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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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

Seventh Session

Pyeongchang, Republic of Korea, 9 - 13 December 2019

PROPOSED DRAFT GUIDELINES ON INTEGRATED MONITORING AND SURVEILLANCE OF FOODBORNE ANTIMICROBIAL RESISTANCE

(Prepared by the Electronic Working Group
led by the Netherlands and co-chaired by Chile, China and New Zealand)

Codex members and observers wishing to submit comments at Step 3 on this document should do so as instructed in CL 2019/83-AMR available on the Codex webpage/Circular Letters: http://www.fao.org/fao-who-codexalimentarius/resources/circular-letters/en/.

Introduction

1. The Sixth Session of the Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance (2018) agreed to re-establish the Electronic Working Group chaired by the Netherlands and co-chaired by Chile, China and New Zealand to prepare a revised version of the Guidelines for integrated monitoring and surveillance of foodborne antimicrobial resistance for consideration by TFAMR07 (2019). The EWG was requested[1] to take into account the discussions at TFAMR06 and to consider the report of the *Joint FAO/WHO Expert Meeting in collaboration with OIE on Foodborne AMR; Role of the Environment, Crops and Biocides*.

2. Codex Members and Observers were invited to register their experts on the Codex electronic platform. A total of 47 Codex Members (46 Member States and 1 Member Organization) and 10 Observers requested registration. The list of Codex Members that actually registered is attached as Appendix II.

3. The EWG organized two rounds of discussions to review the document and to address the specific requests from TFAMR06. The first round for comments was launched in February 2019 and the second in June 2019. For both rounds, the participants had approximately 6 weeks to provide comments on the draft and/or the questions, which were available in English and Spanish on the platform.

4. During the first round of comments the EWG reviewed sections 1-6 and 11-13 to address the specific questions of TFAMR06 in line with The terms of Reference[1] given to the EWG, not reopening agreed text. The EWG also reviewed the presentation of the content of section 7. The EWG received a total of 25 responses from Codex Members and, 6 responses from Observers.

5. During the second round for comments, the participants provided comments on the revised sections 8-10. The EWG received a total of 21 responses from Codex Members and, 5 responses from Observers.

6. A short summary of the answers to the questions and the main responses received by Member Countries and Observers can be found below, as well as explanations to choices made by the EWG.

Summary of the comments from Codex Members and Observers on the questions posted by the Chair and Co-chairs of the EWG related to the proposed draft Guidelines for the integrated monitoring and surveillance of foodborne antimicrobial resistance

7. To address the questions of TFAMR06 on **sections 1-6 and 11-13**, the participants were requested to review and revise the texts in CRD 18. To facilitate the work, the participants were requested to answer the following questions. The questions and the responses received are summarized below:

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1 REP19/AMR, para. 115

a) Should scientific evidence be included in paragraph 3?

The majority of the respondents proposed to keep the current wording.

Advice: To keep "*scientific evidence*".

b) Should the reference to the national food safety system in paragraph 6 remain or be deleted?

The majority of the respondents proposed to keep the sentence. Some respondents suggested to delete the word [comprehensive].

Advice: To keep the reference to the "*national food safety system*" and delete the word "*comprehensive*".

c) Should "international" replace "multi-national" in paragraph 7 or should both terms remain?

The majority of respondents proposed to change "multi-national" by "international".

Few participants propose to keep both. Others mentioned that both terms are synonyms. The Chair and Co-chairs asked the Codex Secretariat which terminology is more appropriate to Codex documents. Codex standards are "international" but in the context of this sentence "multi-national" may also be appropriate as a country cannot create an "international" system and a surveillance system could be "multi-national" (several countries contributing).

Advice: To keep both terms and amend the sentence as proposed: "…*countries may also consider contribution to or creating international, or multi-national or regional, monitoring and surveillance systems*…"

d) Should the words "animals and crops" be deleted from paragraph 13 as they are already included in the definition of food chain or should they remain?

The majority of the respondents proposed to delete "including animals and crops", provided that this is included in the definition in Section 3.

Advice: To delete "*including animals and crops*" and to include it in the definition of food chain in Section 3.

e) How can "feed" be incorporated into the scope? Should the word "feed" be introduced in paragraph 13 or should it be incorporated in the definition of food chain in Section 3?

The majority of the respondents answered that including feed in the definition of food chain is enough to ensure the inclusion of feed in the scope of the guidelines.

Advice: To keep the current definition of food chain which refers to feed, therefore no need to specifically mention it in the scope.

f) Provide a definition for "production environment" or amend as necessary this definition proposed by the Chair of the EWG on the revision the Code of practice to minimize and contain foodborne antimicrobial resistance in Conference Room 20 presented at TFAMR06.

Some respondents did not reply to the question, some others agreed with the definition proposed by the EWG/COP Chair in CRD20, and others proposed different alternatives.

Advice: The following definition captures most of the (elements in the) proposals made by the members of the EWG: "*The ~~immediate~~ vicinity of food, feed, plants/crops/animals to be harvested or processed that has ~~reasonable~~ probability to contribute to foodborne AMR*".

g) Should the reference to the national food safety system in principle 2 remain or should it be deleted?

The majority of the respondents proposed to keep the principle.

Advice: To keep the sentence and to change "*core*" by "*important*" as to align with paragraph 6 in the introduction: "*Monitoring and surveillance systems for AMR and AMU throughout the food chain are a fundamental part of national strategies and plans to minimize foodborne AMR and an important component of a national food safety program*"

h) Should a reference to international standards be included in Principle 3 as to reflect the need for comparable data and to facilitate reporting?

The majority of the respondents proposed to keep the reference to international standards.

Advice: To keep "*international standards*".

i) Consider merging principles 7+10 as they are similar. Provide an alternative for a joint principle.

Advice: A revised joint principle (new 7) is proposed i.e. "*Monitoring and surveillance systems should incorporate to the extent practicable, the capacity for epidemiological investigation and identification of new and emerging foodborne AMR hazards/risks and trends. This could include research projects and epidemiological studies to enhance the technical capability and effectiveness of the integrated monitoring and surveillance system (e.g. new analytical methods, source attribution studies, monitoring of indirect inputs to the food chain, cross-contamination of foods, molecular epidemiology of emerging clones and resistance determinants)*".

j) Should Principle 11 (new 10) remain or should it be deleted?

The majority of the respondents proposed to keep the principle. Some others proposed to delete appropriate, others to keep it and others proposed alternative wording for the principle.

Some respondents commented that such a principle seems inappropriate in a Codex document. The origin of the principles was the concern expressed by some Codex Members that the stepwise approach presented in the guidelines may originate trade barriers. If this is solved in the document, the principle may not be needed anymore.

Advice: To keep it in the current wording and to evaluate later, when the document has been agreed, the need to delete, keep or amend the principle.

k) Should "relationship" be replaced by "level" in paragraph 20?

The majority of the respondents did not support changing the level by relationship. Some of them proposed alternative wording such as linkage to human health, risk to human health, proportionate risk to human health, their potential to pose risk to human health, the level of risk to human health.

Advice: To keep "*relationship*".

l) Need to remove/rephrase the 2 sentences in paragraph 28 as they are going beyond the Codex mandate? Rephrase paragraph 28 in Section 6 to ensure it is not going beyond the Codex mandate.

Some respondents proposed to delete these sentences and others proposed to keep and rephrase.

Advice: To delete second sentence of paragraph 28 "*This should include access to livestock and crop production facilities when conducting epidemiological investigations of multidrug resistant foodborne outbreaks*" and rephrase the first part as "*Competent authorities should need to have access to all sources of antimicrobial use data*". Move paragraph 29 above.

m) Rephrase paragraph 35 in Section 12 as appropriate.

Advice: A revised paragraph is proposed "*Risk communication processes should allow the development of partnerships between the competent authorities and stakeholders. Such partnerships should facilitate communication between parties and the involvement and commitment of stakeholders in the development and implementation of the AMR monitoring and surveillance activities and other related risk management options*".

8. Respecting **section 7**: the EWG reviewed and revised the text in CX/AMR 18/6/6, taking into account the comments of the TFAMR07. Especially the presentation of the content of section 7.3 was revised. The new presentation of this section was welcomed by most. Small amendments were proposed as regards Figure 1.

9. With regard to **sections 8-10**: the text of CX/AMR 18/6/6 were reviewed and revised. In section 8.3, from the 2 proposals presented by the chair, most of the participants preferred to list the sample sources above presenting the sources on a table. In section 8.7, reference to EUCAST and CLSI has not changed and not to specific subgroups within these organizations, as requested by few participants. Some participants proposed to delete some parts of section 9, specially 9.2.3 and 9.2.4. as they considered not in the scope of the document and may overlap OIE text. The Chair has maintained the section as other participants indicated that it is useful. As proposed by the Chair, most of the participants agreed to move/delete some of the subsections in section 10 as explained below.

