutical industry~~[manufacturers], veterinarians [and plant health professionals], [wholesale and retail] distributors[,] ~~and~~ [food] producers[, and consumers] ~~of food-producing animals~~.

~~2.~~ [5.] The marketing authorization procedure has a significant role in establishing the basis for [the responsible and] prudent use of ~~veterinary~~ antimicrobial ~~drugs~~ [agents] ~~in food-producing animals~~ through clear label indications, directions and warning statements.

~~3. A number of codes of practice relating to the use of veterinary antimicrobial drugs and the conditions thereof have been developed by different organisations. These codes were taken into consideration and some elements were included in the elaboration of this Code of Practice to Minimize and Contain Antimicrobial Resistance.~~

~~4.~~ [6.] In keeping with the Codex mission, this Code [of Practice] focuses on antimicrobial use in [the] food~~-producing animals~~[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, the use of authorized products and best practices in the production sector should be followed to minimize the risks associated with the selection and dissemination of resistant microorganisms and determinants.] ~~antimicrobial resistance is also an ecological problem and that management of antimicrobial resistance may require addressing the persistence of resistant microorganisms in the environment. Although this issue is most relevant for CCRVDF with respect to food-producing animals, the same principles apply to companion animals, which also harbor resistant microorganisms.~~

[Scope]

[7. This Code of Practice addresses the risk to human health associated with the presence in food and animal feed, and the transmission through food and animal feed, of antimicrobial resistant microorganisms or determinants. It provides [risk-based] guidance on relevant measures along the food chain to minimize the development and spread of foodborne antimicrobial resistance, including guidance on good practices in agriculture (crops) and animal husbandry and guidance on the responsible and prudent use of antimicrobial agents in agriculture (crops), animal husbandry, and aquaculture. Its objectives are to minimise the potential adverse impact on public health resulting from the use of antimicrobial agents. All actors involved in the authorisation, manufacture, sale and supply, prescription and use of antimicrobials in the food chain together with those involved in the handling, preparation, distribution and consumption of food have a role to play in optimizing the use of antimicrobials and limiting the spread of resistant microorganisms and determinants.]

[8. 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 and recombinant DNA microorganisms[1]; nongenetically modified microorganisms (for example, starter cultures) intentionally added to food with a technological purpose[2]; and certain food ingredients, which could potentially carry AMR genes, such as probiotics[3].]

~~**1. Aims and Objectives**~~

~~5. It is imperative that all who are involved in the authorisation, manufacture, sale and supply, prescription and use of antimicrobials in food-producing animals act legally, responsibly and with the utmost care in order to limit the spread of resistant microorganisms among animals so as to protect the health of consumers.~~

~~6. Antimicrobial drugs are powerful tools for the management of infectious diseases in animals and humans. This Code and existing guidelines for the responsible use of antimicrobial drugs in food- producing animals include recommendations intended to prevent or reduce the selection of antimicrobial resistant microorganisms in animals and humans in order to:~~

- ~~Protect consumer health by ensuring the safety of food of animal origin intended for human consumption.~~
- ~~Prevent or reduce as far as possible the direct and indirect transfer of resistant microorganisms or resistance determinants within animal populations and from food- producing animals to humans.~~
- ~~Prevent the contamination of animal derived food with antimicrobial residues which exceed the established MRL.~~
- ~~Comply with the ethical obligation and economic need to maintain animal health.~~

~~7. This Code does not address environmental issues related to antimicrobial resistance from the use of veterinary antimicrobial drugs but it encourages all those involved to consider the ecological aspects when implementing the Code. Efforts should be made to ensure that environmental reservoirs of veterinary antimicrobial drugs, antimicrobial resistant organisms and resistance determinants are kept to a minimum. In particular:~~

- ~~Regulatory authorities should assess the impact of proposed veterinary antimicrobial drug use on the environment in accordance with national guidelines or recognized international guidelines[4]~~
- ~~Research should be conducted on resistant microorganisms in the environment and the magnitude of resistance determinant transfer among microorganisms in the environment.~~

~~8. The responsible use of veterinary antimicrobial drugs in food-producing animals:~~

- ~~is controlled by the veterinary profession or other parties with the required expertise.~~
- ~~is part of good veterinary and good animal husbandry practice and takes into consideration disease prevention practices such as the use of vaccination and improvements in husbandry conditions.~~

[1] [The food safety assessment on the use of antimicrobial resistance marker genes in recombinant-DNA plants is addressed in the *Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants* (CAC/GL 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* (CAC/GL 46-2003).]

[3] [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).]

[4] ~~VICH (2000). Guidelines on Environmental Impact Assessment for Veterinary Medicinal Products, Phase I. http://vich.eudra.org/pdf/2000/Gl06_st7.pdf~~

- ~~aims to limit the use of veterinary antimicrobial drugs according to their approved and intended uses, and takes into consideration on-farm sampling and testing of isolates from food-producing animals during their production, where appropriate, and makes adjustments to treatment when problems become evident.~~
- ~~should be based on the results of resistance surveillance and monitoring (microbial cultures and antimicrobial sensitivity testing), as well as clinical experience.~~
- ~~does not include the use for growth promotion of veterinary antimicrobial drugs that belong to or are able to cause cross resistance to classes of antimicrobial agents used (or submitted for approval) in humans 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.~~
    - ~~focus on the potential to impact resistance to antimicrobials used in human medicine.~~
- ~~is aimed at all the relevant parties, such as:~~
    - ~~regulatory and scientific authorities;~~
    - ~~the veterinary pharmaceutical industry;~~
    - ~~distributors and others handling veterinary antimicrobial drugs;~~
    - ~~veterinarians, pharmacists and producers of food-producing animals.~~

[Definitions]

[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, 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.]

[Antibiotic: A naturally derived substance 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.]

[Antibacterial: A substance that acts against bacteria.]

[Medically important antimicrobials: Antimicrobial agents important for therapeutic use in humans.]

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

[Treatment of disease: Administration of antimicrobial agents to infected individuals or populations to resolve clinical signs, infection or illness.]

[Control of disease/metaphylaxis: Administration of antimicrobial agents to populations which contain healthy and infected individuals to minimize or resolve clinical signs, infection or illness.]

