CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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

Sixth Session
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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 2018/75-AMR available on the Codex webpage/Circular Letters:
http://www.fao.org/fao-who-codexalimentarius/resources/circular-letters/en/.

Introduction

1. The 5th Session of the Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance (TFAMR05, 2017) decided to establish an electronic working group (EWG) chaired by The Netherlands and co-chaired by New Zealand, Chile and China. The EWG would further develop the Guidelines, based on the general guidance and comments received during the session in order to provide a revised document for comments and consideration at the TFAMR06 (2018).[1]
2. In addition, at the request of the 40th Session of the Codex Alimentarius Commission (CAC40, 2017), the FAO/WHO Expert Meeting on Foodborne Antimicrobial Resistance: Role of the Environment, Crops and Biocides took place in June 2018. The purpose of the expert meeting was to provide scientific advice to inform the work of the Task Force in the above-mentioned areas.[2] In July 2018, FAO[3] and WHO[4] published the summary report of the expert meeting on their respective websites. The final report would be available in October 2018.
3. The conclusions of the expert meeting indicate that there is insufficient knowledge on the amounts and types of antimicrobials applied to crops and those used in terrestrial and aquaculture. Surveillance for antimicrobial use (AMU) and antimicrobial resistance (AMR) in primary food production environments should be implemented in order to obtain additional data that is required for risk assessment and risk management. Terrestrial and aquatic primary food productions system environments and products post-harvest should be considered for inclusion in integrated AMU and AMR surveillance programs.
4. The EWG divided its discussions in two rounds. The first round for comments was launched in February 2018 and the second in July 2018.
5. During the first round of comments, the participants provided comments to the revised sections 1 to 8 as well as specific inputs to address the concerns expressed at the TFAMR05. To facilitate this work, the participants had to answer four specific questions and provide specific inputs for sections 9-15.
6. The participants had approximately 6 weeks to provide comments on the draft and the questions, which were available in English and Spanish on the platform.
7. The EWG received a total of 30 responses from Codex Members and 5 responses from Observers. Not all participants replied to the four specific questions.
8. During the second round for comments, the participants provided comments on the revised section 9, on the stepwise approach to integrated monitoring and surveillance program of AMR available in English and Spanish on the platform for a period of approximately 6 weeks.
9. During the second round for comments, the EWG received a total of 18 responses from Codex Members and 6 responses from Observers.

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[1] REP17/AMR, para. 60
[2] REP17/AMR, paras. 62-64
[3] http://www.fao.org/food/food-safety-quality/scientific-advice/other-scientific-advice/en/
[4] http://www.who.int/foodsafety/areas_work/antimicrobial-resistance/SciAdvTFAMR/en/

10. Below are a summary of the answers to the questions and the main responses received by Codex Members and Observers during the two rounds for comments including explanations on the choices made by the EWG.

Summary of the comments from Codex Members and Observer Organizations on the questions posted by the Chair and Co-Chairs of the EWG in reaction to the discussion that took place at TFAMR05

1. Proposals for the section on stepwise approach to integrated monitoring and surveillance program of AMR that:

- Provide flexibility for implementation of integrated surveillance programs in line with the capacity and priorities of countries.
- Avoid misinterpretation and labeling the status of implementation of national integrated surveillance programs in certain "categories" (="steps") with potential trade implications.
- Clarify on the transition from one-step to another.
- Present the incremental and flexible nature of the approach.
- Present examples to facilitate understanding and implementation of the guidelines (in particular the stepwise approach).

Some countries proposed to apply "phases" instead of "steps" and provided amendments for the text to improve flexibility. Other respondents were in favor of maintaining "steps".

Some participants mentioned that the guidelines should define priorities and allow for expansion based on capacities in the country. The Chair preferred to keep "steps" and introduced "program A, B and C" in a table simplifying the text for requirements for surveillance programs regarding antimicrobial resistance, antimicrobial use and analysis and reporting. This approach also provides the requested flexibility.

2. Proposals for the section on the design of monitoring and surveillance programs that:

- Simplify and integrate the text with WHO and OIE texts, taking into account the risk to human health, available resources and technical capabilities of competent authorities.
- Are realistic and practical.
- Better frame terms like public health, veterinary and pharmaceutical infrastructures.
- Include sampling recommendations regarding sizes and locations.

Some participants commented that the current text was sufficient realistic and practical enough to cover the components of a monitoring and surveillance system. However, they agreed that there was a degree of overlap with other international documents. In addition, too specific recommendations about sampling size and locations may be too prescriptive. Based on the amendments proposed by the respondents, the Chair adjusted the text.

3. Proposals for the section on surveillance of national antimicrobial sales data for use in animals that:

- Broaden this section by the inclusion of other sources of antimicrobial use data beyond sales data.
- Broaden this section by the inclusion of an additional chapter on data for use in plants.

Some participants welcomed broadening the section to include other sources of AMU data and to include crops. Some countries indicated that the advice from the FAO/WHO Expert Meeting on Foodborne Antimicrobial Resistance: Role of the Environment, Crops and Biocides, should provide further guidance for this section. Based on the proposals made by some respondents, the Chair introduced some additional chapters that the TFAMR06 can further develop e.g. units of measurement, denominator, reporting of AMU in crops.

4. Proposals for the section on the review for:

- A new section on evaluation of integrated surveillance programs.

Some participants requested to delete the section on "ineffective use". Some participants provided proposals for a section on "evaluation".

