CODEX ALIMENTARIUS COMMISSION

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Agenda Item 6 **CRD 3**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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

Seventh Session

REPORT OF PHYSICAL WORKING GROUP ON THE PROPOSED DRAFT GUIDELINES ON INTEGRATED MONITORING AND SURVEILLANCE OF FOODBORNE ANTIMICROBIAL RESISTANCE

A physical working group (PWG) was held on 8 December in Pyeongchang, Republic of Korea to consider the proposed draft revision of the Guidelines on integrated monitoring and surveillance of foodborne antimicrobial resistance (CX/AMR 19/7/6) in light of the comments received from Members and Observer organisations in response to CL 2019/83-OCS-AMR. Those comments had been compiled in papers CX AMR 19/7/6 Add.1 and CRD's 5, 8, 9, 10, 12 and 13. The chair of the EWG prepared a revised version of the Draft Guidelines on integrated monitoring and surveillance of foodborne antimicrobial resistance taking into consideration comments received, presented as CRD11. This was used as the basis f or the discussions on the PWG. An overview of the contents of the Guidelines was also shared with the PWG (See Annex 2)

The PWG was chaired by the Netherlands assisted by New Zealand and was open to all Members and Observers attending TFAMR7.

The PWG discussed the proposed draft Guidelines on integrated monitoring and surveillance of foodborne antimicrobial resistance (CRD11) and completed its review of Sections 1 to 7. The PWG made several changes to the text in these sections, as summarised below and reflected in the revised version of the Guidelines attached as Annex 1. Sections 8 to 13 and the Appendix could not be addressed due to time constraints.

The PWG agreed to make the following changes throughout the document:

- Replace "monitoring and surveillance system" with "monitoring and surveillance programme"
- Replace "throughout the food chain" with "along the food chain".
- Replace "progressive approach" with the concept of "continuous improvement", noting that each replacement would need to be considered as there were some contexts in which the term 'progressive' may still be appropriate or necessary

Key discussions and decisions in sections 1-7 were as follows:

Section 1: Introduction and purpose:

Para 1. Agreed with the revisions proposed in CRD11 and further revised the paragraph by deleting 'risk analysis', combining the first and last sentences and inserting 'foodborne' before AMR for clarity.

Para 2, 3: Agreed with the text as proposed in CRD11.

Para 4: Revised to remove use of the word 'essential'.

Para 4bis: Completely revised the paragraph to address concerns regarding reporting of monitoring and surveillance data to international organizations and the potential interpretation that data would only be shared on a reciprocal basis.

Para 5: Agreed with the revisions proposed in CRD11, further revised to clarify that it referred to integrated monitoring and surveillance programs and deleted reference to promotion and protection.

Paras 6, 7: Agreed with the text as proposed in CRD11.

Para 8: Revised the first sentence for clarity but questions were raised as to its necessity. Noted concerns regarding the issue of data comparability and agreed to retain the paragraph in square brackets for further discussion.

Para 9: Deleted reference to design and as there was no consensus on whether to refer to improvement or strengthening of monitoring and surveillance programs, retained 'improve/strengthen' in square brackets.

Moved the last sentence to a new paragraph, changed ‘evolve’ to ‘be assessed on its efficiency’ and inserted ‘foodborne’ before AMR.

Para 10: Agreed with the revisions proposed in CRD11, changed ‘AMR scenarios’ to ‘National situations’, agreed to change ‘gradual’ to either ‘continuous’ or ‘progressive’ for consistency with the remainder of the document, but given the ongoing discussion on regarding use of ‘progressive’ or ‘continuous’ approach, agreed to retain these terms in square brackets for revision once this issue was resolved.

Paras 11, 12. Agreed to retain these under the introduction.

Section 2: Scope

Paras 13, 14: Combined these two paragraphs and edited for clarity.

Para 15: Agreed as proposed in CRD11

Para 16: Moved ’of public health significance’ from the end of the paragraph to immediately after ‘foodborne pathogens’ for clarity.