[Prevention of disease/prophylaxis: Administration of antimicrobial agents to healthy individuals or a population at risk of a specific disease, prior to the onset, with appropriate oversight, dose, and duration.]

Growth promotion: Administration of antimicrobial agents to increase the rate of weight gain and/or the efficiency of feed utilization in animals by other than purely nutritional means. The term does NOT apply to the use of antimicrobials for the specific purpose of treating, controlling, or preventing infectious diseases, even when an incidental growth response may be obtained.

[**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.]

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

[**One Health:** 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 people, animals, plants, and their shared environment.]

[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 AMR risk management options.]

[Principle 2: Biosecurity, adequate nutrition, vaccination, improved production practices, and alternatives to antimicrobial agents[5] should be considered to reduce the need for use of antimicrobial agents.]

[Principle 3: 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 reducing the risk of foodborne antimicrobial resistance. Such guidelines could be included as a part of national action plans on antimicrobial resistance with development and dissemination shared among countries and organisations.]

[Principle 4: The WHO list of Critically Important Antimicrobials, the OIE List of Antimicrobials of Veterinary Importance, and national lists, where available, should be used to set priorities for risk assessment and risk management. The lists should be regularly updated.]

[Principle 5: Responsible and prudent administration in food-producing animals does not include the use for growth promotion of antimicrobial drugs that are considered medically important or are able to cause cross resistance to other antimicrobial drugs, or classes of antimicrobial drugs, 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 publically 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 ~~(e.g. skeletal marking in fish)~~.]

[Principle 7: Antimicrobial agents should only be used in well-defined circumstances for the prevention of a specific disease and follow appropriate oversight, dose, and duration.]

[Principle 8: Only legally authorized antimicrobial agents should be used and all applicable label directions should be followed; 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 CAC/GL77. 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 determinants are among the critical factors to consider when evaluating and determining the effectiveness of implemented risk management measures. Use of medically important antimicrobial drugs in humans and animals, and transmission of pathogens and resistance genes between humans, animals, and the environment are additional factors to consider.]

[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 situation/capacities, and within a reasonable period of time. A stepwise approach may utilized by some countries to properly implement all of the elements in this document.]

[Principle 12: Medically important antimicrobials should be administered or applied only by veterinarians, plant health professionals or other suitably trained person 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 administration when problems become evident.]

[5] [Could include ethnoveterinary approaches, e.g. herbal medicine.]

[**Principle 14:** Administration of antimicrobial agents should be based on sound clinical judgement and where feasible on the results of integrated resistance surveillance and monitoring (bacterial cultures and antimicrobial susceptibility testing), as well as relevant experience.]

[**Principle 15:** The reduce, replace and rethink (RRR) strategy 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 as from a public health perspective.]

Responsibilities of the Regulatory Authorities

9. The national regulatory authorities, which are responsible for granting the marketing authorisation for antimicrobials for use in ~~food-producing animals~~[the food chain], have a significant role in specifying the terms of this authorisation and in providing the appropriate information to the veterinarian [and plant health professionals] through product labelling and/or by other means, in support of [the responsible and] prudent use of ~~veterinary~~ antimicrobial ~~drugs~~[agents] in ~~food-producing animals~~ [the food chain]. It is the responsibility of regulatory authorities to develop up-to-date guidelines on data requirements for evaluation of ~~veterinary~~ antimicrobial ~~drug~~[agent] applications. National governments in cooperation with animal [plant,] and public health professionals should adopt a ~~proactive~~[One Health] approach to promote [the responsible and] prudent use of antimicrobials in ~~food-producing animals~~[the food chain] as an element of a national strategy for the containment of antimicrobial resistance. Other elements of the national strategy should include good animal husbandry [and production] practices, vaccination [and biosecurity] policies and development of animal [and plant] health care at the farm level, all of which should contribute to reduce the prevalence of animal [and plant] disease requiring antimicrobial treatment. ~~Use of veterinary antimicrobial drugs for growth promotion that belong to classes of antimicrobial agents used (or submitted for approval) in humans and animals should be terminated or phased out in the absence of risk analysis, as described in Paragraph 8~~.

~~10. It is the responsibility of the pharmaceutical company or sponsor[6] to submit the data requested by the regulatory authorities for granting marketing authorisation.~~

~~11. The use of antimicrobial agents in food-producing animals requires a marketing authorisation, granted by the competent authorities when the criteria of safety, quality and efficacy are met.~~

- ~~The examination of dossiers/drug applications should include an assessment of the risks to both animals and humans resulting from the use of antimicrobial agents in food- producing animals. The evaluation should focus on each individual veterinary antimicrobial drug but take into consideration the class of antimicrobials to which the particular active principle belongs.~~
- ~~The safety evaluation should include consideration of the potential impact of the proposed use in food-producing animals on human health, including the human health impact of antimicrobial resistance developing in microorganisms found in food- producing animals and their environment associated with the use of veterinary antimicrobial drugs.~~

~~12.~~ [10.]. If dose ranges or different durations of treatment are indicated, the national authorities should give guidance on the approved product labelling regarding the conditions that will minimize the development of resistance, when this information is available.

[11. For more information on antimicrobial drugs for food-producing animals see the OIE Aquatic Animal Health Code Chapter 6.2.4- Responsibilities of competent authorities and Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 1. Marketing authorization.]

~~13. The relevant authorities should make sure that all the antimicrobial agents used in food- producing animals are prescribed by a veterinarian or other suitably trained person authorized in accordance with national legislation or used under conditions stipulated in the national legislation. (See OIE Guidelines for Antimicrobial Resistance: Responsible and Prudent Use of Antimicrobial Agents in Veterinary Medicine (Terrestrial Animal Health Code, Appendix 3.9.3)~~

~~14. No veterinary antimicrobial drug should be administered to animals unless it has been evaluated and authorized for such use by the relevant authorities or the use is allowed through off-label guidance or legislation. Regulatory authorities should, where possible, expedite the market approval process of new veterinary antimicrobial drug formulations considered to have the potential to make an important contribution in the control of antimicrobial resistance.~~

~~[6] As defined in the VICH Good Clinical Practice Guideline, http://vich.eudra.org/pdf/2000/GI09_st7.pdf~~

~~15. Countries without the necessary resources to implement an efficient authorisation procedure for veterinary antimicrobial drugs and whose supply of veterinary antimicrobial drugs mostly depends on imports from foreign countries should:~~