Overview of the most important amendments made in the document based on comments made at the TFAMR05 and the comments received from the members of the EWG

- The word “monitoring” has been included in the title of the Guidelines.
- The sections on the “Purpose of these Guidelines” and the “Use of this document” have been deleted and their content has been reorganized in Section 1 “Introduction and Purpose of the Guidelines”.
- A description of the concept “monitoring and surveillance” has been included in the section on the introduction to assist having a clear understanding of the two concepts in the context of the guidelines.
- The definitions used in the guidelines have been taken from existing Codex, FAO, WHO, and OIE documents and should be aligned with the definitions in the Code of Practice to Minimize and Contain Antimicrobial Resistance (CXC 61-2005).
- The section on a stepwise approach to integrated monitoring and surveillance program of AMR has been reviewed and now includes a description of preliminary tasks before starting the monitoring and surveillance activities and a table with three different programs for a stepwise development of an integrated monitoring and surveillance system. Activities for AMR, AMU and analysis and reporting are presented separately.
- More detailed information about the design of monitoring and surveillance programs on AMR and AMU is presented in two separate sections (sections 8 and 9).
- Section 9 includes a chapter on the reporting of the national antimicrobial sales/use data for use in animals and a separate chapter for the reporting of the national antimicrobial sales/use data for use in crops.
- Some chapters of the section on the review have been merged and others have been moved to the section on other considerations for the implementation of the monitoring and surveillance program. The section on the review has been re-named to be called evaluation of integrated surveillance programs. The chapter on the ineffective use has been deleted.

Conclusions

The EWG concludes:

- Collection and analysis of data on sales and use of antimicrobials (AMU) is essential element of an integrated surveillance program. The Guidelines should further develop the monitoring and surveillance of AMU in animals and crops.
- Crops/food of plant origin should be included in an integrated monitoring and surveillance program of foodborne AMR. Samples collected from the immediate and relevant environment of the food chain (soils where crops are grown, irrigation water, etc.) should complement the integrated monitoring and surveillance systems of foodborne AMR.
- Most participants favored a stepwise approach. This approach would need to take into account Member countries capacities.

Recommendations

The EWG recommends that the TFAMR06:

- Discuss the common definitions in order to align with the definitions of the COP (CXC 61-2005).
- Further develop the section on the surveillance of national antimicrobial sales and use data in animals and crops, especially:
  - the approaches to collection and analysis of data on use of antimicrobials: antimicrobial quantities, animal population, units of measurement;
  - the reporting of the national antimicrobial sales/use data for use in crops.
- Further develop the section on risk communication and training.

APPENDIX I

PROPOSED DRAFT GUIDELINES FOR THE INTEGRATED MONITORING AND SURVEILLANCE OF FOODBORNE ANTIMICROBIAL RESISTANCE

1. Introduction and purpose of the Guidelines

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 management. 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).

For the purpose of these guidelines, "monitoring of AMR and AMU" is the systematic, continuous or repeated, measurement, collection, collation, validation, analysis and interpretation of AMR and AMU related data in defined populations when these activities are not associated with a pre-defined risk mitigation plan or activity. "Surveillance of AMR and AMU" refers to the same activities when these are associated with a pre-defined risk mitigation plan or activity.

An integrated monitoring and surveillance system includes the coordinated and systematic collection of samples at appropriated stages along the food chain and the testing, analysis and reporting of AMR and AMU, including the alignment and harmonization of sampling, testing, analysis and reporting methodologies and practices and the integrated analysis of relevant epidemiological information from in humans, animals, foods, crops and environment to the greatest extent practical.

The data generated by integrated monitoring and surveillance systems provide information for the risk analysis of foodborne AMR. It provides essential input to risk assessment and data 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 public health risk due to resistance microorganisms and resistance determinants.

It also contributes to the promotion and protection of public health by providing information to risk managers about, how resistant infections differ from susceptible infections, and the impact of interventions designed to limit the emergence spread of AMR.

These guidelines are intended to assist governments in the design and implementation of monitoring and surveillance systems for food-borne AMR along the food chain at the national level. Such programs are a fundamental part of national strategies and plans to minimize foodborne AMR and an important component of a comprehensive national food safety system.

Each country should design and implement a system for monitoring and surveillance of foodborne AMR and AMU along the food chain that is appropriate to national circumstances. This should be informed by all available knowledge on priority foodborne risks due to AMR while taking into consideration the international dimension of AMR and the need for data comparability between countries and sectors.

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

National 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 the national situation permits. A gradual approach to monitoring and surveillance should take into account broader capacity issues e.g. availability of information on AMU in humans, animals and crops, human health care infrastructure, human data and reporting, availability of food consumption and agriculture production data, and cross-sector laboratory proficiency and quality assurance.

These guidelines will contribute to the development and implementation of National Action Plans (NAP) on AMR that make the best use of available resources at the national level, with the goal of continuous enhancement as more scientific knowledge, technical capability, data and funding becomes available.

Application of these guidelines should be 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 *Principles and Guidelines for National Food Control Systems* (CXG 82-2013) whenever appropriate.

These guidelines should also be used in conjunction with those already developed by other international standard-setting organizations and 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 OIE standards related to AMR and AMU published in the *Terrestrial Animal Health Code* and the *Aquatic Animal Health Code*.

While these guidelines are aimed at action at national level, countries may consider creating multi-national or regional monitoring and surveillance systems to share laboratory, data management and other resources.

2. Scope

These guidelines cover the design and implementation of an integrated monitoring and surveillance system for foodborne AMR and AMU along the food chain, including animals, crops and the environment.

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.

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

Antimicrobials used as biocides, including disinfectants, are excluded from the scope of these guidelines. In circumstances where a country may decide to include in the integrated system the monitoring and surveillance of biocides, the design and implementation should preferably be broadly consistent with these guidelines to facilitate comparability of data and analysis.

These guidelines will provide aid in the utilization of appropriate AMR and AMU data from humans, animals, crops, food and environment in order to conduct integrated analysis of all these data.

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 databases are highly desirable aspects of integrated monitoring and surveillance systems at the national level.

3. Definitions

Antimicrobial agent: *(*to be aligned with CXC 61-2005)

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[5]. The term antimicrobial agent is collective for antiviral, antibacterial, antifungal and antiprotozoal agents.

Hazard:

A biological, chemical or physical agent in, or condition of, food with the *potential* to cause an adverse health effect[6]. For the purpose of these guidelines, the term hazard refers to AMR microorganism(s) and /or resistance determinant(s)[7].