Para 17: Agreed as proposed in CRD 11

Para 18: Deleted as proposed in CRD 11

Section 3: Definitions

It was agreed to add a preamble to reference the definitions in the other AMR related text namely the Code of Practice and CXG-77. ‘One Health approach to AMR’ was changed to ‘One Health Approach’ to align with the COP. The definitions were otherwise not discussed as all were also included in the COP and it was agreed to align all definitions. The definition for Antimicrobial Resistance (from CXG 77) was included due to its frequent occurrence in the text.

Section 4: Principles

The chapeau text was removed as it was already covered in the introduction.

Principle 1: Agreed as proposed

Principle 2: Revised to include ‘food production environment’, and to add ‘the risk of’ before ‘foodborne AMR’. No consensus were reached on the whether monitoring and surveillance programs were a fundamental part of national strategies, the inclusion or reference to action plans and whether monitoring and surveillance was an important component or contributes to a national food safety system so these aspects were retained in square brackets for further discussion.

Principle 3: Agreed to the proposal in CRD 11 to delete the last part of the sentence regarding reporting but put the remaining text in square brackets as there was no consensus on whether the principle should focus on ‘implementation’ or ‘improvement’ and whether progressive also applied to design of programmes.

Principle 4: Agreed with the proposal in CRD 11 to delete the examples, and additionally deleted ‘policy initiatives’ and replaced ‘support to risk analysis’ with ‘an input into risk analysis’.

Principle 5: Agreed on the proposed revisions in CRD 11, inserted ‘foodborne’ before ‘AMR’ and deleted the rest of the sentence.

Principle 6: Agreed on the proposed revisions in CRD 11, to delete the examples and move them to Section 7 (para 37).

Principle 7: Agreed to delete the second sentence as this was too detailed for a principle.

Principle 8: Put the text relating to external proficiency testing in square brackets for further consideration as part of a principle or whether it was adequate to include it in section 8.

Principle 9: Included ‘where available’ after ‘interpretative criteria’ and put the text relating to sharing/reporting information at the international level in square brackets for further consideration.

Principle 10: This was not discussed and it was agreed to return to this principle only after completion of the remainder of the document to determine if it was needed/appropriate.

Section 5: Risk-based approach

Para 20: Revised ‘relationship with risks’ to ‘potential to pose risks’. Inserted ‘foodborne’ before ‘AMR’ but retained it in square brackets for further discussion.

Para 21: Revised the text by replacing ‘data regarding AMR transmission……..’ to ‘data from other sources when available’ and replaced ‘to protect human plant and animal health’ with ‘to prevent and minimize foodborne AMR’

Para 22: Revised to include ‘scientific’ before the first mention of ‘knowledge’ and to replace the second mention with ‘relevant evidence’. Replaced ‘probable’ with ‘possible’, replaced ‘…..many countries’ to ‘when its limited’ and removed the square brackets from ‘initially’.

Para 23: Agreed to delete

Para 24: Proposed to delete and to consider a new proposal that is included in square brackets for further consideration

Paras 25 and 26: Put the text in square brackets for further consideration under Section 11 (Evaluation)

Section 6: Regulatory framework, policy and roles

Para 27: Agreed as proposed in CRD 11 and additionally ‘counterparts’ was changed to ‘stakeholders’ for clarity and ‘should’ changed to ‘’could’.

Para 28: Agreed as proposed in CRD 11 and additionally the sentence including the examples of stakeholders was deleted.

Paras 29 and 30: Deleted as proposed in CRD11

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

Title: Revised with the deletion of “a progressive approach for’’

Para 31: Put the text relating to progressive in square brackets for further consideration on whether it should be changed to ‘continuous improvement’ and if ‘progressive’ should be introduced before ‘implementation’. Added a reference to the description of ‘continuous improvement’ in CXG 82 in a footnote and deleted ‘enhancement’ at the end of the sentence.

Para 32: Merged with para 31.