- ~~ensure the efficacy of their administrative controls on the import of these veterinary antimicrobial drugs,~~
- ~~seek information on authorizations valid in other countries, and~~
- ~~develop the necessary technical cooperation with experienced authorities to check the quality of imported veterinary antimicrobial drugs as well as the validity of the recommended conditions of use. Alternatively, a national authority could delegate a competent institution to provide quality certification of veterinary antimicrobial drugs.~~

~~16. All countries should make every effort to actively combat the manufacture, advertisement, trade, distribution and use of illegal and/or counterfeit bulk active pharmaceutical ingredients and products. Regulatory authorities of importing countries could request the pharmaceutical industry to provide quality certificates or, where feasible, certificates of Good Manufacturing Practices prepared by the exporting country's national regulatory authority.~~

QUALITY CONTROL OF ANTIMICROBIAL AGENTS

~~17.~~[12. 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.~~, in particular:~~

- ~~to ensure that the quality and concentration (stability) of veterinary antimicrobial drugs in the marketed dosage form(s) is maintained and properly stored up to the expiry date, established under the recommended storage conditions.~~
- ~~to ensure the stability of veterinary antimicrobial drugs when they are mixed with feed or drinking water.~~
- ~~to ensure that all veterinary antimicrobial drugs are manufactured to the appropriate quality and purity.~~

[13. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 2. Quality control of antimicrobial agents and VMP containing medically important antimicrobial agents.]

ASSESSMENT OF EFFICACY

[14. Assessment of efficacy is important to assure adequate response to the administration of antimicrobials.]

[15. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 3. Assessment of therapeutic efficacy.]

~~18. Preclinical data should be generated to establish an appropriate dosage regimen necessary to ensure the efficacy of the veterinary antimicrobial drug and limit the selection of microbial resistant microorganisms. Such preclinical trials should, where applicable, include pharmacokinetic and pharmacodynamic studies to guide the development of the most appropriate dosage regimen.~~

~~19. Important pharmacodynamic information may include:~~

- ~~mode of action;~~
- ~~the spectrum of antimicrobial activity of the substance;~~
- ~~identification of bacterial species that are naturally resistant relevant to the use of the veterinary antimicrobial drugs;~~
- ~~antimicrobial minimum inhibitory and/or bactericidal concentrations;~~
- ~~determination of whether the antimicrobial exhibits time or concentration-dependent activity or co-dependency,~~
- ~~evaluation of activity at the site of infection.~~

~~20. Important pharmacokinetic information may include:~~

- ~~bio-availability according to the route of administration;~~
- ~~concentration of the veterinary antimicrobial drug at the site of infection and its distribution in the treated animal;~~
- ~~metabolism which may lead to the inactivation of veterinary antimicrobial drugs;~~

- excretion routes.

21. The use of fixed combinations of veterinary antimicrobial drugs should be justified taking into account:

- pharmacodynamic (additive or synergistic effects towards the target microorganism);
- pharmacokinetics (maintenance of the concentrations of associated antimicrobials responsible for additive or synergistic effects at the site of infection throughout the treatment period).

22. Clinical data should be generated to confirm the validity of the claimed indications and dosage regimens established during the preclinical phase.

23. Criteria to be considered include:

- parameters for qualitatively and quantitatively assessing efficacy;
- diversity of the clinical cases met when carrying out clinical trials;
- compliance of the protocols of clinical trials with good clinical practice, such as VICH guidelines[7];
- eligibility of the studied clinical cases based on appropriate clinical and microbiological criteria.

ASSESSMENT OF THE POTENTIAL OF VETERINARY ANTIMICROBIAL DRUGS[AGENTS] TO SELECT FOR RESISTANT MICROORGANISMS

[16. The competent authority should assess the potential of medically important antimicrobial drugs to select for resistant microorganisms taking into account CAC/GL77.]

[17. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 4. Assessment of the potential of antimicrobial agents to select for resistance and Chapter 6.10 Risk Analysis for Antimicrobial Resistance Arising from the Use of Antimicrobial Agents in Animals.]

24. Where applicable, data from preclinical or clinical trials should be used to evaluate the potential for target microorganisms, foodborne and/or commensal microorganisms to develop or acquire resistance.

25. Appropriate information should be provided to support an adequate assessment of the safety of veterinary antimicrobial drugs being considered for authorisation in food-producing animals. The regulatory authorities should develop criteria for conducting such assessments and interpreting their results. Existing guidelines for antimicrobial resistance risk assessment, such as the OIE Guideline[8] may be used for more comprehensive information. The type of information to be evaluated in these assessments may include, but is not limited to, the following:

- the route and level of human exposure to food-borne or other resistant microorganisms;
- the degree of cross resistance within the class of antimicrobials and between classes of antimicrobials;
- the pre-existing level of resistance, if available, in pathogens causing gastrointestinal infections in humans (baseline determination);
- the concentration of active compound in the gut of the animal at the defined dosage level.

ESTABLISHMENT OF ADIS (ACCEPTABLE DAILY INTAKE), MRLS (MAXIMUM RESIDUE LIMIT), AND WITHDRAWAL PERIODS FOR VETERINARY ANTIMICROBIAL DRUGS

26. When setting ADIs and MRLs for veterinary antimicrobial drugs, the safety evaluation is carried out in accordance with international guidelines and should include the determination of microbiological effects (e.g., the potential biological effects on the human intestinal flora) as well as toxicological and pharmacological effects.

27. An acceptable daily intake (ADI) and a maximum residue limit (MRL) for appropriate food stuffs (i.e., meat, milk, eggs, fish and honey) should be established for each antimicrobial agent. MRLs are necessary in order that officially recognised control laboratories can monitor that the veterinary antimicrobial drugs are being used as approved. Withdrawal periods should be established for each veterinary antimicrobial drug, which make it possible to produce food in compliance with the MRLs.