One Health approach to AMR: (to be aligned with CXC 61-2005)

An internationally-recognized collaborative and trans-disciplinary approach working at the local, regional, national and global level, to design and implement programs, policies, legislation and research on AMR, in which recognizing the interconnection between humans, animals, plants and their shared environment, multiple sectors communicate and work together with the goal of minimizing the development of AMR and achieving optimal public health outcomes .

Crops/plants: (definition to be discussed and aligned with CXC 61-2005)

Prioritized antimicrobial agents:

For the purpose of integrated monitoring and surveillance, antimicrobial agents prioritized as being of importance to public health e.g. the *WHO List of Critically Important Antimicrobials* (WHO CIA List) and where these exist, national lists based on national official risk analysis and country's unique situation.

Risk-based approach to surveillance and monitoring of foodborne AMR:

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 AMR hazards at a step (or steps) in the food chain and their relationship with risks to human health.

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[5] *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*

[6] Procedural Manual, Codex Alimentarius Commission

[7] *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*

4. Principles

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

- An integrated monitoring and surveillance system for AMR should incorporate an "One Health" approach;
- Monitoring and surveillance programs for AMR and AMU along the food chain are a fundamental part of national strategies and plans to minimize foodborne AMR and a core component of a national food safety system;
- A national monitoring and surveillance program should be tailored to the domestic situation and may be designed and implemented according to a stepwise approach;
- Monitoring and surveillance programs 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);
- Risk analysis should be a guiding principle in the design, implementation and review of a national monitoring and surveillance program 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;
- In using a stepwise approach, priority should be given to the most relevant elements from a public health perspective (e.g. defined combinations of the food commodities, the AMR microorganism and resistance determinants and the antimicrobial agent(s) to which resistance is expressed to be analyzed);
- Monitoring and surveillance programs should incorporate to the extent practical capacity for epidemiological investigation and identification of new and emerging foodborne risks and trends;
- 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);
- A national monitoring and surveillance system should harmonize laboratory methodology, data collection, analysis and reporting across all sectors as part of an integrated approach. Use of internationally recognized, standardized and validated antimicrobial susceptibility testing (AST) methods and harmonized interpretative criteria are essential to ensure that data are comparable at national level and to enhance an integrated approach to data management at the international level;
- Countries should strive to conduct research projects and epidemiological studies to enhance the technical capability and effectiveness of the integrated monitoring and surveillance program (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);
- Data generated from national monitoring and surveillance programs of AMR in imported foods should not be used to inappropriately generate barriers to trade.

5. Risk-based approach

In applying a risk based approach to the design of an integrated monitoring and surveillance system, maximum use should be made of available information on foodborne AMR risks to human health at the national level.

Integrated monitoring and surveillance of AMR and AMU in the food chain provides essential information for risk assessment and risk management decision-making on appropriate control measures in human, plant and animal health.

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 will [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 Antimicrobial Resistance.*

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 Antimicrobial Resistance*. Hazard identification should include human microbiological pathogens and bacterial commensals likely to transmit AMR to humans.

As countries improve their AMR systems over time, a stepwise approach to monitoring and surveillance should increasingly incorporate risk-assessment factors as an important element in design of the program and analysis of data.

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 food chain exposure pathways, changing patterns of AMU. Any adjustments should be properly communicated with reference to methodological changes while retaining valid historical data for trend analysis.

On a risk-based approach, 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 antimicrobial resistance.*

6. Regulatory framework and roles

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, plant health professionals, farmers, professional associations, civil society, consumer organizations, retail and others, will depend on the level of development of the monitoring and surveillance program and the degree of integration. Ideally, all interested parties along the food chain should contribute to the development and implementation of the monitoring and surveillance program.

6.1. Policy and regulatory activities

A national 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 along the food chain in collaboration with the human health, animal health, plant health, environmental and other relevant authorities. Other stakeholders in all relevant sectors should be included and collaborate in line with the 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.

The regulatory activities carried out by the competent authorities should be in response to policy objectives that are embedded in national strategies and NAPs on AMR. Guidance on developing national action plans are outlined in the *WHO Global Action Plan on Antimicrobial Resistance* and specific manuals developed by WHO, FAO and OIE such as the Antimicrobial resistance: a manual for developing national action plans.

The use of antimicrobial agents in the food chain should be subject to regulation as described in the *Code of practice to Minimize and Contain Antimicrobial Resistance* and relevant OIE standards.

6.2. Other activities

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

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 and environmental sectors.

7. A stepwise approach to the implementation of an integrated monitoring and surveillance program of foodborne AMR

A stepwise approach to the design and implementation of an integrated monitoring and surveillance program allows countries to develop a strategy and implement activities to progress according to their own time scales and is a practical response to inevitable variations in monitoring and surveillance objectives, priorities, infrastructure, technical capability, resources and new available scientific information.

The implementation of a stepwise approach should facilitate the achievement of the country’s objectives on AMR and enable continuous improvement.

The stepwise approach to monitoring and surveillance of AMR and AMU that is 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*, chapter 6.9 of the *OIE Terrestrial 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 tasks/actions

7.1.1.Establishing the monitoring and surveillance objectives

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, should take into consideration national action plans, consider knowledge on the AMR and AMU situation and any existing AMR activities in the different sectors (animal, plant and human health sectors). Countries should identify the challenges that they currently face in the implementation of the 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 AMR and AMU, to provide harmonized data that can be easily compared, exchanged, used or aggregated locally, nationally or internationally);
- The comprehensiveness of the surveillance and monitoring program (e.g., data representative of the national situation versus data representative of a regional situation, or data of convenience sampling);
- The setting of proposed timelines (e.g., reporting on an annual basis);
- The 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). A confidentiality policy of the data collected should be in place.

7.1.2. Criteria for prioritization

The establishment of the 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.

Competent authorities should also consider public health implications of AMR, epidemiology of disease and resistance patterns, AMU patterns, information on food production systems, food distribution, consumption patterns and food exposure pathways.