Figure 1: Replaced with the figure presented in CRD12, noting that it may need to be amended following conclusion of discussions on Sections 8-11 of the document.

Para 33: Deleted as proposed in CRD 11

Para 34: Agreed with proposals in CRD 11 and additionally ‘knowledge’ was replaced by ‘relevant evidence’ and bullet 4 was deleted.

Paras 35, 36: Agreed as proposed in CRD 11

Para 37: Agreed as proposed in CRD 11 and examples from principle 6 were already included which the exception of food commodities, which the PWG agreed to delete.

Paras 38-42: Agreed as proposed in CRD11.

Para 43: Changed ‘commodities’ to ‘sample sources’ and inserted ‘based on any existing national data and international recommendations’ in square brackets

Paras 44: New text proposed for bullet 2 inserted in square brackets for further consideration.

Paras 45: Agreed as proposed.

Para 46, 47: Agreed as proposed in CRD11 and additionally ‘enhancement’ was replaced with ‘continuous improvement’.

Other points discussed:

The PWG did not reach consensus on the need to introduce ‘foodborne’ before AMR throughout the document. Some considered it was necessary to clarify to scope of the document, while for others it was sufficient that this was indicated in the title and scope. It was noted that a introducing a sentence defining foodborne AMR, for example in the scope, may be of help.

The chairperson informed the PWG that Subsection 9.6 in the CRD11 document should be included under Section 10.

Annex 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 "One Health" approach for the design and implementation of national programs of monitoring and surveillance of foodborne 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 programs includes the coordinated and systematic collection of data or samples at appropriate stages along the food chain and the testing, analysis and reporting of AMR and AMU. An integrated programs 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/plants and the food production environment. Depending on national priorities, food safety AMR issues, scientific evidence, capabilities and available resources, an integrated monitoring and surveillance programs can be implemented progressively.

4. The data generated by integrated monitoring and surveillance programs provide valuable information for the risk analysis of foodborne AMR. These data could also be useful for epidemiological studies, food source attribution studies and other 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 There is value in sharing standardized and harmonized data from national monitoring and surveillance programs with international organizations.

5. Integrated monitoring and surveillance programs also contribute to public health outcomes by providing information on 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 to gather AMU and foodborne AMR data throughout the food chain.

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

8. [Each monitoring and surveillance program should be designed to be relevant for national circumstances. The design should be informed by~~all~~ available ~~knowledge~~ scientific information on foodborne risks due to AMR~~while taking into consideration the international dimension of AMR~~, where appropriate, and the need for harmonized data collection standards ~~comparability among countries or~~ between sectors.]

9. New scientific knowledge should be incorporated into integrated monitoring and surveillance programs as it becomes available to [improve/strengthen] the programs and to enhance analysis and utility of existing information and data.

9. Bis. Design and implementation of systems should also be assessed on its efficacy when foodborne AMR policies and priorities change at the national and international level.

10. National situations are likely to vary among countries and these Guidelines should be used to foster a [progressive/continuous] 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 [progressive/continuous] approach to monitoring and surveillance should take into account broader capacity issues including the availability of information on AMU and AMR in humans, animals and crops/plants, human and animal clinical AMR data and reporting, availability of food consumption and agriculture production data, and cross-sector laboratory proficiency and quality assurance.

2.

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*.**Scope**

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

15. Although 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 of public health relevance and indicator bacteria.

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

3. Definitions

[The definitions presented in the *Guidelines for risk analysis of foodborne antimicrobial resistance (CXG77-2011) and Code of practice to minimize and contain antimicrobial resistance (CXC 61-2005).*

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

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].

Antimicrobial resistance (AMR)

The ability of a microorganism to multiply or persist in the presence of an increased level of an antimicrobial agent relative to the susceptible counterpart of the same species[2].

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[3].

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[4]. For the purpose of these Guidelines, the term “hazard” refers to AMR microorganism(s) and /or resistance determinant(s)[5].

