



## JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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

#### Fifth Session

### PROPOSED DRAFT GUIDELINES ON INTEGRATED SURVEILLANCE OF 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 the proposed draft Guidelines (Appendix I to this document) should do so as instructed in CL 2017/82-AMR available on the Codex webpage/Circular Letters 2017:

<http://www.fao.org/fao-who-codexalimentarius/circular-letters/en/>.

### Report of the electronic working group for the drafting of the Guidelines on integrated monitoring and surveillance of Antimicrobial Resistance

#### Introduction

1. During the 40<sup>th</sup> Session of the Codex Alimentarius Commission (CAC), the Commission decided that an electronic working group (eWG) chaired by The Netherlands and co-chaired by New Zealand, Chile and China would develop the draft of the new proposal for Guidelines on Integrated Surveillance of AMR to be discussed during the 5<sup>th</sup> Task Force on Antimicrobial Resistance (TFAMR5).
2. For this purpose, Codex Members and Observers were invited to register their experts in the e-platform of Codex. The chair received the request for registration from a total of 55 Codex Members (54 Member States and 1 Codex Member organization) and 14 Codex Observers and the 2 parent organisations. 15 Member States that had requested registration didn't register (some of them expressed difficulties with the registration at the platform). The list of Codex Members is attached as Appendix II.
3. The draft document (in English and Spanish) was uploaded in the platform and a period of approximately 4 weeks was given to the participants to provide comments. Participants were also requested to answer three questions about the future guidelines on integrated monitoring and surveillance of foodborne AMR.
4. The eWG received a total of 29 responses from 26 Codex Members (in some cases more than one reply per Codex Member was received) and 15 responses from 10 Observers. Not all participants replied to the three specific questions. One country not registered replied directly to the chair and co-chair and didn't upload the comment in the e-platform.
5. A short summary of the answers to the questions and the main responses received by Member Countries and Observers can be found below, as well as explanations to choices made by the EWG.

#### **Summary of the comments from Codex Members and Observer Organisations on the questions posted by the chair and co-chairs of the EWG related to the draft Guidelines for the integrated monitoring and surveillance of foodborne antimicrobial resistance**

6. The EWG Chair asked three questions about the guidelines on integrated monitoring and surveillance of foodborne AMR regarding i) the scope of integration, ii) the level of detail and iii) stepwise approach and examples.
7. Not all replied to these three specific questions. The replies of those who did reply are summarized below.

- **Question 1:**  
**What do you think should be the scope of "integration"?**

The scope of integration should refer to the integrated system which includes the analysis of the results (including data from all sectors, incl. human) and include a risk analysis approach to the food chain.

Many expressed that an integrated approach should go further than the coordination of activities on sampling, testing, reporting and analysis of data along the food chain, and include harmonization of procedures.

Integration should not only include monitoring and surveillance of resistance but also the use of antimicrobials in animals and crops, and include potential environmental sources of contamination of the food chain and in humans.

The scope of integration should refer to the integrated system which includes the analysis of the results (including data from all sectors, incl. human) and include a risk analysis approach to the food chain.

WHO AGISAR guidelines were mentioned several times as an example of an integrated system, but monitoring and surveillance of humans cannot be included in the scope of a Codex document.

- **Question 2:  
Taking into account differences between countries on the development in implementation of surveillance systems: what do you think should be the level of detail of the guidelines, especially chapter “Design of monitoring and surveillance programmes”?**

Some respondents were in favour of including a relatively high degree of details in Codex guidelines. Others favoured the inclusion of only basic elements with reference to further details in related documents of Codex, OIE, FAO and WHO. We note that extensive reference to other documents may require periodic updating of the Codex guidelines.

- **Question 3:  
The Guidelines consider a stepwise approach on the development and implementation of monitoring and surveillance systems. Which elements do you think should be included in the guidelines to ensure a stepwise approach? Should the guidelines include examples to illustrate the different steps? Examples of hazard and risk profiles that inform design and implementation?**

Most of the respondents agreed with a stepwise approach as this would facilitate practical uptake at the national level. Many were in favour of examples to illustrate the proposed stepwise approach, especially for countries initiating a programme for the first time.