Information from risk profiles and risk assessments, where these exist should also be used when establishing priorities.

7.1.3.Infrastructure and resources

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 programs described in section 7.3 of these Guidelines can effectively be implemented first and which additional activities could be implemented at a later stage given additional resources and other improvements.

The evolution of surveillance and monitoring programs do not need to strictly follow the program in 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 type of data benefit from a joint analysis, is useful if the programs are aligned on its development.

In advance of launching surveillance activities, the competent authority should carefully consider coordination of sampling and laboratory testing, which interested stakeholders need to be involved in this coordination, and develop a plan for collation of the data in a central location. As part of initial planning, the competent authority should also consider in advance where harmonization and standardization are required to meet monitoring and surveillance objectives.

7.2. Initiating monitoring and surveillance activities

The design of a stepwise monitoring and surveillance system should consider the following principles:

Antimicrobial resistance:

- Targeting the highest priority microorganisms, panels of antimicrobials and commodities (see section 10 of these guidelines) based on country data or international recommendations;
- Identifying the food production and distribution chain, points in the food chain and sampling frequency to undertake sampling to meet monitoring and surveillance objectives;
- Establishing sampling methods, laboratory analysis and reporting protocols; building capacity where required;
- Establishing standardized and harmonized methodologies (e.g., laboratory testing for AST) and best practices with those used in other sectors.

Antimicrobial use:

- Identifying antimicrobial distribution chain from manufacturing or import to end-user including sales/use data providers;
- Identifying the sectors where collection of data would be more relevant;
- Initiating collection and reporting of antimicrobial sales (consumption) and use data in food producing animals and crops (see section 9 of these guidelines) if necessary building a legal framework;
- Implementing of monitoring and surveillance activities through pilot surveys in selected food sectors depending on prioritization (see section 10 of these guidelines).

The phases described below are guidelines for development and enhancement of integrated monitoring and surveillance activities. These guidelines are intended to provide flexibility of options for stages of implementation and expansion, considering resources, infrastructure, capacities, and priorities of countries. They are not intended to provide prescriptive restrictive categories or steps, but rather a continuum of options for implementation.

7.3. Options for stepwise development of integrated monitoring and surveillance of foodborne AMR and AMU programs

ANTIMICROBIAL RESISTANCE			
	PROGRAM A	**PROGRAM B**	**PROGRAM C**
General considerations	• Scope and design of AMR program informed by previous surveys or international experience and recommendations	• Scope and design based on: ○ monitoring findings ○ epidemiology of antimicrobial-resistant bacteria in people ○ refined based on risk profile findings, if appropriate • Additional pro-active surveillance activities (e.g. point prevalence surveys) could be launched	• The scope and design refined based on: ○ monitoring findings ○ epidemiology of antimicrobial-resistant bacteria in people ○ risk profile and/or risk assessment findings, if appropriate • Pro-active monitoring activities (e.g. point prevalence surveys) used as appropriately
Sampling sources(animal/plant species or food commodity Point in the food chain	• Sampling of a limited selection of animals, foods and crops at limited specific stages along the food chain (e.g., farm, crops, slaughterhouse, processing plants, retail)	• Sampling of a broader number of animals, food and crops at higher number of stages along the food chain (e.g., farm, crops, slaughterhouse, processing plants, retail) and related sources (e.g., feed, water)	• Sampling of a broader range of direct and indirect food exposure pathways at all stages along the food chain (e.g. feed, water, waste water, reclaimed water, sewage sludge, manure, surface water)
Sampling plans	• Limited samples collected from the animal/crops/food (e.g., caecal contents vs. carcass swabs) at specific points in the food chain	• Sampling broaden to be more representative of the national population of interest (e.g., surveillance of abattoirs according to slaughter volume)	• Sampling broaden to be fully representative of the national population of interest (e.g., surveillance of abattoirs according to slaughter volume) with stratification within animal species (e.g. broilers, layers, turkeys)
Target microorganisms, bacteria isolated	• Phenotypic testing of representative zoonotic/pathogens (e.g., *Salmonella* spp. and *Campylobacter* spp.) and indicator bacteria (e.g., *E. coli* and *Enterococcus* spp.) for resistance	• Phenotypic testing of a broader range of pathogens and indicator bacteria for resistance • Addition of testing for genetic determinants of resistance	• Phenotypic testing of a broader range of pathogens and indicator bacteria for resistance • Addition of testing for genetic determinants of resistance and mobile DNA elements (e.g. plasmids, transponsors) • AMR testing of animal/plant pathogens may be used to provide additional information about the selection pressure resulting from AMU

ANTIMICROBIAL RESISTANCE			
	PROGRAM A	**PROGRAM B**	**PROGRAM C**
Antimicrobials tested	• Priority 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* or other relevant antimicrobials that have influence on the selection or co-selection of resistance	• Broader range of priority antimicrobials that have been ranked as critically and highly important for human health [as defined by WHO in the *List of Critically Important Antimicrobials for Human Medicine* and a broader range of other relevant antimicrobials that have influence in the selection or co-selection of resistance. Other antimicrobials that are specified in national risk prioritization exercises	• Broader range of priority antimicrobials that have been ranked as critically and highly important for human health [as defined by WHO in the *List of Critically Important Antimicrobials for Human Medicine* and a broader range of other relevant antimicrobials that have influence in the selection and co-selection of for resistance. Additional antimicrobials that are specified in national risk prioritization exercises