Overview of the most important amendments made in the guidelines based on comments received from the members of the EWG

10. The EWG has reviewed the guidelines in line with the Terms of Reference provided by TFAMR06.

- Sections 1-6 and 11-13 have been reviewed as specifically requested in paragraphs 86-108 and 114 and the Terms of Reference in paragraph 115 of the report of TFAMR06 (REP/19/AMR). The most important amendments are:

- The specific reference to animals and crops as part of the food chain in the scope of the guidelines has been deleted. The inclusion of animals, crops and feed in the definition of "food chain" in Section 3 seems enough to clarify that these components are part of the food chain and therefore included in the Scope of the Guidelines.
- An alternative definition for food production environment is provided.
- The reference to the national food safety system in the introduction and in Principle 2 has been kept. The wording in both paragraphs has been aligned.
- Principle 7 and 10 have been merged.
- Principle 11 has not been modified. It is suggested to discuss the convenience to delete or amend this principle on a later stage.
- First and second paragraphs in Section 6 have been reordered. Part of the second paragraph has been deleted and rephrased as to ensure that the content is not going beyond Codex mandate.
- Section 12: Second paragraph has been reviewed.

- The EWG Chair proposed a new presentation of the content of the section 7. The table presenting 3 steps has been deleted and a description on how the different elements of the monitoring and surveillance system can be progressively incorporated to the system has been introduced. Figure 1 has been amended as to reflect that Analysis and Reporting refers to both, AMR and AMU.
- Sections 8-10 has been modified in line with the comments received. Section 10 has been reordered and the following sections have been deleted/combined with section 8:
  - Section 10.1 "Sampling procedures": the content of this section has been moved to Section 8.4 (sampling plans) and 8.7 (laboratories).
  - Section 10.2 "Collection and reporting of resistance data": the content of this section has been moved to Section 8.8.
  - Section 10.4 "Analysis and reporting of results": paragraphs 1-4 have been moved to new section 8.8 "Collection and reporting of resistance data" and paragraph 6 has been moved to Section 10.6 "Integrated analysis of results".
  - Section 10.5 "Target investigation": the content has been merged with section 10.8 "Additional research and targeted investigation".
  - Section 10.7 "Detection and evaluation of emerging risks": this section has been deleted, as it seems not in the scope of the Guidelines

Conclusions

11. The EWG concludes:

- Specific reference to feed, animals and crops/plants when referring to the food chain in Section 2 is not needed to ensure their inclusion into the scope of the Guidelines, provided that these elements are include in the definition of food chain in Section 3.
- A definition of food production environment is provided.
- Principles 2, 7+10 have been revised. The need to keep or amend Principle 11 can be revised on a later stage, when the key elements of the document have been agreed.
- The new presentation of the section 7 is favored by most.
- Deletion/restructuration in sections 8 and 10 has been done, but there is still some overlap.

Recommendations

12. The EWG recommends that the TFAMR:

- Revise the Guidelines to ensure consistency/harmonization in wording.
- Avoid specific references to sections or chapters numbers, especially when referring to other documents (e.g. OIE, Codex standards) as these may change with new editions. Preferably, refer to the content of the chapter or section.
- Align definitions with COP: Agree on a common definition for the term "food production environment".
- Revise Section 7 and Sections 8-10, where possible avoiding overlap, ensuring a clear link between the 3 areas presented in Figure 1 in Section 7 and the subsequent sections and ensuring that the progressive approach for the implementation of the monitoring and surveillance program is well reflected throughout the document. Consider moving some elements (e.g. technical descriptions in sections 8 and 9) to an Annex.

APPENDIX I

PROPOSED DRAFT GUIDELINES ON INTEGRATED MONITORING AND SURVEILLANCE OF FOODBORNE ANTIMICROBIAL RESISTANCE

1. Introduction and purpose

1. World-wide recognition of the importance of antimicrobial resistance (AMR) as a public health threat has led to strong international calls for all countries to develop and implement national strategies and action plans that incorporate an integrated approach to risk analysis. The political declaration adopted during the High-Level Meeting on Antimicrobial Resistance at the General Assembly of the United Nations in 2016 committed Member Countries to developing multi-sectoral national action plans that involve all stakeholders within a "One Health" approach and to improving national systems of monitoring and surveillance of AMR and antimicrobial use (AMU).

2. For the purpose of these Guidelines, monitoring refers to the collection and analysis of AMR and AMU related data and information. Surveillance is the systematic, continuous or repeated, measurement, collection, collation, validation, analysis and interpretation of AMR and AMU related data and trends from defined populations to inform actions that can be taken and to enable the measurement of their impact.

3. An integrated monitoring and surveillance system includes the coordinated and systematic collection of data or samples at appropriated stages throughout the food chain and the testing, analysis and reporting of AMR and AMU. An integrated system includes the alignment and harmonization of sampling, testing, analysis and reporting methodologies and practices as well as the integrated analysis of relevant epidemiological information from humans, animals, foods, crops and the food production environment. Depending on national priorities, food safety AMR issues, scientific evidence, capabilities and available resources, an integrated surveillance system can be implemented progressively.

4. The data generated by integrated monitoring and surveillance systems provide essential information for the risk analysis of foodborne AMR. These data are also essential for epidemiological studies, food source attribution studies and other operational research. It provides information to risk managers about AMR and AMU trends and for the planning, implementation and evaluation of risk mitigation measures to minimize any foodborne public health risk due to resistant microorganisms and resistance determinants.

4.bis Reporting of standardized and harmonized data generated through national monitoring and surveillance systems to international organizations and, in return, use of information generated from global monitoring and surveillance databases is highly desired.

5. It also contributes to the promotion and protection of public health by providing burden of illness information to risk managers about, how infections caused by resistant bacteria differ from infections caused by susceptible bacteria, and the impact of interventions designed to limit the emergence, selection, and dissemination of foodborne AMR.

6. These Guidelines are intended to assist governments in the design and implementation of monitoring and surveillance systems for data on AMU and foodborne AMR throughout the food chain. Such systems are a fundamental part of national strategies and plans to minimize foodborne AMR and are an important component of a national food safety system.

7. While these Guidelines are primarily aimed at action at the national level, countries may also consider contribution to or creating international, or multi-national or regional, monitoring and surveillance systems to share laboratory, data management and other necessary resources.

8. Each monitoring and surveillance system is designed to ensure that it is appropriate for the national circumstances. The design should be informed by all available knowledge on foodborne risks due to AMR while taking into consideration the international dimension of AMR and the need for data comparability between countries or sectors.

9. New scientific knowledge should be incorporated into integrated monitoring and surveillance programs as it becomes available to improve the design of the systems and to enhance analysis and utility of existing information and data. Design and implementation of systems should also evolve as AMR policies and priorities change at the national and international level.

10. AMR scenarios are likely to vary between countries and these Guidelines should be used to foster a gradual implementation of monitoring and surveillance systems at the national level. Identification and implementation of priority activities should be followed by enhancements as resources and capacity develop. A gradual approach to monitoring and surveillance should take into account broader capacity issues including the availability of information on AMU in humans, animals and crops, human health care infrastructure, human clinical AMR data and reporting, availability of food consumption and agriculture production data, and cross-sector laboratory proficiency and quality assurance.

11. These Guidelines should be applied in conjunction with the *Code of Practice to Minimize and Contain Antimicrobial Resistance* (CXC 61-2005). Design and implementation aspects of these Guidelines should specifically take into account the *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance* (CXG 77-2011), as well as other relevant Codex texts including the *Principles and Guidelines for National Food Control Systems* (CXG 82-2013) whenever appropriate.

12. These Guidelines should also be used taking into consideration those already developed by other advisory bodies especially the WHO Advisory Group on Integrated Surveillance of AMR (WHO-AGISAR) *Integrated Surveillance of Antimicrobial Resistance in Foodborne Bacteria: Application of a One Health Approach* and other international standard setting organizations, specially the standards of the Organization of Animal Health (OIE standards) related to AMR and AMU published in the *Terrestrial Animal Health Code* and the *Aquatic Animal Health Code*.

2. Scope

13. These Guidelines cover the design and implementation of an integrated monitoring and surveillance system for foodborne AMR and AMU throughout the food chain, and the production environment.

14. These Guidelines focus on foodborne AMR.

15. Though these Guidelines do not cover the design and implementation of monitoring and surveillance of AMR and AMU in humans, an integrated system within the context of overall risk management of AMR (One Health Approach) would be informed by data, trends and epidemiology regarding AMR and AMU in humans.

16. The microorganisms covered by these Guidelines are those foodborne pathogens and indicator bacteria of public health relevance.

17. Antimicrobials used as biocides, including disinfectants, are excluded from the scope of these Guidelines.

18. Implementation of these Guidelines will facilitate the generation and use of appropriate AMR and AMU data from humans, animals, crops, food and production environment in order to conduct integrated analysis of all these data.

3. 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[1].

Crops/plants

A plant or crop that is cultivated or harvested as food or feed.

Foodborne pathogen

A pathogen present in food, which may cause human disease(s) or illness through consumption of food contaminated with the pathogen and/or the biological products produced by the pathogen.

Food chain

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

Hazard

A biological, chemical or physical agent in, or condition of, food with the *potential* to cause an adverse health effect[2]. For the purpose of these Guidelines, the term “hazard” refers to AMR microorganism(s) and /or resistance determinant(s)[3].

One Health approach to AMR

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

[1] *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*
[2] Procedural Manual, Codex Alimentarius Commission
[3] *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*

Food production environment

The vicinity of food, feed, plants/crops, animals to be harvested or processed that could contribute to foodborne AMR.