#### **Overview of the most important amendments made in the document based on comments received from the members of the eWG**

- The text has been simplified and greater clarity brought to the purpose, definitions, scope and the risk-based approach.
- The scope of the guidelines includes monitoring and surveillance of antimicrobial resistance along the entire food chain, including crops and environment, however the latter needs more development in this draft.
- Biocides have been excluded from the scope.
- A new chapter on use of antimicrobials has been added, with reference to existing AGISAR and OIE work. This needs to be further developed.
- The guidelines do not include monitoring and surveillance of AMR and AMU in humans. Recognizing that an integrated surveillance system should include the coordinated sampling, testing and reporting and analysis of data from all sectors, including humans, the guidelines refer to the need for integrated analysis of results from human monitoring and surveillance.
- A stepwise approach has been further developed in the draft. Some countries expressed the need to include examples to facilitate the comprehension of the document and the value and purpose of these should be a major future discussion topic.
- The definitions used in the guidelines have been largely taken from existing Codex, WHO, OIE and FAO documents. In some cases, working definitions have been specifically developed for use in the context of these draft guidelines.
- "Integrated approach": see summary of comments received to question 1. A working definition is included in the draft guidelines for further discussion.
- For the prioritization of antimicrobials (antimicrobials of highest interest for human health), reference has been made to the WHO publication: "Critically important antimicrobials for human medicine – 5<sup>th</sup> rev. Geneva: World Health Organisation; 2017."

- The appropriate level of detail to include in the guidelines was subject to a number of responses and this will be further discussed and developed by the Task Force. While some responses included detailed sections of text on methods etc., the guidelines will need to remain flexible and current and therefore a high level of prescription (and detail) may need to be avoided. It is worth noting that in a field that is rapidly evolving, excessive detail would likely require periodic updating of the guidelines.
- Some countries emphasized that data obtained from surveillance in imported food should not be used inappropriately to generate barriers to trade and this has been included as a principle.

### **Conclusions**

8. The EWG concludes:

- An integrated monitoring and surveillance system should include the coordinated sampling, testing and reporting of AMR and AMU along the food chain, including the alignment of procedures and methodologies and the integrated analysis of all these data and other information on AMR and AMU as to inform effective risk management across all sectors.
- Collection and analysis of data on use of antimicrobials is essential element of an integrated surveillance programme. The monitoring and surveillance on AMU should be further developed in the guidelines.
- The term Monitoring should be mentioned in the title as to reflect all activities included in the scope of the guidelines.
- Further development of monitoring and surveillance in crops and environment is required to enable an integrated approach to the food chain.
- A stepwise approach with examples is favoured by most. The stepwise approach would need to take into account Member countries capacities.
- A high level of technical prescription need to be avoided as excessive detail would likely require periodic updating of the guidelines.

### **Recommendations**

9. The EWG recommends that the TFAMR:

- Consider the inclusion in the title of the Guidelines “monitoring and”.
- Discuss about the scope of integration as described in the guidelines.
- Elaborate a more complete description of the stepwise approach and prioritizing of components at each step,
- Discuss the need to develop examples to illustrate the stepwise approach.
- Further develop the monitoring and surveillance in crops and environment.
- Further develop the approaches to collection and analysis of data on use of antimicrobials.
- Further develop the chapters: molecular testing, characterization of isolates, analysis of data, review, risk communication and training.

**PROPOSED DRAFT GUIDELINES FOR THE INTEGRATED [MONITORING AND] SURVEILLANCE OF  
FOODBORNE ANTIMICROBIAL RESISTANCE****(for comments at Step 3 through CL 2017/82-AMR)****1. Introduction**

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 commits member countries to developing multi-sectoral national action plans that involve all stakeholders within a “One Health” approach and to improve national systems of monitoring and surveillance of antimicrobial resistance and the use of antimicrobials<sup>1</sup>.

A monitoring and surveillance programme for tracking changes in the AMR of bacteria throughout the food chain, combined with epidemiological information from humans and data on the use of antimicrobials (AM) in humans and animals, is an essential component of a comprehensive national food safety system.

Each country should design and implement a programme for monitoring and surveillance of foodborne AMR and monitoring of use of AMs “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.

Monitoring and surveillance information on AMR along the food chain provides an essential input to risk assessment and decisions by risk managers on control measures to minimise any public health risks due to this exposure pathway. New scientific knowledge should be incorporated in monitoring and surveillance programmes as it becomes available so as to enhance the utility of existing information and data. Design and implementation of programmes should also evolve as AMR policies change at the national and international level.

**2. Purpose of these guidelines**

These guidelines are intended to assist governments in the design and implementation of monitoring and surveillance programmes for food-borne AMR along the food chain at the national level. Such programmes are a fundamental part of national strategies and plans to minimize foodborne AMR. The information generated from these programmes provides essential inputs to:

- Risk analysis
- Assessing trends in occurrence of food borne AMR and AMR determinants (resistant clones, plasmids or genes)
- Providing epidemiological information in case of outbreaks and in incidents of AMR in humans
- Providing data for assessing the impact of control measures at different parts of the food chain in mitigating foodborne risks to consumers
- Availability of information for assessment of risks to animal and plant health
- Guiding and evaluating risk management decisions on more effective or new control measures, either regulatory or non-regulatory
- Providing data inputs to epidemiological studies, food source attribution studies and other operational research
- Risk communication

The guidance provided in this document will contribute to design and implementation of National Action Plans (NAP) that make the best use of available resources at the national level, with the goal of continuous enhancement as more technical capability, data and funding becomes available. As such, these guidelines will assist in promoting a step-wise approach to design and implementation in different countries, both for resistance to, and use of AMs.

