CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 6 **CRD18**

ORINGINAL LANGUAGE ONLY

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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

Seventh Session

Comments of Canada

In light of the discussions during the Physical Working Group meeting on Dec. 8, 2019, we provide this document to facilitate discussions on Sections 7-9 going forward.

Canada suggests that Section 9 still needs some development, particularly for aspects related to dose-based metrics and applicability to plants/crops.

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

7. IMPLEMENTATION OF AN INTEGRATED MONITORING AND SURVEILLANCE PROGRAM FOR FOODBORNE AMR AND AMU

7.1 Preliminary activities

7.1.1 Establishing governance

1. As indicated in the national AMR action plan, competent authorities should develop a One Health governance structure, which supports and provides guidance to the development and continuous improvement of the integrated monitoring and surveillance program.
2. Programs should aspire to effectively use available resources, technical capability and involve various multi-sectoral and international advisory groups and stakeholders as needed for potential cross-sector integration, while seeking continuous improvement.
3. At the outset, the competent authority should identify an individual/ or core team who will be responsible to lead the development and establishment of the program, identify priorities, resource needs, and liaise with key stakeholders.

7.1.2 Setting objectives and priorities

4. The establishment of monitoring and surveillance program objectives is an important initial step in the design and implementation of activities. These objectives should be established in a consultative manner between the competent authorities and interested parties using an evidence-informed approach, such as a scan of existing activities, identification of potential data providers, and existing data (i.e., a situational analysis). In setting the objectives, the competent authorities should take into consideration national action plans, the epidemiology and public health implications of foodborne AMR, AMU patterns, information on food production systems, food distribution, food consumption patterns and food exposure pathways, where the information is available.
5. Part of establishing these objectives is the determination of priorities for microorganisms and resistance determinants, antimicrobials, food commodities, and sample sources for inclusion in the monitoring and surveillance program. These priorities should be informed by national, regional and international public health data and knowledge, where they exists. Competent authorities should identify existing data sources and gaps (with national or regional data as a priority) on AMR and AMU in different sectors. Information from risk profiles and risk assessments, where these exist, should be used.
6. As part of establishing priorities, the competent authority needs to consider the comprehensiveness of the monitoring and surveillance program required to meet the objectives. Considerations for comprehensiveness includes whether passive data is sufficient or if active sampling needs to be conducted (and if so, whether sampling is based on random sampling or convenience sampling) or whether there is a need for census type information (e.g., sampling every farm or having AMU information from every farm).
7. When there are no existing national data to assist with prioritization, the suggested activities as per the WHO AGISAR Guidelines and the OIE Terrestrial and Aquatic Animal Health Codes may be useful.

7.1.3 Developing an operations and communications plan

8. If there are existing monitoring and surveillance programs for other circumstances, such as monitoring of pathogenic foodborne bacteria under food safety programs, the competent authority could consider the possibilities of incorporating or expanding these programs to incorporate aspects related to AMR or AMU to utilize existing infrastructure. Competent authorities should identify the challenges they may face during the implementation of these activities.

9. Once the governance, objective and priorities have been established, the competent authority should determine the infrastructure, capacity, and resources required to meet the objectives. As part of this, the competent authority should identify existing data or sample providers and determine the antimicrobial distribution system for the intended region of the monitoring and surveillance activities.

10. 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 microbiological and epidemiological methods related to the collection, analysis and reporting of the monitoring and surveillance data.

11. The competent authorities should develop an operational plan outlining which elements or components of the monitoring and surveillance program can effectively be implemented first and which could be implemented at a later stage when additional resources become available. The initial scope and design of the program may be informed by previous pilots/surveys or research, if available, and may be informed by national and international experience and recommendations.

12. The setting of proposed timelines for sampling, reporting, and all other surveillance activities should be determined (e.g., reporting on an annual basis).

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

14. The competent authority should determine where the data will be housed, as well as what data will be reported, and how the information will be communicated (e.g., shared in an annual report to interested stakeholders, publication of data to enable further analysis, information exchanged through networks).

15. As part of the operations and communication plan, any needed confidentiality agreements and data management policies should be in place.

16. Implementation of different parts or components of the monitoring and surveillance program can happen at different times. For example, monitoring and surveillance activities on AMR may be implemented at a different point in the operational plan than the activities on AMU. However, as both types of data benefit from a joint analysis, it is useful if the programs are aligned during development and implementation to allow for temporal integrated analysis.