4. Principles

19. These principles should be read in conjunction with the *Guidelines for Risk Analysis of Foodborne AMR*.

- **Principle 1:** An integrated monitoring and surveillance system for foodborne AMR and AMU should follow a “One Health” approach.
- **Principle 2:** Monitoring and surveillance systems for AMR and AMU throughout the food chain are a fundamental part of national strategies and plans to minimize foodborne AMR and an important component of a national food safety program.
- **Principle 3:** A national monitoring and surveillance system should be tailored to the national situation and priorities and may be designed and implemented with the objective of progressive improvement as resources permit; in order to facilitate reporting at the international level ant to ensure that data is comparable international standards should be considered.
- **Principle 4:** Monitoring and surveillance systems should include data on occurrence of AMR and patterns of AMU, in all relevant sectors so as to support risk analysis and policy initiatives (e.g. development of mitigation strategies).
- **Principle 5:** Risk analysis should be a guiding principle in the design, implementation and review of a national monitoring and surveillance systems for AMR, with best practice being informed by expected benefits to public health and in terms of preventing or minimizing the burden to human health.
- **Principle 6:** Priority should be given to the most relevant design elements to be analyzed from a public health perspective (e.g. defined combinations of the food commodities, the microorganism and resistance determinants and the antimicrobial agent(s) to which resistance is expressed).
- **Principle 7:** Monitoring and surveillance systems should incorporate to the extent practicable, the capacity for epidemiological investigation and identification of new and emerging foodborne AMR hazards/risks and trends. This could include research projects and epidemiological studies to enhance the technical capability and effectiveness of the integrated monitoring and surveillance system (e.g. new analytical methods, source attribution studies, monitoring of indirect inputs to the food chain, cross-contamination of foods, molecular epidemiology of emerging clones and resistance determinants).
- **Principle 8:** Laboratories involved in monitoring and surveillance should have effective quality assurance systems in place and participate in external proficiency testing schemes (External Quality Assessment Schemes).
- **Principle 9:** A national monitoring and surveillance system should strive to harmonize laboratory methodology, data collection, analysis and reporting across all sectors according to national priorities and resources as part of an integrated approach. Use of internationally recognized, standardized and validated methods and harmonized interpretative criteria are essential to ensure that data are comparable and to enhance an integrated approach to data management and reporting at the international level.
- **Principle 10:** Data generated from national monitoring and surveillance system of AMR in imported foods should not be used to [inappropriately] generate barriers to trade.

5. Risk-based approach

20. For the purpose of these Guidelines, a risk-based approach is the development and implementation of a monitoring and surveillance system throughout the food chain that is informed by data and scientific knowledge on the likely occurrence of AMR hazards at a step (or steps) in the food chain and their relationship with risks to human health.

21. Integrated monitoring and surveillance of AMR and AMU in the food chain, along with data regarding AMR transmission through food handling, environmental spread or other routes of transmission, provides essential information for risk assessment and risk management decision-making on appropriate control measures in human, plant and animal health.

22. While an integrated monitoring and surveillance system should ideally be designed according to knowledge of possible food-borne AMR risks to public health in the national situation, such knowledge is very limited in most countries. Consequently, most programs should [initially] be designed according to the knowledge that is available on AMR hazards and their potential to result in public health risks. AMR food safety issues may be identified on the basis of information arising from a variety of sources, as described in paragraph 26 of the *Guidelines for Risk Analysis of Foodborne AMR.*

23. Knowledge and information on foodborne AMR hazards, risk factors, etc. should be included on a risk profile as described in the *Guidelines for Risk Analysis of Foodborne AMR*. Hazard identification should include human microbiological pathogens and bacterial commensals that may transmit AMR to humans.

24. As countries improve their AMR systems over time, an approach to the development and implementation of monitoring and surveillance systems should lead to an increased use of generated data for risk assessment.

25. Potential foodborne AMR risks to human health are subject to change over time and an integrated monitoring and surveillance system should be adjusted as new information becomes available e.g. changes in test methodologies, new antimicrobial resistance genes, new food chain exposure pathways, changing patterns of AMU in humans and animals. Any adjustments should be communicated with reference to methodological changes while retaining valid historical data or when relevant updating historical data for trend analysis.

26. The revision of the monitoring and surveillance system should be based on information about hazards and risks incorporated in the risk analysis process as described in the *Guidelines for Risk Analysis of Foodborne AMR.*

6. Regulatory framework, policy and roles

27. An integrated monitoring and surveillance system for AMR and AMU requires good governance and co-ordination by the relevant competent authorities. The competent authorities should develop an overarching policy framework for monitoring and surveillance activities throughout the food chain in collaboration with the human health, animal health, plant health, environmental and other relevant authorities. Other stakeholders in relevant sectors should be included and collaborate in line with the national action plan (NAP) on AMR. Sharing of knowledge and data with international organizations and counterparts can improve the effectiveness of policies taken at local level. Capacity building might help to ensure the implementation of programs for AMR risk management.

28. Competent authorities should need to have access to all sources of antimicrobial use data. Activities related to monitoring and surveillance of foodborne AMR and AMU should involve not only the relevant competent authorities, but a wider range of stakeholders. The level of engagement of stakeholders, including food industry, feed industry, pharmaceutical industry, veterinarians, animal, plant health and environment professionals, farmers, professional associations, civil society, consumer organizations, retail and others, will depend on the level of development of the monitoring and surveillance system and the degree of integration. Ideally, all interested parties along the food chain should contribute to the development and implementation of an integrated monitoring and surveillance system.

29. Stakeholders other than the competent authority, such as veterinarians, plant health professionals, farmers, consumer organizations, civil society, pharmaceutical industry or food and feed industry, retailers and others may carry out monitoring activities e.g. monitoring of AMU on a voluntary basis.

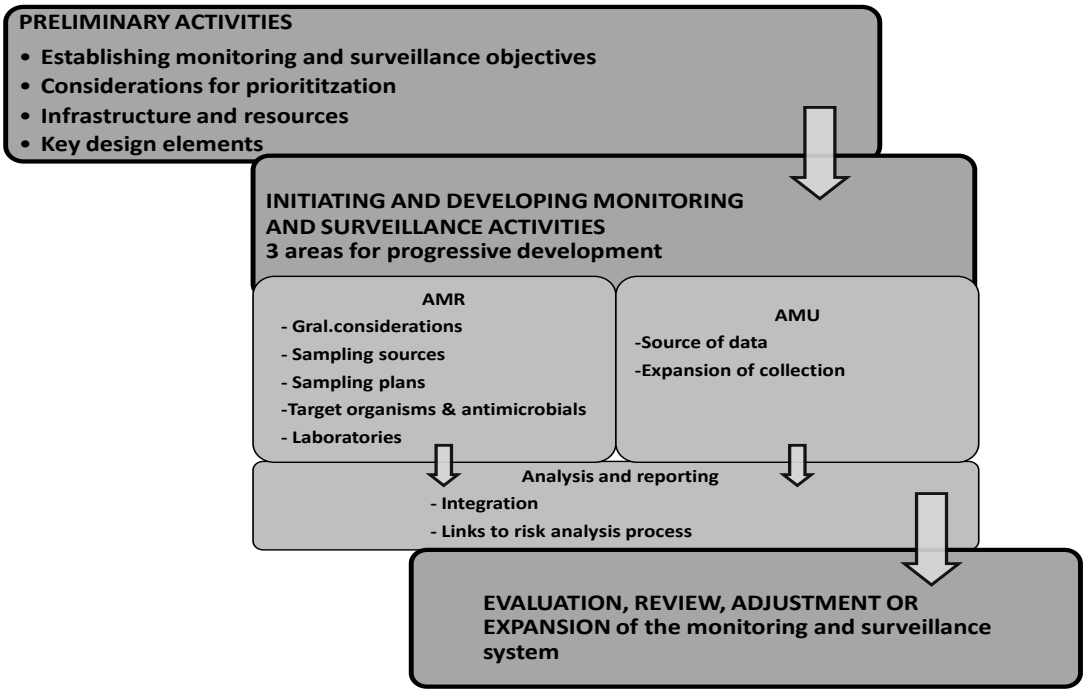
30. Competent authorities responsible for food safety may consider playing an active role in design, analysis and reporting of these activities as part of an integrated “One Health” approach in collaboration with other relevant authorities from the human, animal, plant, food and environmental sectors, recognizing that knowledge and resources available to address certain sectors may be more advance than others.

7. A progressive approach for the implementation of an integrated monitoring and surveillance system of foodborne AMR

31. A progressive approach for the design and implementation of an integrated monitoring and surveillance system allows countries to develop a strategy as well as implement activities to progress according to country-specific scenarios and resources. It is a practical response to inevitable variations in monitoring and surveillance objectives, priorities, infrastructure, technical capability, resources and new scientific information. The implementation of a progressive approach should facilitate the achievement of the country’s objectives on AMR and enable continuous improvement and enhancement.

32. The progressive approach includes: preliminary activities, initiating monitoring and surveillance activities, and evaluation and review of the monitoring and surveillance system.

Figure 1. Progressive approach to the design and implementation of the integrated monitoring and surveillance system for foodborne AMR



33. The progressive approach for monitoring and surveillance of foodborne AMR and AMU presented in these Guidelines is consistent with the *WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach*, and OIE standards and guidelines, especially the chapters on antimicrobial use in the *OIE Terrestrial Animal Health Code* and *OIE Aquatic Animal Health Code* and reporting options of the OIE's guidance for the collection of data on antimicrobial agents used in animals as described in the *OIE Annual Report on the Use of Antimicrobial Agents in Animals*.