One Health approach

A collaborative, multisectoral and trans-disciplinary approach working at the local, regional, national and global

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

levels with the goal of achieving optimal health outcomes, recognizing the interconnection between humans, animals, plants and their shared environment.

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.

- **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 along the food chain and food production environment are [an important/~~fundamental~~] part of national strategies [~~and action plans~~] to minimize the risk of foodborne AMR [and contributes to ~~important component of~~ a national food safety system.]
- **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 implementation/improvement as resources permit.]
- **Principle 4:** Monitoring and surveillance systems should include data on occurrence of AMR and patterns of AMU, in all relevant sectors as an input into risk analysis.
- **Principle 5:** Risk analysis should guide the design, implementation and evaluation of national monitoring and surveillance programs for foodborne AMR.
- **Principle 6:** Priority for implementation should be given to the most relevant foodborne AMR issues to be analyzed from a public health perspective.
- **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.
- **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 l~~a~~boratory methodology, data collection, analysis and reporting across 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, where available, are essential to ensure that data are comparable and to enhance an integrated approach to data management [and sharing data ~~reporting at~~ 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 along the food chain that is informed by data and scientific knowledge on the likely occurrence of [foodborne] AMR hazards at a step (or steps) in the food chain and their potential to pose risks to human health.

21. Integrated monitoring and surveillance of AMR and AMU in the food chain, along with data from other sources when available , provides important information for risk assessment and risk management decision-making on the appropriateness of the control measures to prevent and minimize foodborne AMR...

22. While an integrated monitoring and surveillance system should ideally be designed according to scientific knowledge of probable food-borne AMR risks to public health in the national situation, when its limited programs should initially be designed according to the relevant evidence 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 sources, as described in the *Guidelines for Risk Analysis of Foodborne AMR.*

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.~~]

[Implementation and continuous improvement of monitoring and surveillance systems should ideally lead to an increased use of generated data for input into risk analysis.]

[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, identification of new antimicrobial resistance genes, new ~~food chain~~ exposure pathways throughout the food chain and changing patterns of AMU in humans ~~and~~ animals and plants. 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. As part of a national AMR action plan, the competent authorities should develop an overarching policy framework for monitoring and surveillance activities throughout the food chain in collaboration with human health, animal health, plant health, environmental and other relevant authorities. Other stakeholders in relevant sectors could be included and collaborate in line with the national action plan (NAP) on AMR. Sharing of knowledge and data with international organizations and stakeholders could improve the global understanding of foodborne AMR and effectiveness of policies taken at local level.

28. It is important for competent authorities to have access to relevant sources of antimicrobial use data in their country. Activities related to monitoring and surveillance of foodborne AMR and AMU should involve a wider range of stakeholders. Ideally, all interested parties along the food chain should contribute to the development and implementation of an integrated monitoring and surveillance system.

7. Implementation of an integrated monitoring and surveillance system for foodborne AMR

31. [The concept of continuous improvement facilitates ~~A progressive approach for t~~]The design and [progressive] implementation of an integrated monitoring and surveillance system [and] 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 progressive implementation should facilitate the achievement of the country's objectives on AMR and enable continuous improvement[6]. It includes: preliminary activities, initiating monitoring and surveillance activities, and evaluation and review of the monitoring and surveillance system.

[6] "Continuous Improvement means that a national food control system should possess the capability to learn through a process of review and reform utilising mechanisms that check and evaluate whether the system is able to achieve its objectives." CXG 82 - 2013