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<sup>1</sup> Note that monitoring the use of antimicrobials is implicit in these guidelines for monitoring and surveillance of AMR

### 3. Use of this document

Application of these guidelines should be in conjunction with the *Code of Practice to Minimize and Contain Antimicrobial Resistance* (CAC/RCP 61-2005)<sup>2</sup>. Design and implementation aspects of these guidelines should specifically take into account the *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance* (CAC/GL 77-2011) as well as taking into account other relevant Codex texts including: *Principles and Guidelines for National Food Control Systems* (CAC/GL 82-2013).

These guidelines should also be used in conjunction with those already developed by other international standard-setting organisations and international bodies especially the WHO-AGISAR "Integrated Surveillance of Antimicrobial Resistance in foodborne bacteria; Application of a One Health Approach" and relevant chapters of the OIE Terrestrial Animal Health Code and Aquatic Animal Health Code.

National AMR scenarios are likely to vary between countries and these guidelines should be used to foster a step-wise approach to programme design and implementation at the national level. Identification and implementation of priority baseline activities should be followed by enhancements as the national situation permits. A step-wise approach to monitoring and surveillance should take into account broader capacity issues e.g. availability of information on AM use, adequacy of human health care infrastructure and reporting, availability of food consumption data and agriculture production data, and cross-sector laboratory proficiency and quality assurance.

Information provided from monitoring and surveillance of AMR along the food chain should be combined with information on the amounts and types of antimicrobial agents that are used to best inform risk management decisions.

### 4. Scope

These guidelines cover the design and implementation of an integrated monitoring and surveillance program for AMR and antimicrobial use (AMU) along the food chain, including animals and crops.

These guidelines do not cover design and implementation of monitoring and surveillance of AMR and AMU in humans.

A monitoring and surveillance programme for AMR and AMU along the food chain within the context of overall risk management of AMR (One Health approach) will include design elements, analysis of data and reporting that are common to, and integrated with AMR monitoring and surveillance systems for human and animal health, as well as environmental monitoring,

Reporting of data to international organisations and use of information generated from global monitoring and databases are highly desirable aspects of integrated monitoring and surveillance at the national level.

AMs used as biocides, including disinfectants, are excluded from the scope of these guidelines.

### 5. Definitions

#### One Health approach:

An internationally-recognised approach to designing and implementing programmes, policies, legislation and research on AMR in which multiple sectors communicate and work together to achieve better public health outcomes (WHO reference)

#### 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 (ref. CAC/GL 77-2011)

#### Priority antimicrobial agents:

Antimicrobial agents prioritized as being a public health concern. e.g. the WHO list of critically important antimicrobials<sup>3</sup>.

#### Hazard:

A biological, chemical or physical agent in, or condition of, food with the *potential* to cause an adverse health effect.

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<sup>2</sup> Currently under review

<sup>3</sup>Critically important antimicrobials for human medicine – 5th rev. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO

### Risk-based approach:

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

### Integrated approach to monitoring and surveillance:

For the purpose of these guidelines, a fully integrated approach to the design and implementation of a monitoring and surveillance system includes:

- The coordinated and systematic sampling, testing, analysis and reporting of AMR along the food chain
- Alignment and harmonisation of sampling, testing, analysis and reporting methodologies and practices in humans, animals, plants and the environment to the greatest extent practical
- Integrated analysis of all monitoring and surveillance data and other information on AMR and AMU so as to inform effective risk management across all sectors

### Monitoring of antimicrobial resistance:

The systematic, continuous or repeated, measurement, collection, collation, validation, analysis and interpretation of antimicrobial resistance related data in defined populations when these activities are not associated with a pre-defined risk mitigation plan or activity.

### Surveillance of antimicrobial resistance:

The systematic, continuous or repeated measurement, collection, collation, validation, analysis, interpretation and timely dissemination of antimicrobial resistance related data from defined populations when these activities are associated with a pre-defined risk mitigation plan or activity.

*Note: These data will likely be used in a dynamic manner in the planning, implementation and evaluation of risk mitigation actions.*

## **6. Principles**

These principles should be read in conjunction with the *Guidelines for risk analysis of foodborne antimicrobial resistance* (CAC/GL 77-2011).