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

8. COMPONENTS OF AN INTEGRATED MONITORING AND SURVEILLANCE PROGRAM FOR AMR

18. To ensure that the objectives are met, an integrated monitoring and surveillance program of foodborne AMR should include and systematically review the sampling design, sample sources, and sample plan, the target bacteria and/or resistance genes, laboratory methods, and which antimicrobials or genes to be tested.

8.1 Sampling design

19. The competent authority will need to determine the sampling design required to meet the objectives of the monitoring and surveillance program for AMR. The following are types of sample designs for consideration:

- Investigative, targeted surveillance and short-term *ad hoc* pilot studies. These studies may be used, for example, to obtain data on specific subpopulations or data on animal/plant/crop species or food that cannot be justified for inclusion in routine, ongoing surveillance. Short-term *ad hoc* pilot studies may also be used to test the feasibility and reliability of planned monitoring and surveillance programs, changes in laboratory or data management methodologies, etc.

- Cross-sectional point prevalence surveys. These surveys may be used to collect basic information and compare findings between various populations at particular points in time.

- Longitudinal monitoring. These studies may be used to routinely and continuously collect data over time and provide valuable information on temporal trends. Longitudinal monitoring may be carried out by conducting repeated cross-sectional surveys at fixed intervals.
- Sentinel surveillance, which relies on selected reporting sites or specific providers (e.g., laboratories, farms, veterinarians).
- Comprehensive surveillance (i.e., census-based).

20. To meet the objectives, the monitoring and surveillance program could require new infrastructure and activities designed solely for the purpose of AMR (i.e., active surveillance) or, where available, isolates or information about AMR could be collected through existing programs designed for another purpose (i.e., passive surveillance).

21. When designing a monitoring and surveillance program, an assessment of the likely representativeness of the data is needed to understand the quality of the resulting information.

- The sample size needs to be sufficient enough to meet the monitoring and surveillance objectives. The sample size should be large enough to generate statistically valid results that represents the population from which the samples are collected, and amenable to statistical analysis of temporal or regional trends.
    - Methods and limitations to data interpretation should be fully described and specified. This may include describing the statistical power, precision, and ability to meet the objectives of the monitoring and surveillance program.
    - Statistical methods should be used to calculate the number of samples or isolates needed for testing.
        - Sample size will depend on the purpose of the monitoring and surveillance, the desired precision for estimates of the prevalence of AMR and the magnitude of change in AMR to be detected over a specified period of time in a certain population.
        - Sample size will further depend on the frequency of recovery of the bacteria, the initial or expected prevalence of AMR in that microorganism and the size of the population to be monitored.
- Examples of sampling strategies (simple random sampling, stratified sampling, systematic sampling, etc.) are provided in Codex documents on food hygiene and methods of analysis and sampling (e.g., *General Guidelines on Sampling* (CXG 50-2004)).
- Frequency of sampling.
    - The frequency of testing should be decided on the basis of the surveillance and monitoring objectives. The incidence and seasonality of the microorganisms or diseases under study should be considered.

8.2 Sample sources

22. An integrated monitoring and surveillance program for AMR should reflect the food production in the country and cover samples from all relevant stages of the production to consumption continuum, as set out in the monitoring and surveillance objectives. In an integrated monitoring and surveillance program, samples collected from the farm, slaughter, and retail should be from the same animal species.

23. Options for sample sources at different points of the production to consumption continuum are:

- **Food producing animals (including terrestrial and aquatic animals)**
    - Selection of animal populations should be relevant to the country's production. Samples should be, to the greatest extent possible, representative of the population being targeted as well as representative of a given epidemiological unit (e.g., farm, herd, flock, aquaculture net-pen). The prevalence of the bacterial species should be considered in order to maximize the likelihood of detection.
    - Samples taken from healthy animals destined for slaughter may be collected on-farm, during transport or lairage, or at the slaughterhouse/abattoir. Collection of samples from animals not immediately entering the food chain can provide population-level information about AMR circulating in microorganisms in healthy animals.
    - Prior to slaughter, samples could be taken from pen floors, truck/crate swabs, dust, etc.
    - Samples such as caecal contents or lymph nodes could be taken post-slaughter. In some

animal species, these samples are representative of the pre-slaughter environment and may or may not provide an estimate of AMR arising at the farm-level. Samples collected after slaughter, but before processing (e.g., carcass, rinses and swabs) may provide an estimate of contamination arising from the dressing process or the slaughterhouse environment.