7.1. Preliminary activities

7.1.1. Establishing the monitoring and surveillance objectives

34. The establishment of monitoring and surveillance objectives is an important initial step in the design and implementation of activities. This should be done in a consultative manner by the competent authorities and stakeholders. It should take into consideration national action plans (NAPs) and knowledge of the AMR and AMU situation, as well as any existing activities to address AMR in the different sectors (animal, plant, environment and human health sectors). Competent authorities should identify the challenges that they currently face during the implementation of these activities.

The following aspects should be defined:

- The primary reasons for the data collection (e.g., to evaluate trends over time and space, to provide data useful for risk assessments and risk management, to obtain baseline information on foodborne AMR and AMU, to provide harmonized data that can be easily compared, exchanged, used or aggregated locally, nationally or internationally).
- The comprehensiveness of the monitoring and surveillance program (e.g., nationally or regionally representative data or convenience sampling).
- The setting of proposed timelines (e.g., reporting on an annual basis).
- A description of how the information will be communicated (e.g., shared in an annual report to interested stakeholders, publication and accessibility of data to enable further analysis, information exchange through networks).

35. A confidentiality and data management policy should be in place.

7.1.2. Considerations for prioritization

36. When establishing monitoring and surveillance priorities, competent authorities should consider the epidemiology and public health implications of foodborne AMR, AMU patterns, information on food production systems, food distribution, food consumption patterns and food exposure pathways.

37. Monitoring and surveillance priorities for microorganisms and resistance determinants, antimicrobials, food commodities and sample sources should be informed by national, regional and international data and knowledge where it exists. Competent authorities should identify existing data sources and gaps (national or regional data as a priority) on AMR and AMU in different sectors. Information from risk profiles and risk assessments, where these exist, should also be used.

7.1.3. Infrastructure and resources

38. Once the objectives and priorities have been established, the competent authority should determine the infrastructure, capacity and resources required to meet the objectives and determine which of the elements in the programs described in section 7.2 can effectively be implemented first and which could be implemented at a later stage when additional resources become available.

39. The evolution of surveillance and monitoring programs does not need to strictly follow the order described in these Guidelines; these are logical options for expansion, which may require increasing resources. Programs for AMU monitoring can proceed at a different rate than programs for AMR monitoring and surveillance and vice versa. However, as both types of data benefit from a joint analysis, it is useful if the programs are aligned during development to allow for integrated analysis.

40. In advance of launching the AMR monitoring and surveillance activities, in order to optimize resources and efforts, the competent authority should consider the possibilities of integration of the activities in already ongoing monitoring or surveillance programs or other activities. For example, on ongoing monitoring of pathogenic foodborne bacteria.

41. The competent authority should also carefully consider coordination of sampling and laboratory testing, coordination with relevant stakeholders, and develop a plan for collation and analysis of the data in a central repository. As part of initial planning, the competent authority should also consider where harmonization and standardization are required to meet monitoring and surveillance objectives.

7.1.4. Key design elements to be established before initiating the monitoring and surveillance activities

42. When designing the monitoring and surveillance system, the following elements should be identified and established:

43. Antimicrobial resistance:

- The highest priority microorganisms, panels of antimicrobials and commodities (see section 8) to be targeted based on any existing national data and international recommendations.
- The food production and distribution chain, points in the food chain and sampling frequency to undertake sampling to meet monitoring and surveillance objectives.
- Representative sampling methods, sampling plans, laboratory analysis and reporting protocols.
- Standardized and harmonized methodologies (e.g., laboratory testing) and best practices with those used in other sectors.
- Capacity requirements.

44. Antimicrobial use:

- Antimicrobial distribution chains from manufacturing or import to end-user including sales/use data providers.
- The sectors where collection of data would be most relevant and efficient to meet surveillance objectives.
- An assessment of the need to establish a legal framework before initiating collection and reporting of antimicrobial sales and use data in food producing animals and crops (see section 9) or to start the collection of AMU data on a voluntary basis in agreement with stakeholders that provide the data.

45. Undertaking pilot studies and testing can provide valuable inputs into the design for both AMR and AMU surveillance systems.

7.2. Initiating and developing an integrated monitoring and surveillance system

46. When initiating and developing an integrated monitoring and surveillance system, the following three areas should be considered for progressive development: antimicrobial resistance program, antimicrobial use program and analysis and reporting.

47. The phases described below are guidelines for development and enhancement of integrated monitoring and surveillance system. These Guidelines are intended to provide a continuum of flexible options for implementation and expansion of the system, considering resources, infrastructure, capacity, and priorities of countries.

7.2.1. Antimicrobial resistance program

A. General considerations

48. The initial scope and design of the AMR program may be informed by previous surveys and by national and international experience and recommendations. As the AMR program develops, the scope and design may be refined and adapted as appropriate based on the following factors:

- Monitoring and surveillance findings.
- Epidemiology of antimicrobial-resistant micro-organisms (primarily in humans, but also in the food chain, environment, etc.).
- Risk profile and risk assessment findings.

49.The competent authority may launch additional pro-active monitoring and surveillance activities such as point prevalence surveys or exploratory sampling to determine whether any modifications to the program are needed, e.g. whether a new food commodity should be incorporated into the core surveillance program.

B. Sampling sources and stages in the food chain

50. When identifying the sampling sources to be included in the AMR monitoring and surveillance program, consideration should be given to the major direct and indirect food exposure pathways throughout the food chain.

51. The program can start by targeting a limited selection of sampling sources (e.g. limited number of food-producing animal species, crops/plant species, foods) at specific points in the food chain (e.g. farm, harvest, slaughterhouses, processing plants, retail).

52. Additional sampling sources and stages in the food chain can be incorporated progressively according to priorities and resources as implementation advances. For example, the program can expand to include a broader number of animal species, crop species and food commodities, and other sources such as feed, water, waste water, reclaimed water, sewage sludge, manure, surface water, etc.

C. Sampling plans

53. The sampling plan should describe the sampling procedures required to obtain representative samples for collection from the animal/crops/food commodities or production environment, at the specific point in the food chain (e.g. caecal content or carcass swabs from fattening pigs in slaughterhouses).

54. As the program develops, the sampling plan should gradually broaden to be more representative of the national population of interest, with the ultimate goal of having a sampling plan representative of the national population. For example, surveillance of abattoirs according to slaughter volume, with stratification within animal species (e.g. broilers, layers,) and sample size sufficient to establish prevalence or to detect changes.

D. Target microorganisms

55. The initial program may be based on phenotypic susceptibility testing for resistance of representative zoonotic/pathogens (e.g., *Salmonella* spp. and *Campylobacter* spp.) and indicator bacteria (e.g., *Escherichia coli*). The program may be expanded by including a broader range of foodborne pathogens (e.g. methicillin-resistant *Staphylococcus* aureus (MRSA)) and indicator bacteria *(e.g. Enterococcus* spp).

56. Subsequent program development could include testing for genetic determinants of resistance and mobile DNA elements (e.g. plasmids, transposons).

57. AMR testing of animal/plant pathogens could be used to provide additional information about the selection pressure resulting from AMU.

E. Antimicrobials tested

58. Antimicrobials to be tested should be prioritized based on antimicrobials that have been ranked as highest priority for human health (e.g. as defined by WHO in the *List of Critically Important Antimicrobials for Human Medicine*) and other relevant antimicrobials that have an influence on the selection or co-selection of resistance. Additional antimicrobials specified in national risk prioritization exercises may also be considered for inclusion in the susceptibility testing panels.

7.2.2. **Antimicrobial use program**

A. Source of antimicrobial use data

59. The source of the data collected and the way the data are reported may vary between countries and may change as the implementation of the AMU program develops.

60. A basic source of data regarding antimicrobials intended for use in animals and crops is the collection of antimicrobial sales data from manufacturers and importer/exporter data. Sales data of antimicrobials may be collected in addition, from other sources like wholesalers, retailers, pharmacies, feed mills or other agricultural associations.

61. Through pilot studies competent authorities could explore collection of antimicrobial use data from farmers, veterinarians and plant protection specialists.

62. The AMU-program may evolve to include collection of AMU data from end-user sources , such as collection of use data from veterinary prescriptions and farmers records with increasing national coverage of the data.

B. Reporting

63. The way of analyzing and reporting AMU data may vary depending on the type and source of the data collected, the level of detail of these data and the monitoring and surveillance objectives.

- Reporting of overall amount of antimicrobial agents sold for use in animals and plants/crops may include:
    - Antimicrobial class.
    - Type of intended use (e.g. therapeutic/growth promotion).
    - Animal/plant species groups (e.g. terrestrial/aquatic food producing animals, type of vegetable, fruit).
    - Route of administration.
- Reporting of AMU data could be expanded as follows:
    - Adjusted by the estimated animal population size and land area used for plants/crops, when this information is available.
    - Competent authorities could explore voluntary or regulatory options for stratifying sales data to create estimates of sales by animal/plant species.
    - Overall amount used in animals and crops by antimicrobial class, stratified by type of use, species group and route of administration.
    - Antimicrobial use data presented using different metrics (e.g. Defined Daily Doses (DDD), Defined Course Doses (DCD)).

7.2.3. Analysis and reporting

A. Integrated analysis and reporting

64. The possibilities for integrated analysis and reporting of AMR and AMU data may differ between countries. Factors influencing the degree of integration include the level of development of the monitoring and surveillance system, type of data available, the extent of cross-sectorial collaboration, organizational and legal aspects for data sharing, etc.

65. The integrated analysis and reporting may start by including a sector-specific descriptive analysis and reporting of AMR data from the food chain and analysis and reporting of quantities of antimicrobials intended for use in animals and crops.