ANTIMICROBIAL USE			
	PROGRAM A	**PROGRAM B**	**PROGRAM C**
Source of antimicrobial use data	• Basic source: Sales data of antimicrobials intended for use in animals and crops collected from manufacturers, import/export, etc.	• Direct source: Sales data of antimicrobials collected in addition from other sources like wholesalers, retailers, pharmacies, feed mills, other agricultural associations • Competent authorities could explore pilots for collection of antimicrobial use data from farmers, veterinarians, pharmacies	• End-user source: Collection of use data from veterinarian prescription, farmers use data, pharmacies and other sales data
Reporting	• Overall amount sold for use in animals and crops by antimicrobial class • Type of intended use (e.g. therapeutic/growth promotion) • Antimicrobial use data adjusted by information on estimated animal population size and area of crops, when these information is available	• Overall amount sold for use in animals and crops by antimicrobial class, separate by type of use (therapeutic/growth promotion) and animal/plant species groups (e.g. terrestrial/aquatic food producing animals/companion animals) • 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, separate by type of use, and species group and route of administration • Antimicrobial use data presented using different indicators (e.g. DDD, DCD)

ANALYSIS AND REPORTING			
	PROGRAM A	**PROGRAM B**	**PROGRAM C**
Integrated analysis and reporting	• 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 • Collection of information of different sectors (e.g. humans, animal species, crops, environment), bacterial species, across regions or time, summary of key findings	• Descriptive analysis and reporting of AMR data from the food chain and quantities of antimicrobials intended for use in animals and crops. Isolate based data reporting (i.e. no aggregation) • Identification of sector specific risk/protective factors for AMU or risk/protective factors for AMR could be undertaken • Integration of information across sectors (e.g. humans, animal species, food, crops, environment), across bacterial species, across regions or time, or between use and resistance could be achieved by graphical display of harmonized and standardized data. These graphical displays could show multiple surveillance components at the same time (e.g., bacterial resistance in samples collected from several points along the food-chain up to humans and relevant AMU practices)	• Descriptive analysis and reporting of AMR data from the food chain and quantities of antimicrobials intended for use in humans, animals and crops. Isolate based data reporting (i.e. no aggregation) • Sector specific quantitative epidemiological modelling of risk/protective factors for AMU or risk/protective factors for AMR could be undertaken • Integration of information and statistical modelling across sectors (e.g. humans, animal species, food, crops, environment), across bacterial species, across regions or time, or between use and resistance could be achieved by graphical display of harmonized data. These graphical displays could show 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)
Link with risk management and risk assessment/risk profile	• Prioritizing which AMR food safety hazard(s) need to be evaluated first • Risk managers/policy makers decide whether to develop a risk profile and conduct risk assessment based on the priority AMR food safety hazards	• Conducting risk profiles based on the priority AMR food safety hazards as needed. Launching of qualitative or quantitative risk assessments as needed • Using monitoring and surveillance information to identify risk management options. Using monitoring and surveillance information to evaluate risk management interventions to reduce risk • Engaging in risk communication about priority AMR food safety risks	Additionally to program B • Periodic review and resetting of the risk analysis cycle as monitoring and surveillance data, and new technologies are analyzed and reported • Continuous input of risk assessment information to review and improve monitoring and surveillance as an essential contributor to risk management • Commissioning of ad hoc research projects for risk assessment and surveillance methodological improvement

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

Evaluation and review of the monitoring and surveillance activities are needed to ensure that the monitoring and surveillance objectives are being met and that planned activities are being achieved.

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

- Indicators to effectively track the progress of the monitoring and surveillance program;
- Periodically evaluate the monitoring and surveillance program to ensure quality and that the results are a robust and reliable indicator of AMR or AMU;
- Further detailed risk profiling based on preliminary monitoring and surveillance data;
- Use the data generated from the evaluation of activities and risk profiling to adjust the monitoring and surveillance program if required or to expand to a wider scope of pathogens, foods and antimicrobials, taking into consideration resource allocation and priorities (refer back to preliminary actions);
- Development and inclusion of new monitoring and surveillance tools (e.g. whole genome sequence to facilitate genomic characterization of bacteria).

As resources and capacity may develop, and the design of the monitoring and surveillance program may change periodically, the competent authorities should ensure that all interested stakeholders are kept informed.

The expansion of activities 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 monitoring and surveillance programs for AMR

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

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 strive to include and systematic review the following design elements and technical characteristics:

- Sample sources and sampling methodology to meet the surveillance objectives;
- Sampling plans (representativeness, frequency, sample size, etc.) that are statistically robust enough to provide the desired level of statistical significance and power to detect a difference over time or between populations;
- List of target microorganisms based on public health relevance; (pathogens and indicator bacteria) and resistance determinants and new information or emerging AMR hazards;
- List of antimicrobials to be tested;
- Laboratory testing methodology and quality assurance are appropriate, harmonized and standardized where possible;
- Data management activities (data validation, data storing, data analysis, data sharing and reporting).

8.2. Types of design or sampling plans

Monitoring and surveillance programs may include the following types of design for sample collection:

- Simple cross-sectional point prevalence surveys that can be used to collect basic information and compare between various populations at particular point of time;
- Longitudinal monitoring to routinely and continuously collect data over time. The limitations of longitudinal studies are related to their greater complexity and cost compared with point prevalence surveys, but provides valuable information on trends. Many longitudinal studies are carried out by conducting repeated cross-sectorial surveys at fixed intervals;
- Investigative, targeted surveillance studies (e.g. pilots to test collecting data from new animal species);
- Short-term *ad hoc* studies or projects can be used to test the feasibility of planned programs. They can also enhance the overall technical and analytical value of a national program (e.g. use of new analytical methods);
- Sentinel surveillance.

The design of the monitoring and surveillance program could involve new infrastructure only for the purpose of AMR or AMU (active surveillance) or where available information about AMR and AMU could be collected by an existing program which was designed for another purpose (passive surveillance)

8.3. Sample sources for the collection of isolates for AMR testing

Sources of samples for the collection of the isolates for AMR testing will be based on the objectives, the stage of implementation and the design of the monitoring and surveillance programs and will be determinate by the available resources and the national infrastructure. Data from the samples can be integrated with data from other sources (e.g. human isolates).

Samples should be representative of the population that is targeted and consider the biology of the bacterial species to increase the likelihood of detection and should be representative of given epidemiological unit (e.g. holding of origin, herd, flock).