[7] VICH Good Clinical Practice Guideline , http://vich.eudra.org/pdf/2000/GI09_st7.pdf

[8] Antimicrobial resistance: risk analysis methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin, http://www.oie.int/eng/publicat/rt/2003a_r20314.htm

~~28. Withdrawal periods have to be established for each veterinary antimicrobial drug by taking into account:~~

- ~~the MRLs established for the considered veterinary antimicrobial drug;~~
- ~~the pharmaceutical form;~~
- ~~the target animal species;~~
- ~~the dosage regimen and the duration of treatment;~~
- ~~the route of administration.~~

[ASSESSMENT OF ENVIRONMENTAL IMPACT]

[18. Regulatory authorities should assess the impact of proposed ~~veterinary~~ antimicrobial ~~drug~~[agent~~]~~ use on the environment in accordance with national guidelines or recognized international guidelines.]

[19. For more information on antimicrobial drugs for food-producing animals see the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products guidelines[9].]

[20. Regulatory authorities should consider the environmental aspects of AMR (e.g. pollution from pharmaceutical manufacture, impacts of reusing waste water for irrigation and using manure for soil fertilization, harmonized monitoring and establishment of maximum admissible levels, etc.]

ESTABLISHMENT OF A SUMMARY OF PRODUCT CHARACTERISTICS FOR EACH VETERINARY ANTIMICROBIAL DRUG FOR FOOD-PRODUCING ANIMALS

[21. Regulatory authorities should establish a Summary of Product Characteristics that can be utilized in labelling and as a package insert.]

[22. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 7. Establishment of a summary of product characteristics for each VMP containing antimicrobial agents.]

~~29. The summary of product characteristics contains the information necessary for the appropriate use of veterinary antimicrobial drugs. It constitutes, for each veterinary antimicrobial drug, the official reference of the content of its labelling and package insert. This summary contains the following items:~~

- ~~pharmacological properties;~~
- ~~target animal species;~~
- ~~indications;~~
- ~~target microorganisms;~~
- ~~dosage and administration route;~~
- ~~withdrawal periods;~~
- ~~incompatibilities;~~
- ~~shelf-life;~~
- ~~operator safety;~~
- ~~particular precautions before use;~~
- ~~instructions for the return or proper disposal of un-used or out-of-date products;~~
- ~~any information on conditions of use relevant to the potential for selection of resistance should be included, for the purpose of guidance on prudent use;~~
- ~~class and active ingredient of the veterinary antimicrobial drug.~~

[9] [VICH (2000). Guidelines on Environmental Impact Assessment for Veterinary Medicinal Products, Phase I. http://vich.eudra.org/pdf/2000/Gl06_st7.pdf]

SURVEILLANCE PROGRAMMES

[23. Regulatory authorities should establish systems for the surveillance and monitoring of antimicrobial resistance and antimicrobial use following the Codex *Proposed Draft Guidelines on Integrated Surveillance (CAC/GL xx-xxxx)*, taking into consideration relevant sections of Guidelines for Foodborne Antimicrobial Resistance CAC/GL 77-2011; WHO guidelines on Integrated surveillance of antimicrobial resistance in foodborne bacteria, Application of a One Health Approach (2017); and OIE Terrestrial Animal Health Code Chapter 6.7 Harmonisation 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.]

[24. The surveillance and monitoring of antibiotic resistant bacteria in different production sectors and in different products is necessary for understanding the development and dissemination of antibiotic resistance, providing relevant risk assessment data, and assessing the effectiveness of interventions. Surveillance programmes involve specific and continuous data collection, analysis and reporting that quantitatively monitor temporal trends in the occurrence and distribution of resistance to antibiotics; it also allows the identification of emerging or specific patterns.]

~~30. The relevant authorities should develop a structured approach to the investigation and reporting of the incidence and prevalence of antimicrobial resistance. For the purposes of this Code, priority should be given to the evaluation of antimicrobial resistance in foodborne microorganisms.~~

~~For reasons of efficiency, the methods used to establish such programmes (laboratory techniques, sampling, choice of veterinary antimicrobial drug(s) and microorganism(s)) should be harmonized as much as possible at the international level (e.g. OIE documents on "Harmonisation of National Antimicrobial Resistance Monitoring and Surveillance Programmes in Animals and Animal Derived Food" http://www.oie.int/eng/publicat/rt/2003/a_r20318.htm and "Standardisation and Harmonisation of Laboratory Methodologies Used for the Detection and Quantification of Antimicrobial Resistance" http://www.oie.int/eng/publicat/rt/2003/a_r20317.htm).~~

~~31. Preferably, epidemiological surveillance of antimicrobial resistance should be accompanied by data on the amounts of veterinary antimicrobial drugs used by veterinarians and other authorized users in food-producing animals. These data could be collected using one or more of the following sources:~~

- ~~production data from manufacturers;~~
- ~~importers and exporters;~~
- ~~if possible, data on intended and actual usage from manufacturers, wholesale and retail distributors including feed mills, and veterinary prescription records;~~
- ~~surveys of veterinarians, farmers and producers of food-producing animals.~~
- ~~32. Regulatory authorities should have in place a pharmacovigilance programme 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 programme should form part of the comprehensive strategy to minimize microbial resistance.~~

~~33. 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 endeavour to achieve this re-evaluation~~.

DISTRIBUTION OF ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~[AGENTS] ~~IN VETERINARY MEDICINE~~

[25. 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 veterinarians, plant health professionals, or other suitably trained person authorized in accordance with national legislation.]

[26. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 9. Supply and administration of the VMP containing antimicrobial agents.]

~~34. The relevant authorities should make sure that all veterinary antimicrobial drugs used in food- producing animals are, to the extent possible:~~

- ~~prescribed by a veterinarian or other suitably trained person authorized in accordance with national legislation or used under conditions stipulated in the national legislation;~~
- ~~supplied only through licensed/authorized distribution systems;~~

- ~~administered to animals by a veterinarian or, under the supervision of a veterinarian or other suitably trained person authorized in accordance with national legislation; and that~~
- ~~proper records are kept of their administration (see Paragraph 58, Responsibilities of Veterinarians: Recording section).~~

[27. Where distribution and use are regularly controlled by the competent authorities, targeted checks could be carried out, where appropriate, on prescribers with high levels or concerning patterns of prescriptions.]

CONTROL OF ADVERTISING

[28. Regulatory authorities should assure that advertising of antimicrobial agents is done in accordance national legislation.]

[29. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 10. Control of advertising.]

~~35.~~[30.] Advertising of ~~veterinary~~ antimicrobial ~~drugs~~[agents] should be done in a manner consistent with prudent use guidelines and any other specific regulatory recommendation for the product.