- **Plants/crops**
    - Samples could include plants/crops on the farm, or samples could be collected during transport, processing and packaging.
- **Farm inputs**
    - Sampling of animal feed including regular feed, medicated feed and animal organic fertilizers, and other relevant food production inputs (e.g., bedding) may be considered as part of the integrated monitoring and surveillance program, as they may be a source of resistant bacteria, such as *Salmonella*, which may be transferred to food-producing animals or be a source of plant/crop contamination.
- **Food**
    - Food sampling at processing/packing, wholesale or point-of-sale (retail) should be considered as part of the integrated monitoring and surveillance program and include both domestically produced and imported food sources.
    - The place where the food samples are collected should reflect the production system in the country and the purchasing habits of the consumer (e.g., in open markets or chain stores).
    - The selection of foods for surveillance should reflect human consumption patterns in the country (e.g., beef, chicken, turkey, pork, lamb, fish and vegetables/fruit) and the likely prevalence of AMR, but may be modified periodically in order to capture seasonality of food availability, or where products have been identified as high risk.
- **Food production environment**
    - Sampling of the food production environment could be considered as part of the integrated monitoring and surveillance program.
    - For animals, at the farm-level, samples could include faeces, feed, litter (bedding), dust, fluff, water, soil, sewage, sludge, manure, sediment below aquaculture sites, etc.
    - For plants/crops, at the pre-harvest level, the food production environment samples could include soils, and when appropriate, irrigation water. Sampling soil amendments such as manure and sewage sludge could also be considered. At the post-harvest level, samples could include surfaces, dust, washing or cooling water, etc.

24. Once a sampling structure is established, consistency in sample types and methodology should be maintained for long-term, comparability and accurate interpretation of results.

8.3 Sampling plans

25. The competent authority should develop standard operating procedures for sample collection.

- Procedures should be put in place to ensure that collection of samples is carried out in accordance to the defined sampling design and to guarantee that traceability, security and quality assurance/management are maintained from collection through to analysis and storage.
- Procedures should be in place for storing and transporting the samples (time between sample collection and testing and temperature during transport and storage) in order to maintain sample integrity.
- The competent authority should develop training material of the standard operating procedures for persons collecting the samples.

8.4 Target microorganisms and/or resistance determinants

26. In order to select the target microorganisms and/or resistance determinants, the microorganism's relevance to public health needs to be considered. The microorganisms should include both foodborne pathogens and commensal microorganisms. The following are bacteria for consideration for monitoring and surveillance of AMR from terrestrial animals, aquatic animals, and plant/crops, the selection will be based on monitoring and surveillance objectives and the national circumstances

- Terrestrial Foodborne Pathogens: *Salmonella, Campylobacter,* or other foodborne pathogens

depending on national priorities and objectives.

- Commensal bacteria: *Escherichia coli, Enterococcus faecium/faecalis*
- Aquatic Foodborne Pathogens:*Vibrio* (others?)
- Plant/crop bacteria: based on available evidence and potential risk

27. Whenever possible, the monitoring and surveillance program could include genetic and/or phenotypic analysis of particular isolates that may be a public health concern (e.g., extended spectrum beta lactamases (ESBL), AmpC beta-lactamase, and carbapenemase-producing strains and multidrug-resistant strains).

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

29. The selection of target microorganisms should also take into consideration the presence of high priority AMR genes or mobile genetic elements and horizontal gene transfer in a given bacterial population.

8.5 Laboratories and laboratory testing methods

8.5.1 General

30. - Laboratories participating in the monitoring and surveillance program will need to:

- Perform testing using standardized and validated methods and have trained personnel in the methods used.
- Be accredited in accordance with national and/or international guidance/procedures, or have a validated Standard Operating Procedures on AST.
- Participate in an external quality assurance system testing including proficiency testing in identification, typing, phenotypic and genotypic characterization and AST of the microorganisms included in the monitoring and surveillance program.
- Store isolates and reference strains using methods that ensure viability and absence of change in the characteristics and purity of the strain.
- Have access to a national reference laboratory or an international laboratory (e.g., WHO-collaborative center) that can provide technical assistance if necessary.

8.5.2 Characterization of isolates

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

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

8.5.3 Molecular testing

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

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

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

36. The application of molecular methods and the interpretation of the information derived from them is by nature multidisciplinary. Global agreement on methods, quality standards, analytical schemes, genomic type nomenclature for microorganisms or resistance determinants and interpretational approaches should

be established to prevent variability in the interpretation of molecular test results. Laboratory and technical capacity, data management, data sharing and analytical platforms to link epidemiological and microbiological information at national and international levels are also important considerations.