66. As the program develops:

- More sectors may be included in the descriptive analysis.
- Reporting of individual isolate AMR data (instead of aggregated data) may be considered.
- Enhanced surveillance information may be included through active follow-up or collection of supplementary epidemiological data.
- Linkage of information from various sources may increase to develop more comprehensive analysis across sectors.
- Identification or quantitative epidemiological modelling of sector specific risk/protective factors for AMU or risk/protective factors for AMR can be undertaken.

67. In the initial phase, analysis and reporting may include the collection of information from different sectors (e.g. humans, animal species, plants/crops, food production environment), bacterial species, across regions or time, and a summary of key findings.

68. Subsequent advancement could include integration of information and statistical or epidemiological modelling across the sectors (e.g. humans, animal species, food, plants/crops, food production environment), across bacterial species, across regions (geographical information systems) or time (trend analysis), or between use and resistance. Integration could include graphical display of harmonized data. Graphical charts could illustrate and compare multiple surveillance components at the same time (e.g., bacterial resistance in samples collected from several points along the food-chain up to humans, alignment with findings from whole genome sequencing, and relevant AMU practices).

69. Advanced analytics may be a link between surveillance data and surveillance-based research.

B. Link with risk analysis processes

70. Monitoring and surveillance data can be progressively included in risk analysis activities (risk management and assessment/risk profiling activities) such as:

- Prioritizing which AMR food safety hazard(s) need to be evaluated first.
- Decision-making by risk managers/policy makers on whether to develop a risk profile or conduct a risk assessment based on the priority AMR food safety hazards.
- Conducting qualitative or quantitative risk assessments as needed.
- Identify risk management options, including informing interventions for disease prevention and control and to evaluate risk management interventions to reduce risk.
- Risk communication about priority AMR food safety risks.
- Periodic review and refinement and update of risk analysis in light of new data reported and new technologies.
- Commissioning of *ad hoc* research projects for targeted data collection and for risk assessment and surveillance methodological improvement.

71. Risk assessment findings can continuously be used to review and improve the monitoring and surveillance system.

7.3. Evaluation, review and adjustment or expansion of the monitoring and surveillance program

72. Evaluation and review of the monitoring and surveillance activities are needed to ensure the objectives are being met and that planned activities are being achieved. The evaluation and review should be undertaken at a frequency appropriate to integrate evolving monitoring and surveillance methodologies and to respond to changing national needs as determined by risk analysis.

73. The competent authority should develop a framework and plan to facilitate the evaluation and review of monitoring and surveillance activities (see section 11) which could include the following aspects:

- Indicators to effectively track the progress of the monitoring and surveillance program.
- Periodic evaluation of the monitoring and surveillance program to ensure quality and that the results are a robust, representative and a reliable indicator of AMR or AMU.
- Use of the data generated from the evaluation of activities and risk profiling to adjust the monitoring and surveillance program if required, for example to expand to a wider scope of pathogens, foods and antimicrobials, taking into consideration resource allocation and priorities.
- Development and inclusion of new monitoring and surveillance tools (e.g. whole genome sequencing to facilitate genomic characterization of bacteria).

74. As resources and capacity may increase, and the design of the monitoring and surveillance program may change periodically, the competent authorities should ensure that all interested stakeholders are kept informed. Adjustments or changes in the program should strive to ensure that the ability of the program to identify trends over the time remains.

75. The expansion of system should be done in alignment with the program design in order to continue to meet the monitoring and surveillance objectives in the country.

8. Design of a monitoring and surveillance program for AMR

8.1. Elements of an integrated monitoring and surveillance program for AMR

76. To ensure that the monitoring and surveillance objectives are met, whatever the stage of implementation, an integrated program for monitoring and surveillance of foodborne AMR should include and systematically review the following design elements and technical characteristics:

- Sampling plans (representativeness, frequency, sample size, etc.) that are statistically robust enough to provide the desired level of statistical significance and power to detect differences over time or between populations.
- Sample sources (incl. type of samples) and sampling methodology for the collection of isolates to test AMR.
- Target microorganisms based on public health relevance (foodborne pathogens and indicator bacteria) and resistance determinants taking into account new information on emerging AMR hazards.
- Antimicrobials to be tested and genes to be detected.
- Laboratory testing methodologies and quality control/assurance procedures that are appropriate, harmonized and standardized.
- Data management activities (collection, validation, storage, analysis, sharing and reporting).

8.2. Sampling design

77. Monitoring and surveillance programs may include, but are not limited, to the following types of design for sample collection:

- Cross-sectional point prevalence surveys. These surveys can be used to collect basic information and compare between various populations at particular points in time.
- Longitudinal monitoring. These studies can be used to routinely and continuously collect data over time and provide valuable information on temporal trends. Longitudinal monitoring may be carried out by conducting repeated cross-sectional surveys at fixed intervals.
- Investigative, targeted surveillance and short-term *ad hoc* pilot studies. These studies can be used, for example, to obtain data on specific subpopulations or data on animal/plant species or foodstuffs that cannot be justified for inclusion in routing, ongoing surveillance. Short-term *ad hoc* pilot studies can also be used to test the feasibility and reliability of planned programs, changes in laboratory or data management methodologies, etc.
- Sentinel surveillance which relies on selected reporting sites or specific providers, (laboratories. farms, veterinarians, plant health professionals, etc.) and can be used to obtain high quality data on resistance that cannot be obtained through a passive system.

78. The design of a monitoring and surveillance program may involve new infrastructure and activities only for the purpose of AMR or where available, information about AMR may be collected through existing programs designed for another purposes. For example, detection of AMR in microorganisms isolated in foodborne outbreaks investigations.

8.3. Sample sources

79. Sources of samples for AMR testing will depend on the objectives and the design of the monitoring and surveillance program, as well as the stage of implementation. Available resources and the national infrastructure may also impact decisions regarding the source and collection of samples.

80. An integrated program should reflect the food production in the country and cover samples from all stages of the different food chains. In an integrated program, samples collected from production and retail should be from the same species, e.g. samples from food-producing animals should be taken from the same animal species as retail meat samples.

81. If possible, the origin of the animal or food, crop (e.g. imported or domestic) and any other relevant information should be collected at the time of sampling.

82. Considerations for the selection of possible sample sources at different points of the food chain are described below:

- **Food producing animals**

  Selection of animal populations should be relevant to the country's production system. Samples should be, to the greatest extent possible, representative of the population being targeted as well as representative of a given epidemiological unit (e.g. holding of origin, farm, herd, flock). The prevalence of the bacterial species should be considered in order to maximize the likelihood of detection.

  Samples taken from healthy animals destined to slaughter may be collected on-farm, during transport or lairage, or at the slaughterhouse/abattoir. Collection of samples from animals not immediately entering the food chain can provide population level information on animal health and bacterial populations.

  At farm level, samples could include a variety of samples in the food-producing environment: faeces, feed, litter (bedding), dust, fluff, water, soil, sewage, sludge, manure, etc.

  At the lairage, prior to slaughter, samples could be taken from pen floors, truck/crate swabs, dust, etc.

  Samples such as caecal contents or lymph nodes could be taken post-slaughter. In some species, these samples are only representative of the pre-slaughter environment and may not provide an estimate of AMR arising at the farm level. Samples collected after slaughter but before processing (e.g. carcass, rinses and swabs) may provide an estimate of contamination arising from the slaughterhouse.

- **Plants/crops**

  The selection of crops should be risk-based and relevant to a country's production systems.

  At harvest and farm level, samples could include crops, soils, and when appropriate irrigation water. Sampling soil amendments such as manure and sewage sludge should also be considered.

  At post-harvest level, samples may be taken during transport, processing and packaging and could include samples of the plant/crop, surfaces, dust, washing or cooling water, etc.

- **Farm supplies**

  Sampling of animal feed including regular feed, medicated feed and animal organic fertilizers, and other relevant food production inputs, should be considered as part of the integrated monitoring and surveillance system, as they can be a source of resistant bacteria, such as *Salmonella*, which may be transferred to food-producing animals or be a source of crop contamination.

- **Food**

  Food sampling at processing/packing, wholesale or point-of-sale (retail) should be considered as part of the integrated monitoring and surveillance system and include both domestically produced and imported food sources.

  The place where the food samples are collected should reflect the production system in the country and the purchasing habits of the consumer (e.g. in open markets or chain stores).

  At retail level, the types of food samples could include raw meat (beef, chicken, turkey, pork, etc.), fish or seafood, dairy products, or other edible tissues (liver, kidney, muscle, fat, lung, etc.), raw produce (fruits, vegetables, nuts, etc.) and other minimally processed food. The selection of foods for surveillance should reflect production and consumption patterns in the population and the likely prevalence of AMR but may be modified periodically in order to capture multiple commodities, seasonality, or where products have been identified as high risk.

- **Environment**

  Sampling of the food production environment along the food chain (environment of animals and crops, processing, wholesale facilities and retail outlets) could be considered as part of the integrated monitoring and surveillance system and may include: faecal samples from wildlife and other animals in vicinity of cropping areas, dust, water, bedding, etc.

83. Once a sampling structure is established, consistency in sample types and methodology should be achieved for long-term, comparability and accurate interpretation of results. The feasibility of conducting *ad hoc* pilot studies on a broader range of retail products may be considered.