All advertising of ~~veterinary~~ antimicrobial ~~drugs~~[agents] should be controlled by the relevant authorities.

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

TRAINING OF USERS OF ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~[AGENTS]

~~36.~~[31.] ~~Training should be undertaken to assure the safety to the consumer of animal derived food and therefore the protection of public health.~~ Training should involve all the relevant professional organisations, regulatory authorities, ~~the pharmaceutical industry~~[marketing authorization holders], ~~veterinary~~ schools, research institutes, professional associations[, trade associations] and other approved users such as farmers and producers ~~of food animals~~ and should focus on:

- information on disease prevention and management strategies to reduce the need to use ~~veterinary~~ antimicrobial ~~drugs~~[agents];
- relevant ~~pharmacokinetic and pharmacodynamic~~ information to enable the veterinarian [and plant health professionals] to use ~~veterinary~~ antimicrobial ~~drugs~~[agents] prudently;
- the ability of ~~veterinary~~ antimicrobial ~~drugs~~[agents] to select for resistant microorganisms ~~in food-producing animals~~ that may contribute to animal[, plant] or human health problems; and
- the need to observe responsible use recommendations and using ~~veterinary~~ antimicrobial ~~drugs~~[agents] in ~~animal husbandry~~[production settings] in agreement with the provisions of the marketing authorisations and ~~veterinary~~[professional] advice.

[32. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 11. Training on the usage of antimicrobial agents.]

DEVELOPMENT OF RESEARCH

~~37.~~[33.] The relevant authorities should encourage public and private research to:

- improve the knowledge about the mechanisms of action of antimicrobials in order to optimise the dosage regimens and their efficacy;
- improve the knowledge about the mechanisms of selection, emergence and dissemination of resistance determinants;
- 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 authorisation process, the impact of the proposed use of the ~~veterinary~~ antimicrobial ~~drugs~~[agents] on the rate and extent of resistance development; and
- develop and encourage [good animal husbandry practices and] alternative methods to prevent [and treat] infectious diseases [that would reduce the need to use antimicrobials]

- [develop alternatives to antimicrobials, new antimicrobials, rapid diagnostics, and vaccines, including autogenous vaccines.]
- [determine the potential transfer to fresh produce and other crops of resistant microorganisms and determinants from animal manures used as fertilizer.]

[34. Research should be conducted, as resources permit, on AMR microorganisms in the environment, and if feasible, factors affecting and the magnitude of resistance determinant transfer among microorganisms in the environment.]

COLLECTION AND DESTRUCTION OF ~~UNUSED~~ [OUT-OF-DATE] ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~[AGENTS]

~~38.~~[35. The relevant authorities should develop effective [and compulsory] procedures for the safe collection and destruction of unused or out-of-date ~~veterinary~~ antimicrobial ~~drugs~~[agents].

Responsibilities of ~~the Veterinary Pharmaceutical Industry~~[Manufacturers]

MARKETING AUTHORISATION OF ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~ [AGENTS] ~~FOR FOOD-PRODUCING ANIMALS~~

~~39.~~[36. It is the responsibility of the ~~veterinary pharmaceutical industry~~ antimicrobial agent marketing authorization holders:

- to supply all of the information requested by the national regulatory authority in order to establish objectively the quality, safety and efficacy of ~~veterinary~~ antimicrobial ~~drugs~~[agents]; and
- to ensure the quality of this information on the basis of 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 ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~[AGENTS]

~~40.~~[37.] Only officially licensed/authorized ~~veterinary~~ antimicrobial ~~drugs~~[agents] should be marketed, and then only through approved distribution systems.

- Only ~~veterinary~~ antimicrobial ~~drugs~~[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 ~~veterinary~~ antimicrobial ~~drugs~~[agents] marketed should be provided to the national regulatory authority.

[38. Package size and the strength of antimicrobial formulations should be adapted as far as possible to the approved indications of use (avoidance of improper dosing, overuse and leftovers).]

ADVERTISING

~~41.~~[39.] It is the responsibility of the ~~veterinary pharmaceutical industry~~[marketing authorization holders] to advertise ~~veterinary~~ [medically important] antimicrobial[s] ~~drugs~~ in accordance with the provisions of Paragraph ~~35~~[30] on the Responsibilities of the Regulatory Authorities, Control of Advertising and to not ~~inappropriately~~ advertise [medically important] antimicrobials ~~directly~~ to the ~~food animal~~ producer. [Advertising should only be allowed to persons permitted to prescribe or supply antimicrobial drugs. Promotional campaigns involving economic or material benefits for prescribers or suppliers of antimicrobials should be prohibited.]

TRAINING

~~42.~~[40.] It is the responsibility of the ~~veterinary pharmaceutical industry~~[marketing authorization holders] to participate in the training of users of ~~veterinary~~ antimicrobial ~~drugs~~[agents] as defined in Paragraph ~~36~~[31].

RESEARCH

~~43.~~[41.] It is the responsibility of the ~~veterinary pharmaceutical industry~~[marketing authorization holders] to contribute to the development of research as defined in Paragraph ~~37~~[33]. [Research on the development of alternatives to the use of antimicrobials, new antimicrobials, rapid diagnostics and vaccines would be useful.]

Responsibilities of Wholesale and Retail Distributors

~~44.~~[42.] Retailers distributing ~~veterinary~~ [medically important] antimicrobial[s] ~~drugs~~ should only do so on the prescription of a veterinarian, [plant health professional] or other suitably trained person authorized in accordance with national legislation and all products should be appropriately labelled.

~~45.~~[43.] Distributors should encourage compliance with the national guidelines on the responsible use of ~~veterinary~~ [medically important] antimicrobial[s] ~~drugs~~ and should keep detailed records of all [medically important] antimicrobials supplied according to the national regulations including:

- date of supply
- name of prescribing veterinarian [, plant health professional, or other suitably trained and authorized person]
- name of user
- name of medicinal product
- batch number
- quantity supplied

~~46.~~[44.] Distributors should participate in the training of users of ~~veterinary~~ antimicrobial ~~drugs~~[agents] as defined in Paragraph ~~36~~[30].