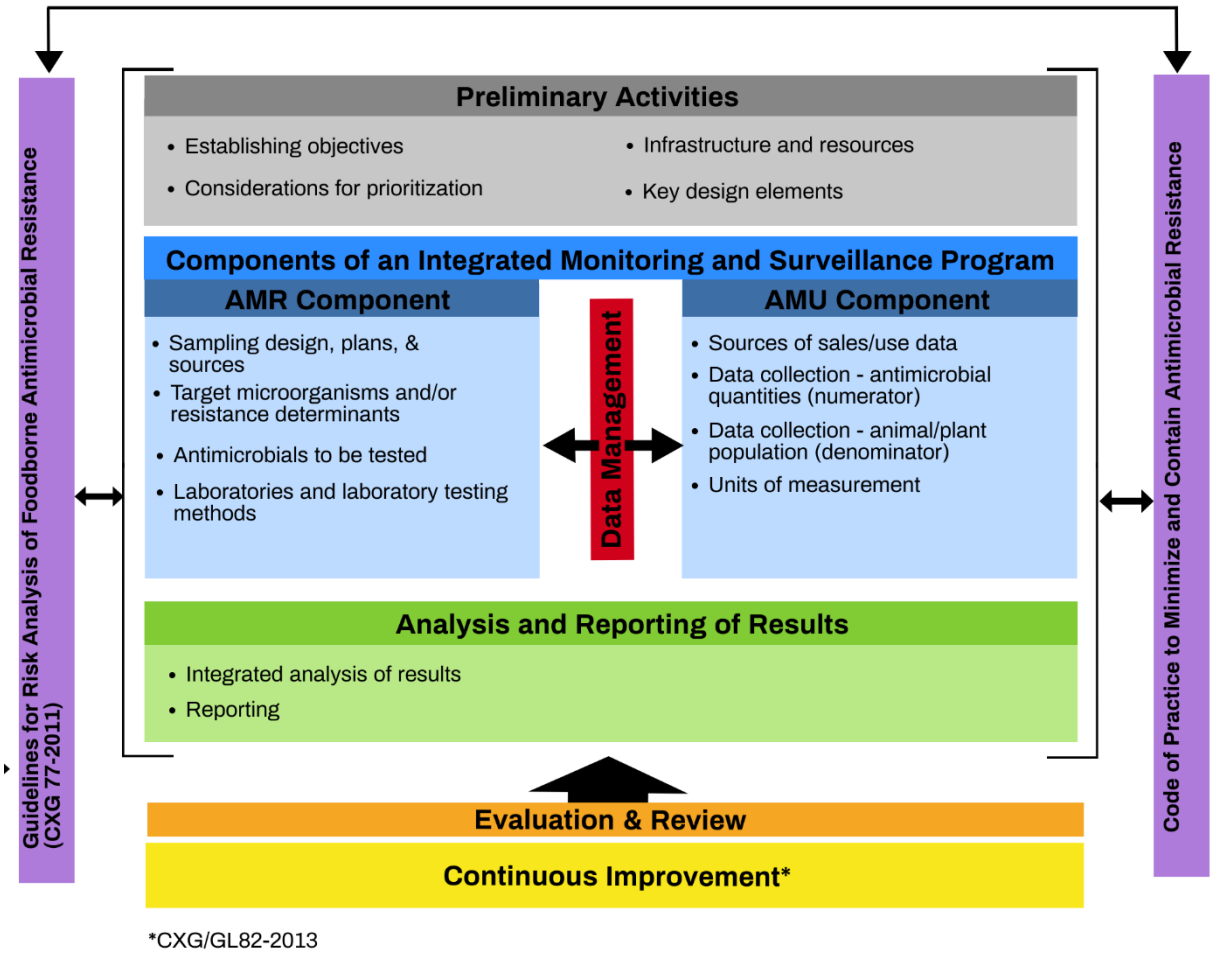

Figure 1. Progressive approach to the design and implementation of the integrated monitoring and surveillance system for foodborne AMR.

7.1. Preliminary activities

7.1.1. Establishing the monitoring and surveillance objectives

34. The establishment of monitoring and surveillance objectives should be done in a consultative manner by the competent authorities and stakeholders. It should take into consideration existing food safety programs and AMR national action plans (NAPs) and relevant evidence 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 for sampling and reporting (e.g., 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 put 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 and outcomes 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, antimicrobial agents and sample sources should be informed by national, regional and international public health 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.