37. Professional development in bioinformatics and genomic epidemiology should be encouraged for microbiologists, risk assessors, epidemiologists and risk managers to facilitate the typing, interpretation, reporting and use of integrated genomic epidemiology data.

38. In some countries, using WGS may cost less than using conventional AST and typing. Countries without current AMR monitoring or surveillance programs may consider WGS when developing their programs. Countries taking this approach should validate WGS findings with conventional AST.

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

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

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

8.5.4 Antimicrobial susceptibility testing

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

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

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

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

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

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

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

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

50. The antimicrobials included in the panel should depend on the target bacteria and the clinical or

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

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

8.5.5 Concentration ranges of antimicrobials

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

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

9. COMPONENTS OF AN INTEGRATED MONITORING AND SURVEILLANCE PROGRAM FOR ANTIMICROBIAL SALES/USE DATA

9.1 Design

54. The following aspects should be taken into account when deciding on the approach to collect antimicrobial sales (i.e., consumption data) or antimicrobial use data.

- The competent authority should identify how antimicrobial agents are distributed for use in agriculture (animals and plants/crops) within the country.
- Potential data holders, including marketing authorization holders, wholesalers, distribution centers, pharmacists, veterinarians, farmers and importers/exporters should be identified as part of this process.
- The competent authority should identify the most appropriate points of data collection and the stakeholders that may provide the data at these points to best meet the monitoring and surveillance objectives.
- The competent authority should develop a protocol to collect qualitative and quantitative information on the antimicrobial agents intended for use in animals or plants/crops, to meet the needs of the monitoring and surveillance objectives.
- The competent authority should identify the scope of the data to be captured in the monitoring and surveillance program, such as the antimicrobial agents, classes or sub-classes to be included in data reporting, based on current known mechanisms of antimicrobial activity and AMR data.
- The competent authority should establish the appropriate technical units of measurement and indicators of antimicrobial sales or AMU for reporting. The units used for reporting sales and use should be chosen to best meet the monitoring and surveillance objectives and could be based on internationally accepted methods (where available), to enable interpretation and data sharing globally.
- The competent authority should identify the type and number of plants/crops and food-producing animals to include in monitoring and surveillance, and their weight in kilograms per year (as relevant to the country of production); the latter provides the context to report the antimicrobial sales or the AMU data.

9.2 Sources of Data

55. Once the point(s) in the antimicrobial distribution chain for data collection has been identified, the source of the data or the type of the data to be collected needs to be chosen.

- As per the OIE Global Database on Antimicrobial Agents Intended for Use in Animals, data sources could include sales data (from wholesalers, retailers, marketing authorization holders, registration authorities, feed mills, pharmacies, farm shops/agricultural suppliers, or industry trade associations), purchase data (wholesalers, retailers, feed mills, pharmacies, agricultural cooperatives, producer organizations), import data (customs declarations), veterinary data (sales, prescriptions), or

antimicrobial use data from farm records.

9.3 Data collection - Antimicrobial quantities (numerator) – animals and plants/crops

56. The choice of the numerator or antimicrobial metric will be based on what is most suitable to meet the monitoring and surveillance objectives.

57. The numerator in the context of antimicrobial sales data (for the purpose of this document also known as antimicrobial consumption data) represents the amount of antimicrobials sold or used.

58. The numerator in the context of AMU data represents the quantities of antimicrobials known to be used in the animal/plant/crop species subjected to the monitoring and surveillance. These data are often provided as farm records or prescriptions issued for antimicrobial use on the farm. For use data, there is also value in reporting the number of farms using select antimicrobial agents, the percentage of animals/plants/crops exposed to antimicrobials, or the average duration of exposure.

59. The minimum data collected to estimate the quantities of antimicrobial agents should be the weight in kilograms of active ingredient of the antimicrobial(s) intended for use in food-producing animal or plant/crop per year. It is possible to estimate total usage by collecting sales data, prescription data, manufacturing data, importer and exporter data or some combinations of these.

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

61. Information on dosage regimens (i.e., dose, dosing interval and duration of the treatment) and route of administration are important elements to include when analyzing and reporting antimicrobial use data.

62. Nomenclature of the antimicrobial agents for both data collection and reporting should comply with international standards (e.g., ATCvet code for veterinary antimicrobial products).

9.3.1 For Animals

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

- WHO: *WHO-AGISAR Guidelines for Integrated Surveillance of AMR in Foodborne Bacteria: Application of a One Health Approach (2017)*.
- OIE: The *OIE Terrestrial Animal Health Code* (Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals), the *OIE Aquatic Animal Health Code* (Monitoring of the quantities and usage patterns of antimicrobial agents used in aquatic animals) and the *Guidance for completing the OIE template for the collection of data on antimicrobial agents used in animals* as included in the *OIE Annual report on antimicrobial agents intended for use in animals*.