Responsibilities of Veterinarians[10] [and Plant Health Professionals]

~~47.~~[45.] The veterinarian ~~is~~[and plant health professionals are] responsible for identifying recurrent disease problems and developing alternative strategies to prevent or treat infectious disease. These may include ~~changes in husbandry conditions and vaccination programs where vaccines are available~~[biosecurity, improved production practices, and alternatives to antimicrobials].

[46. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.6 – Responsibilities of veterinarians.]

~~48. Veterinary antimicrobial drugs should only be prescribed for animals under his/her care, which means that:~~

- ~~the veterinarian has been given responsibility for the health of the animal or herd/flock by the producer or the producer's agent;~~
- ~~that responsibility is real and not merely nominal;~~
- ~~that the animal(s) or herd/flock have been seen immediately before the prescription and supply, or~~
- ~~recently enough for the veterinarian to have personal knowledge of the condition of the animal(s) or current health status of the herd or flock to make a diagnosis and prescribe; and~~
- ~~the veterinarian should maintain clinical records of the animal(s) or the herd/flock.~~

~~49.~~[47.] It is recommended that ~~veterinary~~ professional organizations develop for their members ~~species-specific clinical practice guidelines on the responsible use of veterinary antimicrobial drugs~~[species or sector-specific responsible and prudent antimicrobial use guidelines].

[Within the national action plans, which countries are developing under the Global Action Plan, there should be the recommendation to develop species-specific clinical practice guidelines on the responsible use of veterinary antimicrobial agents. These guidelines would be created by the sector specific veterinary professional organizations.]

~~50.~~[48.] ~~Veterinary a~~[A]ntimicrobial ~~drugs~~[agents] should only be used when necessary and in an appropriate manner:

- A prescription [or order for application] for ~~veterinary~~[medically important] antimicrobial[s] ~~drugs~~ must precisely indicate the treatment regimen, the dose, the dosage intervals, the duration of the treatment, the withdrawal period[, when appropriate,] and the amount of antimicrobial to be delivered depending on the dosage, ~~the number, and the weight of the animals~~[and the characteristics of the individual or population] to be treated;
- [The delivered amount should be limited only for the treatment concerned. It should also indicate the animal keeper/owner and the identification of the animal(s) to be treated;]
- All ~~veterinary [medically important]~~ antimicrobial[s] ~~drugs~~ should be prescribed [or applied] and used according to [label directions and] the conditions stipulated in the national legislation.

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

~~51.~~[49.] [For food-producing animals, the]~~The~~ appropriate use of ~~veterinary~~ [medically important] antimicrobial[s] ~~drugs~~ in practice is a clinical decision which 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 animals, which may have been exposed to pathogens, may need to be treated without recourse to an accurate diagnosis and antimicrobial susceptibility testing in order to prevent the development of clinical disease and for reasons of animal welfare.

~~52.~~[50.] Determination of the choice of a ~~veterinary~~ antimicrobial [agents] ~~drug~~ by:

- The expected efficacy of the treatment based on:
    - the ~~clinical~~ experience of the veterinarian [, plant health professional or suitably trained and authorized person];
    - the spectrum of the antimicrobial activity towards the pathogens involved;
    - the ~~epidemiological~~ history of the ~~rearing~~[production] unit particularly in regards to the antimicrobial resistance profiles of the pathogens involved. ~~Ideally~~[Whenever possible], the antimicrobial profiles should be established before the commencement of treatment. [If this is not possible, samples should nevertheless be taken before start of the treatment to allow, if necessary, for adjustment of therapy based on sensitivity testing.] Should a first antimicrobial treatment fail or should the disease recur, the use of a second ~~veterinary~~ antimicrobial ~~drug~~[agent] should be based on the results of microbiological tests;
    - the appropriate route of administration;
    - results of initial treatment;
    - [previous published scientific information on the treatment of the specific disease;]
    - ~~known pharmacokinetics/tissue distribution to ensure that the selected veterinary antimicrobial drug is active at the site of infection;~~
    - ~~prognosis~~[the likely course of the disease].
- The need to minimize the adverse health impact from the development of microbial resistance based on:
    - the choice of the activity spectrum of the ~~veterinary~~ antimicrobial ~~drug~~[agent] [(narrow-spectrum antimicrobials should be a preferred choice whenever possible/appropriate)];
    - the targeting of specific microorganism;
    - known or predictable susceptibilities using antimicrobial susceptibility testing;
    - optimized dosing regimens;
    - the use of effective combinations of ~~veterinary~~ antimicrobial ~~drugs~~[agents];
    - the importance of the antimicrobial drugs to veterinary and human medicine; and,
    - the route of administration.

~~53. If the label conditions allow for some flexibility, the veterinarian should consider a dosage regimen that is long enough to allow an effective recovery of the animal but is short enough to limit the selection of resistance in foodborne and/or commensal microorganisms.~~

OFF-LABEL USE

~~54.~~[51.] [For food-producing animals, the]~~The~~ off-label use of a veterinary antimicrobial drug may be permitted in appropriate [(exceptional)] circumstances and should be in agreement with the national legislation in force including the administrative withdrawal periods to be used. It is the veterinarian's responsibility to define the conditions of responsible use in such a case including the therapeutic regimen, the route of administration, and the duration of the treatment. Off-label use of [medically important] antimicrobial growth promoters should not be permitted.

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

RECORDING

~~55.~~[52.] [For food-producing animals, records]~~Records~~ on veterinary antimicrobial drugs should be kept in conformity with national legislation. Veterinarians may refer to recording information as covered in the relevant national legislation.~~11~~

In particular, for investigation of antimicrobial resistance, veterinarians should:

- record the antimicrobial susceptibility testing results;
- investigate adverse reactions to veterinary antimicrobial drugs, including lack of expected efficacy due to antimicrobial resistance, and report it, as appropriate, to the regulatory authorities [(through a pharmacovigilance system)].

~~56.~~[53.] [For food-producing animals, veterinarians]~~Veterinarians~~ should also periodically review farm records on the use of veterinary antimicrobial drugs to ensure compliance with their directions.

TRAINING

~~57.~~[54.] ~~Veterinary~~ ~~p~~[P]rofessional organizations should participate in the training of users of ~~veterinary~~ antimicrobial ~~drugs~~[agents] as defined in Paragraph ~~36~~[31].