(e.g. defined combinations of the food commodities, the microorganism and resistance determinants and the antimicrobial agent(s) to which resistance is expressed

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 described in section 8, 9 and 10 can effectively be implemented first and which could be implemented at a later stage when additional resources become available.

39. The evolution of a monitoring and surveillance system 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 order to optimize resources and efforts, the competent authority should consider the possibilities of integration or expansion of the AMR or AMU monitoring and surveillance activities in other already ongoing activities. For example, on ongoing monitoring of pathogenic foodborne bacteria under food safety programs.

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 sample sources (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. [Identification of the sectors where collection of data would be most relevant and efficient to meet surveillance objectives. For example, see OIE Terrestrial Animal Health Code Article 6.9.4 for information regarding efficient and practical sources of antimicrobial use data, including veterinary medicinal product registration authorities, wholesalers, retailers, pharmacists, veterinarians, feed stores, feed mills and pharmaceutical industry associations. A possible mechanism for the collection of this information is to make the provision of appropriate information by pharmaceutical manufacturers to the regulatory authority one of the requirements of antimicrobial registration.]

- 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 (section 8), antimicrobial use program (section 9) and integrated analysis and reporting (section 10).

47. The elements described in the next sections are guidelines for the development and continuous improvement 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.

8. Components of an integrated monitoring and surveillance program for AMR

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.

76. To ensure that the monitoring and surveillance objectives are met, an integrated program for monitoring and surveillance of foodborne AMR should include and systematically review the following elements/components :

- Sampling design
- Sampling plans
- Sample sources
- Target microorganisms and resistance determinants .
- Antimicrobials to be tested.
- Laboratory testing methodologies and quality control/assurance procedures.
- Data management activities (collection, validation, storage, analysis, sharing and reporting).

8.1. Sampling design

77. the following types of design for sample collection should be considered by the competent authority:

- 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.
- 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.
- 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.

- Comprehensive surveillance (e.g. census based)

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

8.2. Sample sources

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.

80. An integrated program should reflect the food production in the country and cover samples from all relevant 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.

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, wastewater, reclaimed water, sewage sludge, manure, surface water, etc.

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 input**

  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.

- **Food production 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..

8.3. 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 food 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.

84. The representativeness of the data obtained is essential to ensure high 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.

- 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.

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 or monitoring.

  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 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/commodities: Animals, plants/crops, food, feed, environment or epidemiological units of interest.

  Selection of strata (levels) or risk clusters (groups) to best meet surveillance objectives

- Target microorganisms and resistance determinants.
- 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 under study should be considered. Samples can be collected monthly or periodically throughout the year from different sites, in sufficient numbers, to identify trends.
- Development of standard operating procedures for sample collection: .
    - 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 for collection of samples in accordance with the defined sampling strategy and to guarantee that traceability, security and quality assurance/management are maintained from collection through to analysis and storage.

Samples should be collected by trained persons following the standard operating procedures.

8.4. Target microorganisms and resistance determinants

55 + 56. The initial program may be based on phenotypic susceptibility testing for resistance of representative zoonotic/pathogens and commensal bacteria and may be expanded by including a broader range of foodborne pathogens, commensal bacteria and testing for genetic determinants of resistance and mobile DNA elements (e.g. plasmids, transposons).

86. In order to target appropriate bacterial species and resistance determinants, the 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 bacteria: *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 potential intestinal pathogenic flora from terrestrial animals respectively, with potential risk for resistance.

89. Target microorganisms for aquatic animals and food of non-animal origin should be determined based on available evidence and relevance to public health and may include *Salmonella* spp. and *Listeria monocytogenes.* In aquatic animals the inclusion of *Vibrio parahemolyticus* should be considered.

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.