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

    - Baseline information.
    - **Option 1**: Quantities of antimicrobial agents sold for/used in food-producing animals by antimicrobial class, with the possibility to separate by type of use.
    - **Option 2**: Quantities of antimicrobial agents sold for/used in food producing animals by antimicrobial class, with the possibility to separate by type of use and species group.
    - **Option 3**: Quantities of antimicrobial agents sold for/used in food producing animals by antimicrobial class, with the possibility to separate by type of use, species group and route of administration.

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

66. For animals, if the quantities of antimicrobial agents used can be determined by animal species, then there is the option of converting the kilograms of active ingredients into dose-based metrics (e.g., Defined Daily Doses for animals, or Defined Daily Course Doses for animals). The value of converting to dose-based metrics is to adjust for the different daily doses labelled for use of these antimicrobials (i.e., antimicrobial products differ in the volume required to achieve the desired therapeutic effect).

9.3.2 For Plants/crops

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

- Baseline information on what antimicrobials are registered for use in which plants/crops.
- Collection of amounts sold/used in plants/crops:
    - **Option 1**: Overall amount sold for/used in plants/crops by antimicrobial class, with the possibility to separate by plant/crop type (e.g., fruit trees, grains, vegetables, field vegetables vs greenhouse vegetables, nuts).
    - **Option 2**: Overall amount sold for/used in food and feed plants/crops by antimicrobial class, with the possibility to separate by plant/crop type and specific plants/crops (e.g., apple orchards, walnuts, greenhouse tomatoes).
    - **Option 3**: Overall amount sold for/used in food and feed plants/crops by antimicrobial class, with the possibility to separate by plant/crop type and specific plants/crops, and specific disease and pathogen.
- Reporting of the national antimicrobial sales/use data for use in plants/crops could consider collecting relevant data from farms and agriculture lands where waste derived fertilizers and antimicrobials as pest-control products are applied.

9.4 Data Collection – Denominators - Animal or plant/crop population

68. The desired denominator for reporting of antimicrobial sales or AMU should be determined in advance.

69. A denominator representing the animal population at risk or plant/crop population at risk of being treated with the antimicrobials is important for contextualizing the consumption data and should facilitate the reporting and the comparability of data.

70. The denominator chosen should be representative to the animal species, plant/crop species, production type, etc.

- For animals, the denominator in the context of antimicrobial sales data could be the animal population at risk of being treated (with antimicrobials)
    - This denominator should consider the country's available data on animal populations and animal weights and reflect the surveillance design and objectives.
    - The OIE provides a biomass denominator suitable for global reporting of quantities of antimicrobial agents intended for use in animals. Different production practices and slaughtering or marketing weights make it challenging to develop one biomass calculation that would be equally applicable to every national situation, therefore calculation of the national animal population is desirable for reporting at national level. The European Surveillance of Veterinary Antimicrobial Consumption project has provided a methodology for the calculation of such animal population for sales data reported at EU level; this methodology has been adopted by other countries outside of the EU (e.g., Canada). Furthermore, the US Food and Drug Administration recently published a proposal for the estimation of the animal population. Other examples of denominators may be the total weight of slaughtered or marketed animals, animal years, kg live weight sold or slaughtered.
    - For animals, AMU collected from sampled farms, the number of animals and the time they are under surveillance is critical context for reporting AMU data. Common denominators reported in the literature for sampled farms include 1,000 animal-days or 100 animal-days.
    - For plants/crops, the denominator in the context of antimicrobial agent sales data is the anticipated plants/crops at risk of being exposed to antimicrobials.

i. Currently, there are no standards for reporting a denominator for the quantities of antimicrobials sold for use in plants/crops. Options for denominators could include quantities (kg) of harvested plants/crops or quantities of hectares of land (greenhouses?) used for plant/crop production at risk of being exposed to antimicrobial agents.

9.5 Indicator

71. Indicators are the result of dividing the numerator by the animal/plant/crop population denominator.

72. The choice of indicator for reporting antimicrobial sales and AMU in specific food producing animal species or plant/crops should reflect the objectives of the monitoring and surveillance program.

73. Examples of indicators are: mg of active substance/kg of animal biomass, number of Defined Daily Doses for animals (DDDvet)/1000 animal-days, number of Defined Course Dose for animal (DCDvet)/1000 animal-days.