Responsibilities of Producers

~~58.~~[55.] Producers are responsible for preventing disease outbreaks and implementing health and welfare programmes on their farms. They ~~may, as appropriate,~~ [should] call on the assistance of ~~their~~ veterinarian[, plant health professional] or other suitably trained person authorized in accordance with national legislation. All people involved with ~~food-producing animals~~[the food chain] have an important part to play in [preventing disease and] ensuring the responsible [and prudent] use of ~~veterinary~~ antimicrobial ~~drugs~~[agents].

~~59.~~[56.] Producers ~~of food-producing animals~~ have the following responsibilities:

- to use ~~veterinary~~ antimicrobial ~~drugs~~[agents] only when necessary and not as a replacement for good management and farm hygiene, or other disease prevention methods such as vaccination;
- to implement a health plan in cooperation with the veterinarian [, plant health professional, or other suitably trained person authorized in accordance with national legislation] ~~in charge of the animals~~ that outlines preventative measures ~~(e.g. mastitis plan, worming and vaccination programmes, etc.)~~;
- to use ~~veterinary~~ antimicrobial ~~drugs~~[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 health professional or other suitably trained person authorized in accordance with national legislation] familiar with the animals ~~and~~[or] the production site;
- ~~to isolate sick animals and dispose of dead or dying animals promptly under conditions approved by relevant authorities;~~
- to comply with the storage conditions of ~~veterinary~~ antimicrobial ~~drugs~~[agents] according to the approved product labelling;
- to address hygienic conditions regarding contacts between people (veterinarians, [plant health professionals,] breeders, owners, children) and the ~~animals~~[populations] treated;
- to comply with the recommended withdrawal periods to ensure that residue levels in ~~animal derived~~[the] food do not present a risk for the consumer;
- to not use out-of-date ~~veterinary~~ antimicrobial ~~drugs~~[agents] and to dispose of all unused ~~veterinary~~ antimicrobial ~~drugs~~[agents] in accordance with the provisions on the product labels [and national legislation];
- to inform the veterinarian[, plant health professional, or other suitably trained person authorized in accordance with national legislation] in charge of the [production] unit of recurrent disease problems;

~~11 Veterinarians can also refer to the "Recommended International Code of Practice for Control of the Use of Veterinary Drugs CAC/RCP 38-1993."~~

- to maintain all clinical and laboratory records of microbiological and susceptibility tests ~~if required by the national regulatory authority~~. These data should be made available to the ~~veterinarian~~[professional] in charge of ~~treating the animals~~[treatment] in order to optimize the use of ~~veterinary~~ antimicrobial ~~drugs~~[agents].
- to keep adequate records of all ~~veterinary~~ antimicrobial ~~drugs~~[agents] used, including the following:
    - name of the ~~veterinary~~ antimicrobial ~~drug~~[agent]/active substance and batch number;
    - name of supplier;
    - date of administration;
    - identification of the ~~animal or group of animals~~[production unit] to which the ~~veterinary~~ antimicrobial ~~drug~~[agent] was administered;
    - ~~clinical conditions~~[disease] treated;
    - quantity and duration of the antimicrobial agent administered;
    - withdrawal periods;
    - result of laboratory tests;
    - result of treatment;
    - name of the prescribing veterinarian [, plant health professional] or other suitably trained person authorized in accordance with national legislation.
- To ensure sound management of ~~animal~~ wastes and other materials to ~~avoid~~ [minimize] dissemination of antimicrobial agents and resistance determinants into the environment;
- To prevent the unnecessary contact with and transmission of resistant bacteria to all personnel, including farm workers;
- To assist the relevant authorities in surveillance programs related to antimicrobial resistance.

[57. The responsible and prudent use of antimicrobials must be supported by continuous efforts in disease prevention to minimise infection during production and decrease the volume of antibiotics used. 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, and implementing national or international good animal husbandry, aquaculture, or agricultural practices. Disease prevention through the use of vaccines and other measures 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 colonisation of some bacterial pathogens) should be considered and applied wherever appropriate and available.]

[58. Concerted efforts of all stakeholders within the entire food chain is required to minimize and contain foodborne antimicrobial resistance. While such efforts mainly focus on 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 (CAC/GL 63-2007).]

[Responsibilities of Consumers]

[59. Consumers have an important role to play to minimize and control antimicrobial resistance. By practicing safe food handling techniques, following health recommendations, and maintaining awareness of antimicrobial resistance information, consumers can minimize the risk of contracting and spreading infectious bacteria thereby further reducing the need for antibacterials. Consumer should:

- Take antibiotics only when needed;
- Use a food thermometer to ensure that foods are cooked to a safe internal temperature: 145°F (63°C) for whole beef, pork, lamb, and veal (allowing the meat to rest for 3 minutes before carving or consuming), 160°F (71°C) for ground meats, and 165°F (74°C) for all poultry, including ground chicken and ground turkey;
- Wash hands after touching raw meat, poultry, and seafood. Also wash work surfaces, cutting boards, utensils, and grill before and after cooking;
- Keep food below 40°F and refrigerating foods within 2 hours of cooking (1 hour during the summer heat);

- Separate raw meat, poultry, seafood and eggs from fresh produce and ready-to-eat foods to avoid cross contamination. Use different cutting boards to prepare raw meat or poultry and any food that will be eaten without cooking;
- Wash hands after contact with feces, animals or animal environments;
- Report suspected outbreaks of illness from food to local health department; and
- Review Competent Authority's traveler's health recommendations when preparing to travel to a foreign country.

[Advocacy and Communication]

[60. The successful control of antimicrobial resistance along the food chain requires the involvement and cooperation of all parties along the food chain. These include the relevant authorities and stakeholders such as the manufacturers, veterinarians and plant health professionals, wholesale and retail distributors, producers, and consumers who are involved in the authorisation, production, control, importation, exportation, distribution and use of antimicrobial agents.]

[61. Advocacy and communication strategies should identify relevant target audiences, such as policy makers, health, veterinary and agricultural professionals, farmers, players in the food industry, the media and the general public, who all have a responsibility in minimising antimicrobial resistance along the food chain.]

[62. Advocacy and communication efforts at the international and national levels should aim to raise awareness of the importance of antimicrobials in treating bacterial infections and the public health challenges of antimicrobial resistance, including within a food safety perspective.]