For plants, samples from priority crop species could also be taken at farm level.

Although samples from both healthy animals and sick animals are useful for monitoring and surveillance, samples from healthy animals should be the primary focus because such samples can provide better measure of AMR in animals entering the human food supply chain. Isolates from sick animals are useful for detecting novel resistance patterns.

For food producing animals at farm level, samples from animals and their related environment could include: faeces, feed, litter (bedding), dust, fluff, water, soil, etc.

At holding level (lairage and abattoir), samples can be taken from pen floor, truck/crate swabs, dust, etc.

At the slaughter and post-slaughter stage, samples could taken at the evisceration point (e.g.ceacal contents, lymph nodes) or after slaughter but before processing (e.g.carcass rinses and swabs)..

At retail level, the types of food samples could include meat (beef, chicken, turkey, pork, etc.), fish, dairy product, other edible tissues (liver, kidney, etc.), vegetables and processed food. The selection of foods for surveillance should reflect consumption patterns in the population and likely prevalence of AMR, but may be modified periodically in order to capture multiple commodities.

Once the sampling structure is stablished, the feasibility of conducting ad hoc studies on a broader range of retail products may be considered.

In an integrated program samples collected from food-producing animals should be taken from the same animal species as retail meat samples. An integrated program should cover samples from all stages of the different food chains including crops.

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

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

8.4. Sampling plans for AMR data collection

When designing monitoring and surveillance programs, representativeness of the data obtained is essential to ensure quality information. Irrespective of the stage, an adequate sampling design is required to interpret data and compare results, and to ensure that data obtained from the selected population under investigation (AUS) is representative of the target population and amenable to statistical analysis of temporal or regional trends.

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

- Sampling strategy: active or passive surveillance;
- Target populations: animal/food/crops and target bacterial populations and resistance determinants;
- Selected epidemiological units (flocks, holding);
- Point in the food chain where the samples will be taken;
- Frequency of sampling;
- Statistical power and goals of testing (precision of point estimates versus sensitivity to change over time;
- Required sample size with estimates of statistical power to detect changes in antimicrobial resistance patterns with sufficient precisions and statistical power;
- Number of isolates/samples;
- Selection of strata or risk clusters to best meet surveillance objectives.

Sample selection strategy for collection of samples for AMR testing

Sampling may be active (prospective) or passive (samples collected for other purposes), random or systematic, statistically-based or convenience-based. Sentinel surveillance, which relies on specific providers, healthcare facilities, laboratories, or other sources reporting a disease or condition under surveillance, may also be employed.

Examples of sampling strategies (Simple Random Sampling, Stratified Sampling, Systematic Sampling, etc.) are provided by Codex documents on food hygiene and methods of analysis and sampling.

Frequency of collection of samples for AMR testing

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 bacteria 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.

Sample size for collection of samples for AMR testing

Statistical methods should be used to calculate the number of samples or isolates needed for testing (sample size). The choice of sample size depends on the purpose of the study, on the desired precision for estimates of the prevalence of resistance and the magnitude of change in resistance to be detected over a specified period of time in a certain population. It further depends on the frequency of bacterial recovery, the initial or expected prevalence of resistance in that bacterial species and the size of the population to be monitored. It also depends on the desired level of statistical significance and power to detect a difference over time or between populations.

Example of sample size calculation can be found at national or international publications.

8.5. Target microorganisms and resistance determinants

Bacterial species should be chosen considering public health aspects, including the epidemiology of foodborne diseases, and should include both foodborne pathogens and indicator organisms of commensal bacteria.

Salmonella is a key foodborne pathogen and should therefore be included in an integrated monitoring and surveillance program. Other foodborne pathogens like *Campylobacter* should also be strongly considered, as well as other pathogens depending on national or regional situation and risks (e.g. *Vibrio)*.

Indicator organisms of commensal intestinal bacteria may contaminate food and can harbor transferable resistance genes. Commensal bacteria such as *E. coli* and *Enterococcus faecium/faecalis spp.* should be used as indicators of Gram negative and Gram positive intestinal flora.

Whenever possible the monitoring and surveillance program should include genetic and/or phenotypic analysis of particular isolates that may be a public health concern such as ESBL- AmpC and carbapenemase-producing strains and MDR strains.

Tests for virulence factors, AMR genes, gene transferability and gene sequencing can also be applied as resources and capacity permits.

8.6. Laboratories

Laboratories participating in the monitoring and surveillance program should:

- Isolate, identify, type and further characterize target bacteria from the different sample types, by using internationally accepted reference methods or alternatively other analytical methods validated according to internationally accepted validation methodology;
- Be accredited in accordance with national and/or international regulations or at least have a validated Standard Operating Procedure on AST for the monitoring purposes in place;
- Be involved in an external quality assurance systems including proficiency test in identification, typing, phenotypic and genotypic characterization and susceptibility testing of the microorganisms included in the monitoring and surveillance system;
- Perform antimicrobial susceptibility testing using standardized and validated methods (at least phenotypic and selected genotypic methods to confirm selected phenotypes);
- Store isolates for a period of time using methods that ensure viability and absence of change in strain properties;
- Have access to a national reference laboratory or an international laboratory (e.g. WHO-collaborative center) that can provide technical assistance if necessary.

8.7. Antimicrobial susceptibility testing

8.7.1.Methods and interpretative criteria

Susceptibility testing methods (disk diffusion or minimum inhibitory concentration (MIC) methodologies) 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.

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

Interpretation of results for disc diffusion or MICs, should also be done according to EUCAST or CLSI standards and should include quantitative results (disk diffusion zone diameters or minimal inhibitory concentrations values) as well as categorization of the isolate (resistant or susceptible, wild-type or non-wild type) and the cut off value used for interpretation.

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.

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

The use of epidemiological cut-off values, 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 more adequate in case of treatment decisions related to pathogenic bacteria.

Detailed information on interpretation of antimicrobial susceptibility test results and quality control can be found 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

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

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 volumes that are used in the relevant agricultural sectors and their influence in the selection or co-selection of resistance.