- Monitoring and surveillance programmes for AMR should be a core component of a national food safety system;
- Monitoring and surveillance programmes should include patterns of use of AMs so as to support risk analysis and policy initiatives;
- Risk analysis should be a guiding principle in the design, implementation and review of a national monitoring and surveillance programme for AMR, with best practice being informed by expected benefits in terms of minimising the burden of human illness;
- Programmes for monitoring and surveillance of AMR should incorporate an integrated approach (“One Health”);
- A national monitoring and surveillance programme should be tailored to the domestic situation and be designed and implemented according to a step-wise approach;
- In using a step-wise approach, priority should be given to the most relevant elements from a public health perspective (e.g. combinations of bacterial species/ food to be analysed);
- Monitoring and surveillance programmes should incorporate capacity for epidemiological investigation and identification of new and emerging foodborne risks;
- Laboratories involved in monitoring and surveillance should have effective quality assurance systems in place and participate in external proficiency testing;
- Laboratory methodology, data collection, analysis and reporting should be aligned and harmonised across all sectors in national AMR systems as part of an integrated approach;

- Ad hoc operational research projects and epidemiological studies should be carried out to enhance the technical capability and effectiveness of the monitoring and surveillance programme (e.g. new analytical methods, food source attribution studies, monitoring of indirect inputs to the food chain, cross-contamination of foods, molecular epidemiology of emerging clones and resistance determinants);
- National programmes should strive to harmonise components, methodologies and interpretative criteria with international guidance so as to enhance an integrated approach to information management at the international level;
- Data generated from national monitoring and surveillance programmes of AMR in imported foods should not be used to inappropriately generate barriers to trade.

## 7. Risk-based approach

The *Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance* (CAC/GL 77-2011) incorporate the following steps:

- Preliminary risk management activities
- Risk assessment
- Identification and selection of risk management options
- Implementation of control measures
- Monitoring and review.
- Risk communication

In applying a risk based approach to the design of a monitoring and surveillance programme (equivalent to step 5 in the Codex risk analysis framework), 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 in the food chain provides essential information for risk assessment and risk management decision-making on appropriate control measures.

While monitoring and surveillance programmes 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 programmes will [initially] be designed according to the knowledge that is available on AMR hazards (and their determinants) and their potential to result in public health risks.

This knowledge should be included on a risk profile (ref. CAC/GL 77-2011)). 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 step-wise approach to monitoring and surveillance should increasingly incorporate risk-assessment factors as an important element in design of the programme and analysis of data.

Potential foodborne AMR risks to human health are subject to change over time and monitoring and surveillance should be adjusted as new information becomes available e.g. changes in test methodologies, new food chain exposure pathways, changing use patterns of AM. Any adjustments should be properly communicated with reference to methodological changes.

## 8. Regulatory framework and roles

Activities related to monitoring and surveillance of AMR should involve not only the Competent Authority, but also a wider range of stakeholders in various roles. The level of integration of stakeholder roles including food industry, pharmaceutical industry, veterinarians, farmers, professional associations, retail and others will depend on the level of step-wise development of the programme and the degree of integration. Ideally, all stakeholders along the food chain should contribute to the development and implementation of the monitoring and surveillance system.

### 8.1 Regulatory policy framework

Integrated monitoring and surveillance programmes for AMR at the national level require good governance and co-ordination by the relevant Competent Authorities if they are to be effective and sustainable. The Competent Authorities responsible for food safety should provide an overarching policy framework for monitoring and surveillance activities along the food chain in collaboration with the human health, animal health and environmental sectors. Sharing of knowledge with international counterparts might improve the effectiveness of policies taken at local level.

The regulatory activities carried out by the Competent Authorities should be in response to policy objectives that are embedded in national strategies and action plans for managing AMR. Guidance on developing national action plans are outlined in the WHO Global action plan on antimicrobial resistance (reference Global Action Plan on Antimicrobial Resistance, WHO, 2015).

The use of antimicrobial agents in the food chain should be subject to regulation as described in *Code of practice to Minimize and Contain Antimicrobial Resistance* (CAC/RCP 61-2005; under review) and relevant OIE standards.

## 8.2 Non-regulatory activities

Stakeholders other than the Competent Authority may carry out non-regulatory monitoring activities e.g. monitoring of the use of AMs on a voluntary basis by non-government stakeholders such as veterinarians, farmers and the pharmaceutical industry.

Competent authorities responsible for food safety should play an active role in design, analysis and reporting of non-regulatory activities as part of an integrated “One Health” approach.

## 9. A stepwise approach to integrated monitoring and surveillance programme of AMR

A stepwise approach to guidance on design and implementation of integrated monitoring and surveillance programmes allows countries to progress according to different time scales and this is a practical response to inevitable variations in infrastructure, technical capability and budgets level. Clear guidance on a stepwise approach should also facilitate continuous improvement.

The stepwise approach on the monitoring and surveillance of AMR and the use of AMs that is presented in these guidelines references WHO AGISAR Guidelines for integrated surveillance of AMR in foodborne bacteria<sup>4</sup> and reporting options of OIE Guidance for the collection of data on antimicrobial agents used in animals<sup>5</sup>).