[63. Advocacy campaigns should be tailored to the specific stakeholder groups. Campaigns targeted at the agricultural sectors should include good animal husbandry or agricultural practices and the prudent use of antimicrobials. Those at the food industries should reinforce prevention of contamination and food hygiene practices. National guidelines and education programmes should promote best practices, including correct treatment, measures to prevent and reduce the transmission of pathogens, infection control and hygiene measures.]

[64. The engagement and consultation of stakeholders prior to enforcement or introduction of prudent use policies or measures are critical for successful implementation. Regulatory authorities should engage all relevant stakeholder groups.]

[65. Establishment of an Adhoc scientific AMR Newsletter with the objective of collection of recent advances in AMR specially in the field of the tripartite organizations (FAO, WHO and OIE), Codex universities and institutions; with relevance to the development and transmission of food-borne antimicrobial resistance in the food chain (with special emphasis on the genera of Enterobacteriaceae (*E.coli* O157H7, *Salmonella, Shigella, Campylobacter* and *Vibrio cholera*).

~~**Conclusions**~~

~~60. Veterinary antimicrobial drugs are very important tools for controlling a great number of infectious diseases in both animals and humans. It is vital that all countries put in place the appropriate systems to ensure that veterinary antimicrobial drugs are manufactured, marketed, distributed, prescribed and used responsibly, and that these systems are adequately audited.~~

~~61. This document is designed to provide the framework that countries may implement in accordance with their capabilities but within a reasonable period of time. A stepwise approach may be appropriate for a number of countries to properly implement all of the elements in this document.~~

~~62. The continued availability of veterinary antimicrobial drugs, which are essential for animal welfare and animal health and consequently human health, will ultimately depend on the responsible use of these products by all those involved in the authorisation, production, control, distribution and use of antimicrobials in food-producing animals.~~

~~**End Notes**~~

~~[1]A. Franklin, J. Acar, F. Anthony, R. Gupta †T. Nicholls, Y. Tamura, S. Thompson, E.J. Threlfall, D. Vose, M. van Vuuren, D.G. White, H. C. Wegener & M.L. Costarrica. Antimicrobial resistance: harmonization of national antimicrobial resistance monitoring and surveillance programmes in animals and in animal-derived food. Rev. sci. tech. Off. Int. Epiz., 20 (3), 859-870. http://www.oie.int/eng/publicat/rt/2003/a_r20318.htm~~

~~[2]D.G. White, J. Acar, F. Anthony, A. Franklin, R. Gupta, †T. Nicholls, Y. Tamura, S. Thompson, E.J. Threlfall, D. Vose, M. van Vuuren, H. C. Wegener & M.L. Costarrica. Antimicrobial resistance: standardization and harmonization of laboratory methodologies for the detection and quantification of antimicrobial resistance. Rev. sci. tech. Off. Int. Epiz., 2001, 20 (3), 849-858. http://www.oie.int/eng/publicat/rt/2003/a_r20317.htm~~

List of Abbreviations [Acronyms] Used in this Code

ADI — Acceptable Daily Intake

CAC — Codex Alimentarius Commission

CAC/RCP — Codex Alimentarius Commission/Recommended Code of Practice CCRVDF Codex Committee on Residues of Veterinary Drugs in Foods FAO Food and Agriculture Organization of the United Nations

MRL — Maximum Residue Limit

OIE — Office International des epizooties/International Office of Epizooties

VICH — International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products

WHO — World Health Organization

Glossary of Definitions and Terms

Veterinary Antimicrobial Drug

Veterinary antimicrobial drug(s) refers to naturally occurring, semi-synthetic or synthetic substances that exhibit antimicrobial activity (kill or inhibit the growth of microorganisms). Where anticoccidial products have antibacterial activity, they should be considered as veterinary antimicrobial drugs, except where this is precluded by national legislation.

Disease Treatment/Therapeutic Use

Treatment/Therapeutic Use refers to use of an antimicrobial(s) for the specific purpose of treating an animal(s) with a clinically diagnosed infectious disease or illness.

Disease Prevention/Prophylactic Use

Prevention/Prophylactic Use refers to use of an antimicrobial(s) in healthy animals considered to be at risk of infection or prior to the onset of clinical infectious disease. This treatment includes:

- control of the dissemination of a clinically diagnosed infectious disease identified within a group of animals, and
- prevention of an infectious disease that has not yet been clinically diagnosed.

Growth Promotion

Growth Promotion refers to the use of antimicrobial substances to increase the rate of weight gain and/or the efficiency of feed utilization in animals by other than purely nutritional means. The term does NOT apply to the use of antimicrobials for the specific purpose of treating, controlling, or preventing infectious diseases, even when an incidental growth response may be obtained.

Appendix II

List of Participants

Codex Members

1. Argentina
2. Australia
3. Austria
4. Belgium
5. Brazil
6. Canada
7. Chile
8. China
9. Colombia
10. Costa Rica
11. Czech Republic
12. Denmark
13. Ecuador
14. Estonia
15. Finland
16. France
17. Germany
18. Guatemala
19. Guyana
20. Hungary
21. India
22. Ireland
23. Italy
24. Japan
25. Kenya
26. Malaysia
27. Netherlands
28. New Zealand
29. Nigeria
30. Norway
31. Poland
32. Republic of Korea
33. Russian Federation
34. Singapore
35. Spain
36. Sudan
37. Sweden
38. Switzerland
39. Thailand
40. Tunisia
41. Uganda
42. UK
43. Uruguay
44. USA

Codex Member Organization

1. European Union

Codex Observers

1. Biotechnology Innovation Organization (BIO)
2. Consumers International
3. Crop Life International
4. Food and Agriculture Organization (FAO)
5. Food Drink Europe
6. Health for Animals
7. Inter-American Institute for Cooperation on Agriculture (IICA)
8. International Association of Consumer Food Organizations (IACFO)
9. International Council of Grocery Manufacturers Association (ICGMA)
10. International Dairy Federation (IDF)
11. International Feed Industry Federation (IFIF)
12. International Poultry Council
13. Intl Meat Secretariat (IMF)
14. SSAFE
15. The European Feed Manufacturer's Federation (FEFAC)
16. The International Commission on Microbiological Specifications (ICMSF)
17. World Health Organization (WHO)
18. World Organization for Animal Health (OIE)