8.4. Sampling plans

84. When designing a monitoring and surveillance program, representativeness of the data obtained is essential to ensure quality information. Adequate sample size and design must be considered to enable valid interpretation of the data and comparability of the results and to ensure that data obtained from the selected population under investigation is representative of the target population and amenable to statistical analysis of temporal or regional trends. Methods and limitations to data interpretation should be fully described and specified.

85. The following elements should be defined when designing the sampling plan:

- Sampling strategy: Active or passive surveillance.

  Sampling may be active (prospective) or passive (samples collected for other purposes), random or systematic, statistically-based or convenience-based. Sentinel surveillance may also be employed.

  Examples of sampling strategies (Simple Random Sampling, Stratified Sampling, Systematic Sampling, etc.) are provided in Codex documents on food hygiene and methods of analysis and sampling (e.g. *General Guidelines on Sampling* (CXG 50-2004))

- Target populations: Animals, plants/crops, food, feed or environment.
- Target microorganisms and resistance determinants.
- Epidemiological units.
- Point in the food chain where the samples will be taken.
- Frequency of sampling.
- For surveys and periodic studies, the frequency of testing should be decided on the basis of the defined objectives. The incidence and seasonality of the microorganisms or diseases under study should be considered. Samples can be collected monthly or periodically throughout the year from different sites, in sufficient numbers, to identify trends.
- Statistical power and goals of testing (precision of point estimates versus sensitivity to change over time).
- Required sample size (number of isolates/samples) to detect changes in antimicrobial resistance patterns with sufficient precision and statistical power.

  Statistical methods should be used to calculate the number of samples or isolates needed for testing Sample size will depend on the purpose of the study, the desired precision for estimates of the prevalence of AMR and the magnitude of change in AMR to be detected over a specified period of time in a certain population. It will further depend on the frequency of recovery, the initial or expected prevalence of AMR in that microorganism and the size of the population to be monitored; Examples of sample size calculation can be found in national or international publications.

- Selection of strata (levels) or risk clusters (groups) to best meet surveillance objectives.
- Samples should be collected by trained persons authorized to do so (e.g. third-party accreditation).
- Procedures for storing and transporting the samples (time between sample collection and testing and temperature during transport and storage) in order to maintain sample integrity.
- Procedures should be put in place to ensure that collection of samples is carried out in accordance with to the defined sampling strategy and to guarantee that traceability, security and quality assurance/management are maintained from collection through to analysis and storage.

8.5. Target microorganisms and resistance determinants

86. In order to target appropriate bacterial species and resistance determinants, the bacteria's relevance to public health must be considered. Bacterial species studied should include both foodborne pathogens and indicator organisms or commensal bacteria.

87. *Salmonella* is a key foodborne pathogen to be included in an integrated monitoring and surveillance program as it is found in human and animal species. The inclusion of *Campylobacter* (*C. coli, C. jejuni*) is also strongly advised, as well as other food borne pathogens depending on national or regional epidemiology and risks (e.g. *Vibrio, Listeria monocytogenes)*.

88. Commensal intestinal bacteria including *Escherichia coli* and *Enterococcus faecium/faecalis* can contaminate food and harbor transferable resistance genes. These species can serve as indicators of Gram-negative and Gram-positive intestinal microflora from terrestrial animals respectively.

89. Target microorganisms for aquatic animals and food of non-animal origin should be determined based on available evidence and risk.

90. Whenever possible the monitoring and surveillance program should include genetic and/or phenotypic analysis of particular isolates that may present a public health concern (i.e. extended spectrum beta lactamases (ESBL) - AmpC beta-lactamases (AmpC) and carbapenemase-producing strains and multidrug-resistant strains).

91. Tests for virulence factors, sequencing of AMR genes, mobile genetic elements (transposons, integrons, plasmids) and molecular typing can also be applied as resources and capacity permit.

92. The selection of target microorganisms should also be influenced by the presence of high priority AMR genes or mobile genetic elements and horizontal gene transfer in a given population.

8.6. Laboratories

93. Laboratories participating in the monitoring and surveillance program should:

- Perform bacterial isolation, identification (to species level), typing, phenotypic and genotypic characterization and antimicrobial susceptibility testing (AST) using standardized and validated methods and have trained personnel in the methods used.
- Be accredited in accordance with national and/or international regulations or have a validated Standard Operating Procedure on AST for the monitoring purposes in place.
- Participate in an external quality assurance system including proficiency testing in identification, typing, phenotypic and genotypic characterization and AST of the microorganisms included in the monitoring and surveillance program.
- Store isolates and reference strains using methods that ensure viability and absence of change in the characteristics and purity of the strain.
- Have access to a national reference laboratory or an international laboratory (e.g. WHO-collaborative center) that can provide technical assistance if necessary.
- Be equipped with facilities and have procedures to maintain sample integrity (e.g. storage temperature and time between sample reception and analysis) and traceability.

8.7. Antimicrobial susceptibility testing

8.7.1. Methods and interpretative criteria

94. Susceptibility testing methods (disk diffusion or minimum inhibitory concentration (MIC) methodologies) that are standardized and validated by recognized organizations such as the European Committee on Antimicrobial Susceptibility Testing (EUCAST) or Clinical and Laboratory Standards Institute (CLSI) should be used to ensure reliable and comparable data.

95. Quality control strains of bacteria should be used according to international standards e.g. from EUCAST or CLSI. The strains used should be designed to provide quality control for all antimicrobial agents tested. The quality control strains should be maintained and propagated according to the same recommendations, and results of the quality control strains should be used to determine if results for other tested bacteria are valid before interpreting and reporting the results.

96. Interpretation of results for disc diffusion or minimum inhibitory concentrations (MICs), should also be done consistently according to EUCAST rational documents or CLSI standards, and should include quantitative results (disk diffusion zone diameters or MIC values). Categorization of the isolate should also be done based on the epidemiological cut off value (ECOFF) (wild-type or non-wild type) and when available based on clinical breakpoint (resistant, intermediate or susceptible) used for interpretation. Data interpretations using ECOFFs can be very useful as for the temporal analysis of AMR trends. The interpretative category used, ECOFF or clinical breakpoint, should be included in the reporting, interpretation and analysis of data.

97. Primary quantitative data should be maintained in order to allow comparability of results e.g. with human data, for early recognition of emerging resistance or reduced susceptibility and in order to maximize ability to analyze and compare results across sample sources.

98. Quantitative results are also necessary for the analysis of resistance patterns over time and when retrospective data analysis is needed due to changes in clinical breakpoints or ECOFFs.

99. The use of ECOFFs, as interpretive criteria will allow for optimum sensitivity for detection of acquired resistance and comparability between isolates from different origins (e.g. food, animal species). The use of clinical breakpoints may differ between animal species but may be adequate in the case of treatment decisions related to pathogenic bacteria.

100. Detailed information on interpretation of AST results and quality control are described in the *WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach*.

8.7.2.The panel of antimicrobials for susceptibility testing

101. The panel of antimicrobials for susceptibility testing should be harmonized as to ensure continuity and comparability of data. Attempts should be made to use the same antimicrobial class representatives across sample sources, geographic regions, and over time.

102. The antimicrobials included in the panel should depend on the target bacteria and the clinical or epidemiological relevance of these antimicrobials and should allow for the tracing of isolates with particular patterns of resistance. The antimicrobials included should also take into account the quantities used in the relevant agricultural sectors and their influence in the selection or co-selection of resistance. Antimicrobials that would give the best selection of cross-resistance profiling should be selected. Antimicrobials not used in veterinary medicine, but which have the potential for co-selection of resistance due to gene linkage can also be included (e.g. chloramphenicol resistance in *Salmonella*.).

103. Suggested panels of antimicrobials by bacteria for inclusion for AST can be found in the *WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach*. National lists of important antimicrobials can also be used to guide the selection of antimicrobials to be included in the panel.

8.7.3.Concentration ranges of antimicrobials

104. The concentration ranges used, should ensure that both ECOFFs and clinical breakpoints, when available, are included in order to allow comparability of results with human data. The concentration range of each antimicrobial agent should also cover the full range of allowable results for the quality control strain(s) (QC strain(s)) used for each antimicrobial agent.

105. Examples of suggested ranges of concentrations of antimicrobials can be found at CLSI and EUCAST and also at *WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach*.

8.7.4.Characterization of isolates

106. Whenever possible characterization of bacterial isolates (genus, species, and additional microbial subtyping) should be undertaken.

107. Microbial typing refers to the application of laboratory methods capable of characterizing, discriminating and indexing subtypes of microorganisms. Typing methods can be classified into two main groups: phenotypic methods, focusing on observable or measurable morphological or biochemical properties of an organism and genotypic methods, for investigating the genetic code of the organism. There are multiple typing methods available for most organisms. The choice of typing method depends on the objective and needs to be feasible for the intended use. Other factors that may influence the choice are the cost, ease of use, accessibility, capacity and capabilities to perform a specific method.

8.7.5.Molecular testing

108. Molecular testing such as polymerase chain reaction (PCR), micro and nano arrays, Sanger-sequencing, pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST) or whole genome sequencing (WGS), may be used for the detection of resistance determinants and epidemiological analysis

109. Molecular characterization such as WGS is also an important tool for use in the rapid identification of clusters, outbreak investigations, determination of epidemic source and transmission chains, detection of emergence and investigation of the spread of new resistant strains or resistance determinants; and source attribution by linking to molecular monitoring of pathogens or resistant microorganisms or resistance determinants in humans, animals, food and environmental reservoirs.