### Pre-requisites

Monitoring and surveillance should focus on priority bacterial species and or determinants of AMR, priority AMs e.g. WHO list of critically important antimicrobials for human medicine (reference<sup>6</sup>) and a range of sample sources as determined at the national level. Establishing priorities should be informed by national and international data and knowledge that incorporates public health aspects, epidemiology and AMU patterns, information on agricultural production systems, food consumption patterns and food exposure pathways will enhance risk profiling and risk assessment.

### Step 1

- Monitoring of AMR to a range of priority AMs that have been ranked as highest priority for human health [as defined by WHO in the list of CIAs for human medicine, reference].
- Testing of representative pathogen and indicator bacteria for resistance.
- Sampling from a limited number of food exposure pathways at limited stages along the food chain e.g. slaughterhouse or retail meats.
- Aggregation of national sales data for AMs e.g. collection of data on overall amount sold for/used in animals by antimicrobial class, with the possibility to separate by type of use.
- Analysis and reporting of data from the food chain.

### Step 2

- Scope and design elements informed by a risk profile
- Monitoring and surveillance of AMR to a broader range of priority AMs 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, reference].
- Testing of a range of pathogens determinants and indicator bacteria for resistance.

<sup>4</sup> <http://apps.who.int/iris/bitstream/10665/255747/1/9789241512411-eng.pdf?ua=1>

<sup>5</sup>

[http://www.oie.int/fileadmin/Home/fr/Our\\_scientific\\_expertise/docs/pdf/AMR/Survey\\_on\\_monitoring\\_antimicrobial\\_agents\\_Dec2016.pdf](http://www.oie.int/fileadmin/Home/fr/Our_scientific_expertise/docs/pdf/AMR/Survey_on_monitoring_antimicrobial_agents_Dec2016.pdf)

<sup>6</sup> [http://www.who.int/foodsafety/areas\\_work/antimicrobial-resistance/cia/en/](http://www.who.int/foodsafety/areas_work/antimicrobial-resistance/cia/en/)



- Sampling from a number of food exposure pathways along the food chain e.g. red meat, poultry, aquaculture products and other related sources (e.g. feed, water).
- Pro-active surveillance activities as informed by monitoring and human epidemiology.
- Alignment of food chain methodologies and practices with those used in other sectors.
- Aggregation of national and regional sales data for AMs e.g. collection of data on overall amount sold for/used in animals by AM class, with separation by type of use and species group.
- Integrated analysis and reporting of data from the food chain, and other sources as available.

### Step 3

- Scope and design elements informed by a risk profile and risk assessment.
- Monitoring and surveillance of AMR to a broad range of AMs that are important for human health [as defined by WHO list of Critically Important Antimicrobials, reference].
- Testing of a wide range of pathogen bacteria / determinants and indicators for susceptibility.
- Sampling from a range of direct and indirect food exposure pathways along the food chain e.g. red meat, poultry, aquaculture products, food plants, animal feed, waste water.
- Pro-active surveillance activities as informed by monitoring and human epidemiology.
- Alignment of food chain methodologies and practices with those used in other sectors.
- Aggregation of national and regional sales data for AMs e.g. collection of data on overall amount sold for/used in animals by AM class, with separation by type of use and species group and route of administration.
- Integrated analysis and reporting of data from the food chain and other sectors (“One Health” approach).
- Period review and resetting of the risk analysis cycle as monitoring and surveillance data, together with new technology, is analysed and reported.

Table 1: Description of steps

Step	Scope	Programme	Design	Analysis and reporting
1	Priority AMs and foods as defined at national level	Monitoring of pathogens / indicators in a limited range of foods for susceptibility to priority AMs  Collection of national AM sales/use data as available	Informed by previous surveys and international experience and recommendations	Limited to monitoring data from the food chain
2	Priority AMs and representative foods	Monitoring of a range of pathogens / pathogen determinants and indicators in a number of foods along the food chain Surveillance Collection of national AM sales/use by type of use and species group	Informed by risk profile  Alignment of methodologies across sectors  Pro-active surveillance as informed by monitoring  Review and resetting of design as needed	Co-ordinated and systematic analysis and reporting of data from along the food chain
3	AMs, foods and pathogens / determinants as determined by risk profile	Monitoring of a range of pathogens / pathogen determinants and indicators in a range of foods along the food chain; monitoring of indirect sources	Based on risk profile  Alignment of methodologies across sectors	Co-ordinated and systematic analysis and reporting of data from along the food chain

		<b>Surveillance</b> Collection of national and regional AM sales/use by type of use and species group, and route of administration	Pro-active surveillance as informed by monitoring and human health epidemiology  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 methodological improvement	Integration of data from human sources in co-ordinated analysis and reporting
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## 10. Design of monitoring and surveillance programmes

Many options are available in regard to design of integrated monitoring and surveillance programmes for AMR. The design will be primarily determined by the resources available and the technical capability of the Competent Authorities. An ability to change the design in response to new policy objectives, changes in scientific knowledge and risk assessment is a key attribute for ensuring continuous improvement of the programme. Design should proactively introduce new elements and measures in a timely manner so as to minimise food-borne transmission of AMR.