Suggested panel of antimicrobials by bacteria for inclusion for AST can be found at *WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach*. National list 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

The concentration ranges to be used, should ensure that both epidemiological cut off values and clinical breakpoints are included in order to make comparability of results with human data possible. The concentration range of each antimicrobial agent should also cover the full range of allowable results for the QC strain(s) used for each antimicrobial agent.

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

8.7.4.Characterization and subtyping of isolates

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

Microbial typing refers to the application of laboratory methods capable of characterising, 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, strictly applying different methods for investigating the genetic code of the organism for characterization purposes. There are multiple typing methods available for most organisms. The choice of typing method is linked to the resolution needed to fulfil the objective of the investigation and needs to be practically feasible for the intended use. The cost, ease of use, accessibility, capacity and capabilities to perform a specific method need to be acceptable.

8.7.5.Molecular testing

The use of molecular testing such as polymerase chain reaction (PCR), sanger-sequencing, pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST) or Whole Genome Sequencing (WGS), may contribute to the monitoring of AMR, the detection of resistance genes and epidemiological analysis.

The use of molecular characterization such as WGS is also an important tool for the rapid detection of outbreaks, risk factors and epidemic source, investigation of transmission chains, detection of emergence and spread of new drug resistant strains; source attribution by linking to molecular monitoring of pathogen in humans, animals, food and environment reservoirs.

For example of the use of molecular testing could be useful for the enhanced surveillance and early warning of resistant pathogens of high public health impact such as carbapenemase-producing *Enterobacteriaceae*.

The application of molecular methods and the interpretation of the information derived from them will require multidisciplinary interpretation, global agreement on analytical and interpretational approaches, laboratory and technical capacity, data management and analytical platform to link epidemiological and microbiological information at national and international level. For appropriate and successful use of molecular surveillance data, national, international and cross-sector agreements on quality standards, analytical schemes and genomic type nomenclature for the bacterial pathogen or resistance determinants under monitoring should be established in collaboration with national and international reference laboratories.

Training and professional development in bioinformatics and genomic epidemiology should be carried out for public health microbiologists, epidemiologists and risk managers about analysis, reporting, interpretation and use of integrated genomic epidemiology data.

In some countries, using WGS costs less than using conventional microbiology, including isolation, detection and molecular typing. Countries without current AMR surveillance programs may consider focusing on WGS in developing surveillance programs. Countries taking this approach should do some surveillance using conventional microbiology to monitor for previously undetected resistance genes. WGS approaches to surveillance are particularly suited to data sharing and there are several international initiatives to collect and share WGS data.

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

9. Surveillance of national antimicrobial sales and use data in animals and crops

9.1. Key aspects to consider when developing surveillance of antimicrobial sales/use data in animals and crops

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

- The distribution of antimicrobials for use in agriculture (animals and crops) within the country should be mapped and interested parties should be identified (e.g. marketing authorization holders, wholesalers, distribution centers, pharmacist, veterinarians, farmers, importers/exporters);
- The most appropriate points of data collection should be identified and the stakeholders that may provide the data at these points;
- A protocol on the collection of data should be developed to captures qualitative and quantitative information on the antimicrobials;
- 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;
- The desired technical units of measurement and indicators on antimicrobial consumption or use should be established;
- 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 use data may be further organized by crop type, animal species, by route of administration (e.g. in-feed, in-water, injectable, oral, intramammary, intra-uterine, topical), by 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

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:
  Chapter 2.3 (Surveillance of use of antimicrobials in animals) and chapter 2.4. Data management to support surveillance of antimicrobial use of the *WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach*.

  The AGISAR guidance provides details for:
  - Surveillance of national antimicrobial sales data;
  - Surveillance of antimicrobial consumption by animal species;
  - Continuous collection of consumption data by animal species;
  - Collection of data from a sample of farms;
  - Stratification of sales data.

- OIE:
  Chapter 6.9 (Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals) of the *OIE Terrestrial Animal Health Code*, Chapter 6.3 (Monitoring of the quantities and usage patterns of antimicrobial agents used in aquatic animals) of the *OIE Aquatic Animal Health Code* 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 the use of antimicrobial agents in animals*.

  Chapter 6.9 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 the use of antimicrobial agents 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; overall amount sold for/used in animals by antimicrobial class, with the possibility to separate by type of use;
  - Option 2; overall amount sold for/used in use animals by antimicrobial class, with the possibility to separate by type of use and species group;
  - Option 3; overall amount sold for/used in 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 can be exposed to the antibiotics (see below).

9.2.2. Antimicrobial quantities (numerator)

To be further developed

- The minimum data collected should be the weight in kilograms of the active ingredient of the antimicrobial(s) used 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 any combination of these.
- For active ingredients present in the form of compounds or derivatives, the mass 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 mass of active entity should be stated.
- Information on dosage regimens (dose, dosing interval and duration of the treatment) and route of administration are elements to include when estimating antimicrobial usage in food-producing animals.

9.2.3. Animal population (denominator)

To be further developed

- The desired denominator for reporting indicators of antimicrobial consumption or use should be determined in advance. This denominator should reflect the surveillance design and objectives. For example, the animal biomass is appropriate for national sales data, whereas 1,000 animal-days is an example of an appropriate denominator for antimicrobial use data from a sample of farms.

- For the estimated animal biomass, that can be exposed to antimicrobials should be calculated. The European Surveillance of Veterinary Antimicrobial Consumption project has provided a methodology for the calculation of such animal population; the methodology which has been adopted by other countries outside of the EU (e.g., Canada and Japan). Furthermore, the US Food and Drug Administration recently published a proposal for the estimation of the animal population and the OIE is currently working to provide a biomass denominator suitable for global reporting of quantities of antimicrobial agents intended for use in animals.
- 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.

- The total number of 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.