110. The use of molecular testing may be useful for the enhanced surveillance and early warning of resistant microorganisms of high public health impact such as ESBL/AmpC/carbapenemase-producing *Enterobacteriaceae*.

111. The application of molecular methods and the interpretation of the information derived from them is by nature multidisciplinary. Global agreement on methods, quality standards, analytical schemes, genomic type nomenclature for microorganisms or resistance determinants and interpretational approaches should be established to prevent variability in the interpretation of molecular test results. Laboratory and technical capacity, data management data sharing and analytical platforms to link epidemiological and microbiological information at national and international level are also important considerations.

112. Basic training and professional development in bioinformatics and genomic epidemiology should be carried out for microbiologists, risk assessors, epidemiologists and risk managers to facilitate the typing, interpretation, reporting, and use of integrated genomic epidemiology data.

113. In some countries, using WGS may cost less than using conventional AST and typing. Countries without current AMR monitoring or surveillance programs may consider WGS when developing their programs. Countries taking this approach should validate WGS findings with conventional AST. WGS approaches to surveillance are particularly suited to allow for comparison of molecular data sharing and there are several international initiatives to collect and share WGS data.

114. There are limitations to the applicability of WGS data to the risk assessment process when no correlative AST data exist. These can include whether the presence of a resistance determinant in a given isolate or sample is in fact casual of a resistant foodborne pathogen hazard and if a resistance determinant confers a clinically relevant resistance phenotype. When acquired resistance genes are identified and correlative AST data does not exist, laboratories should confirm phenotypic expression using AST.

115. It is important that laboratories undertaking molecular characterization of isolates have quality assurance programs in place for the wet and dry laboratory components of the analysis.

116. There is substantial scientific knowledge which indicates that predicting the resistance phenotype from WGS data is now possible with a high level of accuracy for certain organism and genes. New approaches are also coming through with the application of machine learning techniques for the determination of MIC. Once sequence data are generated and stored (with appropriate metadata) these data can be used for retrospective surveillance (e.g. in the case of newly discovered resistance determinants). The use of WGS also allows the integration of resistance data with other relevant data for public health such as virulence determinants.

8.8. Collection and reporting of resistance data

117. The information collected and recorded may differ depending on the step in the production chain, sampling design and the specific public health objectives.

118. Information for each individual sample should include:

- General description of the sampling design and randomization procedure.
- Specific information about the origin of the sample: food producing animal species, epidemiological unit, plant/crop, environmental or food category, country of origin, type of sample, stage of sampling in the food chain, date and place of sampling, and isolation date, etc.
- General information to identify the isolate, bacterial species, serovar, other subtyping information as appropriate (e.g.: phage type, molecular type, etc.).
- Specific information about the isolation of the bacteria and the AST: date of testing, specific information about the methods used, quantitative results (e.g. MICs in mg/L), etc. In the case of qualitative results interpretative criteria should be recorded (e.g. AST results including criteria used to identify resistant or non-wild type isolates). It is also necessary to report the International standard used for the interpretation of the results.

119. Reporting of results from the monitoring and surveillance program should be timely and preferably include information on individual isolates, specific information about sampling and methods as describe above.

120. Antimicrobial susceptibility testing methods and interpretive criteria should be clearly described, and differences transparently explained to show where data may and may not be directly comparable.

121. When results of PFGE, MLST, WGS or other DNA analysis for an individual isolate are available, tests for genetic linkage and homogeneity can be carried out between the isolate and bacteria isolated from humans, food, agricultural, livestock and aquatic products and environment.

122. The *WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach* provides detailed information about interpretation of antimicrobial susceptibility results, data analysis and reporting.

9. Collection of national antimicrobial sales and use data in animals and plants/crops

9.1. Elements of an integrated monitoring and surveillance program for antimicrobial sales/use data

123. The following aspects should be taken into account when deciding on the approach to collect antimicrobial sales or use data.

- Identification of how antimicrobials are distributed for use in agriculture (animals and crops) within the country. Contributing parties, including marketing authorization holders, wholesalers, distribution centers, pharmacists, veterinarians, farmers and importers/exporters should be identified as part of this process.
- Identification of the most appropriate points of data collection and the stakeholders that may provide the data at these points.
- Establishment of the principles for ensuring confidentiality of data supplied at national level (e.g. personal or proprietary data)Development of a protocol on the collection of data to captures qualitative and quantitative information on the antimicrobials.
- Identification of the antimicrobial agents, classes or sub-classes to be included in data reporting, based on current known mechanisms of antimicrobial activity and antimicrobial resistance data.
- Nomenclature of antimicrobial agents should comply with international standards where available.
- Establishment of the technical units of measurement and indicators of antimicrobial sales or use The units used for reporting sales and use should be based on internationally accepted methods, to enable interpretation and data sharing globally.
- Identification of the type and number of crops and food-producing animals by species, type of production and their weight in kilograms for food production per year (as relevant to the country of production) is essential basic information.
- The way of organizing the reporting of antimicrobial sales or use data may be further organized by crop type, animal species, animal categories, age groups, and by route of administration (e.g. in-feed, foliar spray, in-water, injectable, oral, intramammary, intra-uterine, topical), type of use (therapeutic vs non-therapeutic, pest-control in crops), etc.

9.2. Reporting of the national antimicrobial sales/use data for use in animals

9.2.1. International guidance on monitoring and surveillance of antimicrobial sales and use data in animals

124. The following international guidance should be taken into consideration when developing a national surveillance and monitoring system for antimicrobial sales or use data in animals:

- WHO:
  WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach (2017).

  The AGISAR guidance provides details for:

  - Surveillance of national antimicrobial sales data.
  - Surveillance of antimicrobial consumption by animal species.
  - Continuous collection of antimicrobial consumption data by animal species.
  - Collection of data from a sample of farms.
  - Stratification of sales data.

- OIE:
  The *OIE Terrestrial Animal Health Code* Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals, the *OIE Aquatic Animal Health Code* (Monitoring of the quantities and usage patterns of antimicrobial agents used in aquatic animals) and the *Guidance for completing the OIE template for the collection of data on antimicrobial agents used in animals* as included in the *OIE Annual report on antimicrobial agents intended for use in animals*.

  The relevant Chapter of the OIE Terrestrial Animal Health code provides information about the sources of antimicrobial data (basic, direct, end-use and other sources) and about the types and reporting formats of antimicrobial usage data.

The OIE *Annual report on antimicrobial agents intended for use in animals* provides a detailed template for the collection of data on antimicrobials used in animals, with different options for the level of reporting of antimicrobial data. The information can be divided as follows:

- Baseline information.
- **Option 1**: Quantities of antimicrobial agents sold for/used in food-producing animals by antimicrobial class, with the possibility to separate by type of use.
- **Option 2**: Quantities of antimicrobial agents sold for/used in food producing animals by antimicrobial class, with the possibility to separate by type of use and species group.
- **Option 3**: Quantities of antimicrobial agents sold for/used in food producing animals by antimicrobial class, with the possibility to separate by type of use, species group and route of administration.
- Whenever possible the above data should be provided with an estimate of the animal population that has been exposed to the antibiotics (see below).

125. Data on quantities of antimicrobials sold and used at national level may differ. Proper analysis of the data collected, and additional information may be necessary to understand these differences. For example, differences in data source, different data providers, stocks in some points of the supply chain could be reason for differences between sales and use data.

9.2.2. Antimicrobial quantities (numerator)

126. Numerator in the context of antimicrobial data consumption represents the amount of antimicrobials sold or used

127. The minimum data collected to estimate the amount of antimicrobials should be the weight in kilograms of active ingredient of the antimicrobial(s) intended for use in food-producing animals per year. It is possible to estimate total usage by collecting sales data, prescription data, manufacturing data, import and export data or some combinations of these.

128. For active ingredients present in the form of compounds or derivatives of product/presentation, the strength of each active entity of the molecule should be recorded. For antimicrobial agents expressed in international units, the factor used to convert these units to kilograms of active entity should be applied.

129. Information on dosage regimens (dose, dosing interval and duration of the treatment) and route of administration are important elements to include when assessing antimicrobial usage in food-producing animals.

9.2.3. Animal population (denominator)

130. The denominator in the context of antimicrobial consumption is the animal population at risk for being treated (with antimicrobials).

131. Variables such as number of animals per farm/species/categories/production, weight of the animals in the population, or differences in how animal species metabolize antimicrobials are important for the interpretation and assessment of the amount of antimicrobials sold or used (numerator). A denominator representing the animal population at risk of being treated with the antimicrobials should enable a better overview/indication of the consumption data and should facilitate the reporting and the comparability of data. The denominator chosen should be representative to the species, production type, etc.

132. The desired denominator for reporting of antimicrobial sales or use should be determined in advance. This denominator should consider the country's available data on animal populations and animal weights and reflect the surveillance design and objectives. Examples, of denominators include the animal biomass for national sales data, or 1,000 animal-days for antimicrobial use data from a sample of farms.

- The estimate animal biomass of food producing species at risk of being treated with antimicrobials should be calculated. The OIE provides a biomass denominator suitable for global reporting of quantities of antimicrobial agents intended for use in animals. Different productions practices and slaughtering or marketing weights make it challenging to develop one biomass calculation that would be equally applicable to every national situation, therefore calculation of the national animal population is desirable for reporting at national level. The European Surveillance of Veterinary Antimicrobial Consumption project has provided a methodology for the calculation of such animal population for sales data reported at EU level; this methodology has been adopted by other countries outside of the EU (e.g., Canada). Furthermore, the US Food and Drug Administration recently published a proposal for the estimation of the animal population.