### 10.1 Prerequisites to design

#### 10.1.1 Step-wise approach

A step-wise approach is key to ensuring continuous enhancement of a monitoring and surveillance programme. The following aspects should be taken into account in deciding on an appropriate initial step in design and implementation:

- Public health infrastructure and knowledge of AMR
- Veterinary infrastructure
- Pharmaceutical infrastructure and distributions systems
- Existing national survey data
- National strategies and action plans
- Budget
- Laboratory capacity and performance
- Type of agricultural, aquatic and livestock production systems and practices
- Other relevant national circumstances, including historical data

#### 10.1.2 Information sources

The Competent Authorities responsible for food safety should consider all available information on:

- Existing national [and international] surveys and/or programmes (regulatory and voluntary)
- Type and use of AMs along the food chain
- Food-borne pathogens occurring in each exposure pathway
- Food supply and distribution systems
- Food consumption patterns and habits
- Foodborne illness data in humans [and animals] that has been attributed to AMR
- International guidance published by international organisations

As with infrastructure and capability considerations above, the extent of the information available and the ability to access and integrate this information will depend on the national situation and the information needs of the initial step that is taken in monitoring and surveillance.

### 10.1.3 Risk profile

Developing a risk profile from available information on hazards and risks (CAC/GL 77-2011) is an important prerequisite to design and should include quantitative information on the likely presence of hazards and associated information, including:

- Lists of critically important (CZ) antimicrobials
- Emerging foodborne AMR threats
- Changing antimicrobial use patterns
- Epidemiology of potential transmission of resistance from food to humans
- Factors affecting foodborne AMR human exposure e.g. food chain hygiene, cooking of foods.
- The likely presence of foodborne microbiological hazards (foodborne AMR microorganism and /or determinants) along the food chain(s) to be monitored
- Lists of AMs prioritised as important for public health
- Use patterns of AMs along the food chain
- Indirect pathways for contamination of food
- Factors affecting human exposure to foodborne hazards e.g. food chain hygiene, cooking of foods
- Epidemiology information on potential transmission of resistance from food to humans
- Any risk assessment information that is available

Risk profiling will utilise the above sources and any other relevant information to describe the potential foodborne risks of transmission of AMR in the particular food chain setting. The extent of the risk that is undertaken will depend on the national situation and the design and implementation step that is being initiated. In many situations, very little risk-based information will be available to draw on and the risk profile will be primarily based on an accumulation of information on hazards and likely exposure through the food chain.

## 10.2 Elements of an integrated monitoring and surveillance programmes

Whatever the step that is utilised, an integrated programme for monitoring and surveillance of AMR along the food chain should strive to include systematic development of the following design elements and technical characteristics:

- Monitoring structure for the food chain
- Sample sources and sampling methodology
- Sampling plans (representativeness, frequency, sample size, etc) that are statistically robust to determine trends in AMR over time
- List of target microorganisms; (pathogens and indicators) and resistance determinants
- Laboratory testing methodology and quality assurance
- Data management including method of Data analysis, sharing and reporting

## 10.3 Types of structure design

- Monitoring programmes may include the following types of design or studies: 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 for a long period of time. The limitations of longitudinal studies are related to their greater complexity and cost compared with point prevalence surveys, but provide valuable information on trends. In the most simple circumstances one or two target microorganisms can be intensively monitored at regular intervals, e.g. every other year.
- Investigative, targeted surveillance studies

- Short-term *ad hoc* studies or projects that can enhance the overall technical and analytical value of a national programme e.g. use of new analytical methods.

#### 10.4 Sample sources

Sources of samples will be determined by the step that is designed. Data from the samples can be integrated with data from other sources e.g. human isolates.

Samples from animals and related sources along the food chain should include:

Samples from food-producing animals (e.g. faeces), feed, litter, water, soil, etc. taken at farm or crops. Although samples from both healthy animals and sick animals are useful for surveillance, samples from healthy animals should be the primary focus for monitoring and surveillance because such samples can provide an unbiased measure of AMR in source animals for the human food supply. Samples collected from food-producing animals should be taken from the same animal species as retail meat food samples in an integrated programme

At holding stage, sample can be taken from holding pen floor, truck/crate swabs, dust, etc.

In the post-slaughter stage, samples can be caecal contents, carcass rinsates and swabs, lymph nodes, etc.

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

Food samples should reflect the purchasing habits of the consumer (e.g. in open markets or chain stores).