9.2.4. Units of measurement

To be further developed

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

To be further developed

- Baseline information on what antimicrobials are registered for use in which crops.
- Collection of amounts sold/used in crops:
  - Option 1: overall amount sold for/used in crops by antimicrobial class, with the possibility to separate by crop type (eg. fruit trees, grains, vegetables);
  - Option 2: overall amount sold for/used in food and feed crops by antimicrobial class, with the possibility to separate by 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 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 are applied as pest-control products;
- 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. Sampling procedures

Samples should be collected by persons authorized to do so (third party accreditation).

Procedures should be put in place to ensure that collection of samples is carried out in accordance to the defined sampling strategy and to guarantee that traceability, security and quality management are maintained from collection through to analysis and storage.

Temperature, time between sample collection and testing, and storage of the samples are important aspects that may influence the results. During transport and storage of the samples in the laboratory measures to maintain the cold chain should be implemented.

10.2. Collection and reporting of resistance data

To ensure appropriate analysis of the integrated surveillance and monitoring program it is important that relevant information about the sampling procedure and the individual samples are collected and recorded in a national central database.

The information collected and recorded may differ depending on the step that is designed and specific public health objectives.

Information for each individual sample should include:

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

10.3. Management of data

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

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

Ongoing validation of the data should be ensured.

A description of sampling designs, stratification and randomization procedures per animal populations and food categories should be provided with the data.

Ideally, isolate-level data should be collected and stored. at isolate. level (report separately each bacterial species and animal population/food combination)

10.4. Analysis and reporting of results

Reporting of results from the monitoring and surveillance system should be timely and preferably include information for each individual isolate, including information about microbiological methods used for isolation, the identification of the isolate, the bacterial species (serovar), specific information about the sampling (food category, place of sampling, sampling strategy, date of sampling), AST results, etc.

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.

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.

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 resistant bacteria isolated from humans, food, agricultural, livestock and aquatic products and environment.

Results of AMR should be compared with results of AMU so that the data can be used when implementing policies to ensure proper use of antimicrobials.

Whenever possible, data from monitoring and surveillance of AMR should be analyzed though a One Health approach, combined with information on AMU in primary production (animals and crops) in national settings, and AMU in human medicine, and also the many pathways among people, animals, crops and their shared environment connecting resident bacterial populations.

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

10.5. Targeted investigation

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.

10.6. Integrated analysis of results

Combined analysis of results and data of a program of integrated monitoring and surveillance of antimicrobial resistance in foodborne bacteria comprises the syntesis 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, and also provision of the detailed methodology of the surveillance system and epidemiological context.

The data may originate from different surveillance systems, and comparability is an important factor to consider in the design of the surveillance programs. The analytical approach chosen should allow the investigation of the relationship between consumption and resistance within the animal, plant/crops and human populations, as well as additional associations between equivalent data within all relevant populations.

One of the objectives of those integrated analysis would be the study of the associations between the data by use of e.g. ecological studies or point prevalence studies. Statistical analysis like univariate ((logistic regression) and multivariate analysis can be used as appropriate.

Integration of data from foodborne human isolates

Data from relevant human isolates should include data from those more relevant foodborne pathogens according to national epidemiological information (e.g. Salmonella, Campylobacter) and whenever possible commensal flora such as *E. coli* and potentially also *Enterococcus*. The surveillance of human clinical isolates should not only allow to follow trends in the occurrence of resistance to antimicrobials relevant for treatment but also to follow trends in the occurrence of resistance to other antimicrobials of public or animal health importance, and for the comparison with isolates from the food chain and the environment.

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

Guidance on conducting antimicrobial resistance surveillance among isolates from humans is provided by the WHO Global Antimicrobial Resistance Surveillance System (GLASS).

10.7. Detection and evaluation of emerging risks

This could include the design of monitoring and surveillance system performance indicators and disease prevention metrics for the evaluation of public health benefits of system implementation, including definition of short-, medium-, long term indicators.

10.8. Additional research and targeted investigation

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.

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,

11. Evaluation of integrated surveillance programs

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.

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

As part of broader risk communication plans for national strategies and NAPs, there are specific requirements for communicating the results of ongoing monitoring and surveillance program – industry, consumers, international organizations etc.

The value of consultative and risk communication processes in developing partnerships and achieving commitment to activities to optimize and reduce use of antimicrobials and preserve the effectiveness of antimicrobial agents in humans, animals and plants/crops.

Additional guidance on how to communicate risk can be found in the *Working Principles for Risk Analysis for Food Safety for Application by Governments* and the *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance*.

13. Training

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.

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 program. This should include the capacity to train personnel in the collection, analysis and reporting of the monitoring and surveillance data.

APPENDIX II

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Codex Members

1. Argentina
2. Australia
3. Austria
4. Bolivia
5. Brazil
6. Burkina Faso
7. Canada
8. Chili
9. China
10. Colombia
11. Costa Rica
12. Croatia
13. Denmark
14. Dominican Republic
15. Ecuador
16. Egypt
17. Finland
18. France
19. Germany
20. Italy
21. Japan
22. Kazakhstan
23. Kenya
24. Malaysia
25. Mexico
26. Morocco
27. The Netherlands
28. New Zealand
29. Nigeria
30. Norway
31. Peru
32. Poland
33. Republic of Korea
34. Russian Federation
35. Singapore
36. South Africa
37. Spain
38. Sweden
39. Thailand
40. United Kingdom
41. United States of America
42. Uruguay

Codex Member Organization

1. European Union

Codex Observers

1. Consumers International (CI)
2. CropLife International
3. European Feed Manufacturers' Federation (FEFAC)
4. FoodDrinkEurope
5. HealthforAnimals
6. Inter-American Institute for Cooperation on Agriculture (IICA)
7. International Association of Consumer Food Organizations (IACFO)
8. International Council of Grocery Manufacturers Associations (ICGMA)
9. International Dairy Federation (IDF)
10. International Feed Industry Federation (IFIF)
11. International Meat Secretariat (IMS)
12. Organisation Mondiale de la Santé Animale (OIE)