8.5. 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 guidance/procedures or have a validated Standard Operating Procedure for the monitoring purposes in place.
- Participate in an external quality assurance system testing including proficiency testing in identification, typing, phenotypic and genotypic characterization and AST of the microorganisms included in the monitoring and surveillance program.
- Be equipped with facilities and have procedures to maintain sample integrity (e.g. storage

temperature and time between sample reception and analysis) and traceability.

- 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.
- Have trained personnel in the methods used..

8.6. 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. 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 internationally 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 tables 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). 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. Quantitative reuslta are also necessary for quantitative microbiological risk assessment.

99. The use of ECOFFs, as interpretative 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. When phenotypic testing is done, the panel of antimicrobials for susceptibility testing should be harmonized across the national monitoring and surveillance system 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.

58. Antimicrobials to be tested should be prioritized based on antimicrobials that have been ranked with higher

priority as 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.

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 classes and 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.Molecular testing

108. Molecular testing such as polymerase chain reaction (PCR), micro and nano arrays, Sanger-sequencing, 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 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. Molecular testing, in particular WGS, 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 is important 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..

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. Sequence data generated and stored (with appropriate metadata) 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, production class, 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 described 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, plant production, 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 data analysis and reporting.

9. Components of an integrated monitoring and surveillance program for antimicrobial sales and use data in animals and plants/crops

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

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

- Identification of how antimicrobials are distributed for use in agriculture (animals and plants/crops) within the country.
- Data holders, 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 to best meet the monitoring and surveillance objectives.
- Establishment of the principles for ensuring confidentiality of data supplied (e.g. personal or proprietary data).
- Development of an approach (i.e. protocol) to collect qualitative and quantitative information on the antimicrobials intended for use in animals or plants/crops.
- Identification of the scope of the data to be captured in the monitoring and surveillance system such as 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.
- Establishment of the appropriate 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 (where available) , 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 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. Sources of sales/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.

Data sources could include sales data (from marketing authorization holders, wholesalers, retailers, registration authorities, feed mills, pharmacies, farm shops/agricultural suppliers, or industry trade associations), purchase data (wholesalers, retailers, feed mills, pharmacies, agricultural cooperatives, producer associations) import/export data (customs declarations), veterinary data (prescriptions) or antimicrobial use data from farm records.

60. A basic source of data regarding antimicrobials intended for use in animals and crops is the collection of antimicrobial sales. Care should be taken to avoid double reporting.

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

62. The 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.

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.

9.3. Data collection: Antimicrobial quantities (numerator)

126. The numerator in the context of antimicrobial use data represents the amount of antimicrobial agents sold or used.

127. The minimum data collected to estimate the amount of antimicrobials sold should be the number of packages sold per package presentations of the antimicrobial(s) intended for use in food-producing animals or plants/crops per year. The competent authority can then calculate these sales to the basic unit: weight in kilograms of active substance.

127.bis. For the estimation of use data, quantities of antimicrobials known to be used in the animal or plants/crops species under monitoring and surveillance, other units may also be applicable, such as number of animals treated with the relevant antimicrobials.

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 when analysing antimicrobial usage in food-producing animals.

129 bis. Nomenclature of antimicrobial agents should comply with international standards where available (i.e. ATC vet code).

A. For 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).

B. For 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.

9.4. Data collection: Animal/plant population (denominator)

130. The denominator in the context of antimicrobial sales or use is the animal or plant population at risk for being treated with or potentially exposed to antimicrobials and should be determined in advance.

131. Variables such as number of animals or plants (measured in hectares or greenhouses) per farm/species/categories/production, weight of the animals in the population, are important for the interpretation and assessment of the amount of antimicrobials sold or used (numerator).

A denominator representing the animal or plant 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 animal species, plant species, production type, etc.

132. The desired denominator for reporting of antimicrobial sales or use should be determined in advance.

A. For animals

- The denominator in the context of antimicrobial sales data is the animal population at risk of being treated with antimicrobials.
- This denominator should consider the country's available data on animal populations and animal weights and reflect the surveillance design and objectives. The estimated 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. However different productions practices and slaughtering or marketing weights make it challenging to develop one biomass calculation method that would be equally applicable to every national situation, therefore calculation of the national animal population is desirable for reporting at national level.
- For use data from sampled farms, 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.