- For sampled farm data, the number of animals and the time they are under surveillance is critical context for reporting antimicrobial use data. Common denominators reported in the literature for sampled farm data include 1,000 animal-days or 100 animal-days.
- Other examples of denominators may be the total weight of slaughtered or marketed animals, animal years, kg live weight sold or slaughtered, etc.
- The total number of food-producing animals by species, type of production and animal weight in kilograms for food production per year (as relevant to the country of production) is important information that should be collected where possible.

9.2.4. Units of measurement

133. Standardized units of measurement for reporting antimicrobial sales and use in specific food producing animal species should be used

134. Examples of units are: mg of active substance/kg of animal biomass, number of Defined Daily Doses for animals (DDDvet), number of Defined Course Dose for animal (DCDvet), etc.

135. Units of measurement described in international guidelines to collect antimicrobial use data should be used where possible (OIE instructions for collecting antimicrobial use data).

9.3. Reporting of the national antimicrobial sales/use data for use in plants/crops

136. The following aspects should be taken into account when deciding on the approach to collect antimicrobial sales or use data:

- Baseline information on what antimicrobials are registered for use in which plants/crops.
- Collection of amounts sold/used in plants/crops:
    - **Option 1**: Overall amount sold for/used in plants/crops by antimicrobial class, with the possibility to separate by plant/crop type (e.g. fruit trees, grains, vegetables, field vegetables vs greenhouse vegetables, nuts).
    - **Option 2**: Overall amount sold for/used in food and feed crops by antimicrobial class, with the possibility to separate by plant/crop type and specific crops.
    - **Option 3**: Overall amount sold for/used in food and feed crops by antimicrobial class, with the possibility to separate by plant/crop type and specific crops, and specific disease and pathogen.
- Collection of relevant data from farms and agriculture land where waste derived fertilizers and antimicrobials as pest-control products are applied.
- Other plausible entry routes of antimicrobials in crop production such as but not limited to land application of biosolids, animal by-products and municipal waste.
- Reporting of the national antimicrobial sales/use data for use in crops should consider collecting relevant data from farms and agriculture lands where waste derived fertilizers and antimicrobials as pest-control products are applied.

10. Other considerations for the implementation of the monitoring and surveillance program

10.1. Management of data

137. To ensure consistent collection and analysis of resistance data, sampling information should be recorded down to individual sample level and should be kept in a national digital database where possible.

138. To properly manage test results and data generated through of the integrated monitoring and surveillance program, a digital database that guarantees security, confidentiality and integrity of data is needed. At a national level, one common location of data is preferred, with one database for AMR information and one database for AMU information.

139. The database should allow the appropriate and easy extraction of data when required and for expansion as the integrated monitoring and surveillance program improves.

140. Ongoing (or regular) validation of the data should be ensured.

141. A description of sampling designs, stratification and randomization procedures per animal populations and crop/plant, environmental or food categories should be provided with the data.

142. For AMR ideally, data should be collected and stored at isolate level with each bacterial species and sample source reported to the database separately.

10.2. Analysis and reporting of results

143. Results of AMR monitoring and surveillance should be compared with results of AMU monitoring and surveillance to evaluate trends over time and that the data can be used as described in CAC/GL 77/2011 for risk analysis purposes and to inform the development and implementation of appropriate risk management options and policies to ensure responsible and prudent use of antimicrobials and to address foodborne AMR.

144. Results of AMR and AMU monitoring and surveillance should be published annually where resources allow. When available, summary reports about AMR in humans, agricultural, livestock and aquatic products and environment can be published.

145. Data from the samples and use data can be integrated with data from other sources (e.g. human isolates).

10.3. Integrated analysis of results

146. Combined analysis of results and data of a program of integrated monitoring and surveillance of AMR in foodborne bacteria comprises the comparison and synthesis of AMU in humans, animals and crops and AMR data across all sectors including humans, food-producing animals, plants/crops, retail foods, and the environment. The detailed methodology of the surveillance system and epidemiological context should also be incorporated to the analysis. Where data is available, exposure pathways among people, animals, crops and their shared environment connecting resident bacterial populations could be incorporated to the analysis.

147. The data may originate from different monitoring and surveillance systems, and comparability is an important factor to consider in the design of the monitoring and surveillance program. The choice of analytical approaches should allow the investigation of the relationship between use and resistance within the animal, plant/crops and human populations, as well as additional associations between equivalent data within all relevant populations, provided that AMR and AMU data are representative. Appropriate statistical analysis such as univariate (logistic regression) and multivariate analysis should be used to ensure accuracy.

Integration of data from foodborne human isolates

148. Integrated monitoring and surveillance of foodborne AMR should be aligned with surveillance in human populations to ensure comparability of results and inferring relationships between AMR and AMU. Key considerations for data analysis include analysis of relevant human isolates to include data from significant foodborne pathogens according to national epidemiological information (e.g. *Salmonella*, *Campylobacter*) and, whenever possible, commensal flora such as *E. coli* and *Enterococcus*. Integration of results with surveillance of human clinical isolates should facilitate identifying trends in resistance to specific antimicrobials important for human treatment, as well as identify trends in the occurrence of resistance to other antimicrobials of human and animal importance. The surveillance of human isolates will allow comparison with isolates from the food chain and environment.

149. Isolates obtained for AMR surveillance should also include representative isolates from sporadic and outbreak foodborne disease cases.

150. Guidance on conducting antimicrobial resistance surveillance of human isolates is provided by the WHO Global Antimicrobial Resistance Surveillance System (GLASS).

10.4. Additional research and targeted investigation

151. Additional research in the national setting to improve the understanding and knowledge of AMR e.g. food source attribution studies, point prevalence studies, surveys, etc. should be considered.

152. Other targeted investigation which is not included in the routine AMR monitoring and surveillance program may be needed at national or local level as risk management response to surveillance activities and actions, e.g. incorporating real-time “Critical Resistance” Alert Systems.

11. Evaluation of integrated surveillance programs

153. The evaluation of an integrated monitoring and surveillance system promotes the best use of data collection resources and provides assurance that systems operate effectively. Evaluation of systems also provides assurance the data and information reported is robust and surveillance objectives are being met.

154. The steps in developing an evaluation framework include:

- Identify the skills needed by evaluators.
- Describe the monitoring and surveillance system to be evaluated, including the objectives and desired outcomes (this may include a subsection of the entire system such as the sample collection component, laboratories, analysis and reporting).
- Identify key stakeholders for the evaluation.
- Identify key performance criteria to be evaluated.
- Collect evidence against the key performance criteria.
- Report results on evaluation.
- Draw conclusions on components of the evaluation.
- Share evaluation outcomes with stakeholders.

12. Risk communication

155. The implementation strategy of the monitoring and surveillance system should include the development a of risk communication plan which defines the objectives, the evaluation process and allows for timely improvement of the plan.

156. Risk communication processes should allow the development of partnerships between the competent authorities and stakeholders. Such partnerships should facilitate communication between parties and the involvement and commitment of stakeholders in the development and implementation of the AMR monitoring and surveillance activities and other related risk management options.

157. An integrated monitoring and surveillance system of foodborne AMR will generate data and information of interest to the competent authorities and a wide range of stakeholders, including risk managers, veterinarians, farmers, food manufacturers, retailers, consumers, etc. Special attention should also be given to the communication strategy between the competent authorities and the different stakeholders.

158. Additional guidance on how to communicate risk can be found in the *Working Principles for Risk Analysis for Food Safety for Application by Governments* (CXG 62-2007) and the *Guidelines for Risk Analysis of Foodborne AMR*.

13. Training and capacity building

159. A tiered approach to the implementation of this guidance at the national level is recommended. Programs should aspire to use effectively available resources, technical capability and take advantage of potential for cross-sector integration while seeking continuous improvement.

160. Training programs such as capacity development programs carried out by FAO/WHO/OIE should include capacity to train the personnel of the relevant competent authorities in different aspects of the monitoring and surveillance system. This should include the capacity to train personnel in the collection, analysis and reporting of the monitoring and surveillance data.

APPENDIX II

LIST OF PARTICIPANTS

Chair

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Codex Members

- Armenia
- Australia
- Belgium
- Brazil
- Canada
- Chile
- China
- Costa Rica
- Denmark
- Finland
- France
- Germany
- Ghana
- India
- Iran
- Ireland
- Japan
- Kazakhstan
- Macedonia
- Madagascar
- Malaysia
- Morocco
- Mexico
- Netherland
- New Zealand
- Nicaragua
- Nigeria
- Norway
- Poland
- Republic of Korea
- Russian Federation
- Saudi Arabia
- Singapore
- Slovakia
- Sweden
- Switzerland
- Thailand
- Uganda
- United Kingdom
- United States
- Uruguay

Codex Member Organization

- European Union

Codex Observers

- Consumers International (CI)
- The Consumer Goods Forum (CGF)
- CropLife International
- HealthforAnimals
- International Association of Consumer Food Organizations (IAFCO)
- International Dairy Federation (IDF)
- International Feed Industry Federation (IFIF)
- International Meat Secretariat (IMS)
- World Organisation for Animal Health (OIE)
- World Veterinary Association (WVA)