#### 10.5 Sampling plans

When designing monitoring and surveillance programmes, representativeness of the data obtained is essential to ensure quality information. Irrespective of the step, an adequate sampling design is required to interpret data and compare results, and to ensure that data obtained from the selected population under study is representative of the whole population and amenable to statistical analysis of temporal trends.

Examples of sampling methods are: Simple Random Sampling (SRS), Stratified Sampling, Systematic Sampling, etc<sup>7</sup>.

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

- Samples selection strategy: retrospective/prospective
- Target animal populations/food/crops
- Selected epidemiological units (flocks, holding)
- Frequency of sampling
- Statistical power and goals of testing (precision of point estimates versus sensitivity to change over time)
- Sampling size with estimates of statistical power to detect changes in antimicrobial resistance patterns.
- Number of isolates/samples
- Selection of strata or risk clusters
- Point in the food chain where the samples will be taken

##### *Selection strategy and principle*

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.

##### *Frequency of sampling*

For surveys and periodic surveillance studies, the frequency of testing should be decided on the basis of the incidence and seasonality of the bacteria or diseases under surveillance. Samples can be collected monthly or periodically throughout the year from different sites, in sufficient numbers, to identify trends.

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<sup>7</sup> Guidance on sampling methods is provided by the Codex documents CCFH and CCMAS

### Sampling size

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 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; depends on the initial or expected prevalence of resistance and the size of the population to be monitored; depends on the desired level of statistical significance and power to detect a difference.

Example of sample size calculation can be found at EFSA Technical specification on harmonised monitoring AMR 2012; 10(6):2742.

## 10.6 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 programme. 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. *Staphylococcus*, *Clostridium* or *Vibrio*).

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

Whenever possible the monitoring and surveillance programme 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.

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

## 10.7 Laboratories

Laboratories participating in the monitoring and surveillance program should:

- isolate, identify and type target bacteria from the different matrices, 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
- be involved in a quality assurance systems including proficiency test in identification, typing and susceptibility testing of the microorganisms included in the monitoring and surveillance system;
- perform antimicrobial susceptibility testing using standardised and validated methods (both phenotypic and/or genotypic);
- store isolates for a period of time by 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 centre) able to provide technical assistance if necessary.

## 10.8 Antimicrobial susceptibility testing

### 10.8.1 Methods and interpretative criteria

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

Quality control (QC) strains of bacteria should be used according to international recommendations e.g. from EUCAST. 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 the other bacteria tested 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 the quantitative results (disk diffusion zone diameters or minimal inhibitory concentrations values) as well as the categorisation of the isolate (resistance or susceptible).

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 analyse 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, rather than 'clinical' breakpoints, as interpretive criteria will allow for optimum sensitivity for detection of acquired resistance.

Detailed information on interpretation of antimicrobial susceptibility test results and Quality control can be found at WHO AGISAR Guidelines for Integrated surveillance of AMR in foodborne bacteria.

#### 10.8.2 The panel of antimicrobials for susceptibility testing

The panel of antimicrobials for susceptibility testing should be harmonised as to ensure continuity and comparability of data, and attempts should be made to use the same antibiotic 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 the antimicrobials and should allow for the tracing of isolates with particular patterns 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.

#### 10.8.3 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 possible comparability of results with human data. 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.

#### 10.8.4 Characterisation of isolates

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

*To be further elaborated*

#### 10.8.5 Molecular testing

Use of molecular testing such as Whole Genome Sequencing (WGS), detection of genes of resistance.

*To be further elaborated.*

### **11. Surveillance of national antimicrobial sales data for use in animals**

This chapter on antimicrobial use should be read in conjunction with:

- 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 Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) guidance on Integrated Surveillance of Antimicrobial Resistance in Foodborne Bacteria,
- Chapter 6.8 (Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals) of the 2016 OIE Terrestrial 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.

#### **11.1 Key aspects to consider when developing surveillance of antimicrobial sales data**

The distribution of antimicrobials for use in animals within the country should be identified.

The most appropriate points of data collection should be identified.

A protocol on the collection of data should be developed.

The estimated animal biomass that can be exposed to antimicrobials should be calculated. [In the EU the ESVAC project has provided a methodology for the calculation of such animal population. The FDA has recently published a proposal for the estimation of the animal population and the OIE is currently working to provide a worldwide estimate of the animal population for country.]

## **11.2 Reporting of the national antimicrobial sales data for use in animals**

The OIE <sup>8</sup> 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 above).

The AGISAR guidance provides details on the collection of:

- 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

## **12. Implementation of the monitoring and surveillance programme**

### **12.1 Sampling procedures**

Samples should be collected by persons authorised to do so (third party accreditation – ref. CCFICS).

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 and duration of transport, and storage of the samples are important aspects as it may influence the results. During transport and storage of the samples in the laboratory measures to maintain the cold chain should be implemented.