B. For plants/crops

- The denominator in the context of antimicrobials sales data is the plants/crops at risk of being exposed to antimicrobials.
- Plant production could be measured as quantities (kg) of harvested crops or quantities of hectares of land used for crop production at risk of being exposed to antimicrobial agents.

9.5. 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)/1000 animals/day, number of Defined Course Dose for animal (DCDvet)/1000 animals/days, etc.

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

9.6. Management of data

137. To ensure consistent collection and analysis of resistance data, sampling information should be recorded down to individual sample and isolate 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.

10. Integrated analysis and reporting of results

10.1. Integrated analysis of results

143. Results of AMR monitoring and surveillance should be compared with results of AMU monitoring and surveillance to evaluate trends over time, between regions, across host species, across bacterial species or antimicrobial classes.

The data can be used as described in CAC/GL 77/2011 for risk assessment 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.

145. Resistance data from the samples and use data can be integrated with data from other sources (e.g. human isolates) for comparative analysis and reporting.

146. Combined analysis of data from an integrated monitoring and surveillance of AMR in foodborne bacteria can include the comparison and synthesis of AMU in humans, animals and plants/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 considered in the analysis. Where data is available, exposure pathways among people, animals, plants/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. 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 and multivariate analysis (e.g. logistic regression) should be used to ensure proper interpretation of results.

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 may also include isolates from sporadic and outbreak foodborne disease cases.

10.2. Reporting of results

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.

144. The reporting of the monitoring and surveillance information should be timely. 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.

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 that the data and information reported are robust and surveillance objectives are being met.

72. 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.

154+73. The competent authority should develop a framework and plan to facilitate the evaluation and review of monitoring and surveillance activities which could include the following aspects:

- 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.

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.

12. Risk communication

[155.

156.] Proposal to delete

158. 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* (CXG 77-2011).

13. Training and capacity building

159. A progressive 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:

Information from Section 7: Progressive approach.

7.2.2. Antimicrobial use program

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.

Annex II

PROPOSED DRAFT GUIDELINES ON INTEGRATED MONITROING AND SURVEILLANCE OF FOODBORNE ANTIMCROBIAL RESISTANCE

1. Introduction
2. Scope
3. Definitions
4. Principles
5. Risk-based approach
6. Regulatory framework and roles
7. A progressive approach to an integrated monitoring and surveillance program for AMR
   - 7.1. Preliminary activities
     - 7.1.1. Establishing the monitoring and surveillance objectives
     - 7.1.2. Considerations for prioritization
     - 7.1.3. Infrastructure and resources
     - 7.1.4. Key design elements to be established before initiating monitoring and surveillance
   - 7.2. Initiating and developing an integrated monitoring and surveillance system

8. Components integrated monitoring and surveillance program for AMR
   - 8.1. Sampling design
   - 8.2. Sample sources
   - 8.3. Sampling plans
   - 8.4. Target microorganims and resistance determinants
   - 8.5. Laboratories
   - 8.6. Characterization of isolates
   - 8.7. AST (methods and interpretative criteria, panel for susceptibility testing, concentration ranges, molecular testing)
   - 8.8. Collection and reporting of resistance data

9. Components of an integrated monitoring and surveillance program for antimicrobials sales and use data in animals
   - 9.1. Design of an integrated M&S program for antimicrobial sales/use data
   - 9.2. Sources of sales/use data
   - 9.3. Data collection: antimicrobial quantities (numerator): animals/plants
   - 9.4. Data collection: animal/plant population (denominator): animals/plants
   - 9.5. Units of measurement
   - 9.6. Management of data

10. Integrated analysis and reporting of results
    - 10.1. Integrated analysis of results
    - 10.2. Reporting of results

11. Evaluation of integrated surveillance program

12. Risk Communication

13. Training