### **12.2 Collection and reporting of data**

To ensure an appropriate analysis of the integrated surveillance and monitoring programme it is important that relevant information about the sampling procedure and the individual sample is collected and recorded.

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 randomisation procedure
- General information to identify the isolate, bacterial specie, serovar, etc
- Specific information about the origin of the sample: food producing animal or food category, country of origin, type of sample, stage of sampling in the food chain, place, date of sampling and isolation, etc.
- Specific information about the isolation of the isolate and the AST: date of testing, specific information about the method, quantitative results (e.g. MICs in mg/L), etc. In case of qualitative results interpretative criteria should be recorded.

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<sup>8</sup> OIE Annual report on the use of antimicrobial agents in animals

### 12.3 Management of data

To properly manage test results and data of the integrated monitoring and surveillance programme, a database that guarantees the security, confidentiality and integrity of the data is needed. At national level, one common database is preferred.

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.

Ideally, data should be stored at isolate level including information about.

### 12.4 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.

WHO AGISAR Guidelines 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, 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 coming up with policies to ensure proper use of antimicrobials.

Information provided from monitoring and surveillance of AMR should be analyzed combined with information on the amounts of antimicrobial agents that are used in primary production in national settings, especially with regard to direct use associated with the food chain. Sources of such data include

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.

### 12.5 Targeted investigation

Targeted investigation which is not included in the routine AMR monitoring and surveillance programme 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.

## 13. Review

### 13.1 Integrated analysis of results

Combined analysis of results and data of a programme of integrated surveillance of antimicrobial resistance in foodborne bacteria comprises the bringing together of antimicrobial use in humans and animals and antimicrobial resistance data across all sectors including humans, food-producing animals, retail foods, and the environment, and also provision of the detailed methodology of the surveillance system

#### *Integration of data from foodborne human isolates*

Data from relevant human isolates should include data from those foodborne pathogens more relevant according to national epidemiological information (e.g. Salmonella, Campylobacter) and whenever possible commensal flora such as E. coli and potentially also Enterococcus from healthy humans. 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 antimicrobial resistance 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).

### 13.2 Detection and evaluation of emerging risks

*To be further elaborated.*



### **13.3 Ineffective use**

The Competent Authority should have in place a pharmacovigilance programme for the reporting of adverse reactions to antimicrobials containing veterinary medicinal products and antimicrobial agents, including lack of the expected efficacy, so that this information can be used to review use with respect to the potential for AMR.

### **13.4 Operational research**

Investment in operational research in the national setting to improve the understanding and knowledge of AMR e.g. food source attribution studies.

## **14. Risk communication**

As part of broader risk communication plans for national strategies and action plans, there are specific demands in regards to communicating the results of ongoing surveillance programme – industry, consumers, international organisations etc.

*Ref Codex Risk Analysis principles for governments and CAC/GL 77-2011.*

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 and animals.

*To be further developed.*

## **15. Training**

A tiered approach to implementation at the national level is required, proportional to each step. Programmes should aspire to effective use of available resources, technical capability and potential for cross-sector integration while seeking continuous improvement.

Training programs should include capacity to train the relevant personnel of the relevant competent authority in the different aspects of the monitoring and surveillance programme. This should also include capacity to train personnel in the capture, analyse and reporting of the monitoring and surveillance data.

**Appendix II****List of Participants****Codex Members**

1. Argentina
2. Australia
3. Austria
4. Brazil
5. Canada
6. Chili
7. China
8. Colombia
9. Costa Rica
10. Czech Republic
11. Denmark
12. Dominican Republic
13. Estonia
14. Finland
15. France
16. Guatemala
17. Hungary
18. India
19. Ireland
20. Japan
21. Malaysia
22. The Netherlands
23. New Zealand
24. Norway
25. Poland
26. Republic of Korea
27. Russian Federation
28. Singapore
29. Slovakia
30. South Africa

31. Sweden
32. Switzerland
33. Thailand
34. Tunisia
35. Uganda
36. United Kingdom
37. United States of America
38. Uruguay

**Codex Member Organization**

1. European Union

**Codex Observers**

1. Safe Supply of Affordable Food Everywhere (SSAFE)
2. Biotechnology Innovation Organization (BIO)
3. International Council of Grocery Manufacturers Associations (ICGMA)
4. FoodDrinkEurope
5. Health for Animals
6. International Meat Secretariat (IMS)
7. Organisation Mondiale de la Santé Animale (OIE)
8. European Feed Manufacturers' Federation (FEFAC)
9. Consumers International (CI)
10. CropLife International
11. International Poultry Council (IPC)
12. Inter-American Institute for Cooperation on Agriculture (IICA)
13. International Association of Consumer Food Organizations (IACFO)
14. International Dairy Federation (IDF)