CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 4 and 5 **CRD3**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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

Fifth Session

Comments of European Union

AGENDA ITEM 4 PROPOSED DRAFT REVISION OF THE CODE OF PRACTICE TO MINIMISE AND CONTAIN ANTIMICROBIAL RESISTANCE (CAC/RCP 61-2005)

Mixed Competence

European Union Vote

This document contains contributions from Codex Members and Observers, including potential areas of consensus, identified in the Electronic Working Group (EWG) held 26 July to 31 August 2017. New and revised text in [square brackets] is proposed for further comment and potential adoption at TFAMR5. Similarly, the working group identified potential consensus around existing text that could be deleted. All text proposed for replacement or deletion is accordingly noted by ~~strikethrough~~ for further comment and consideration at TFAMR5.

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[List of Acronyms Used in the Document]

ADI	Acceptable Daily Intake
AMR	Antimicrobial Resistance
AMU	Antimicrobial Use
CAC	Codex Alimentarius Commission
CAC/RCP	Codex Alimentarius Commission/Recommended Code of Practice
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Foods
FAO	Food and Agriculture Organization of the United Nations
MRL	Maximum Residue Limit
OIE	Office International des epizooties/International Office of Epizooties, World Organisation for Animal Health

VICH International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products

VMP Veterinary Medicinal Product

WHO World Health Organization

Introduction

[1. Antimicrobial resistance poses a complex, global public health challenge. Within the food production to consumption continuum, there is a need to address the **emergence**, selection and dissemination of resistant microorganisms and resistance determinants. The development of strategies for good practices in agriculture (crops), aquaculture and animal husbandry including the responsible and prudent use of antimicrobials **agents** in all sectors following a One Health approach will form a key part of multi-sectoral national action plans to address risks of foodborne antimicrobial resistance.]

[2. This Code of Practice is an integral part of risk analysis focusing on risk management options and should be read in conjunction with other Codex texts including the *Proposed Draft Guidelines on Integrated Surveillance (CAC/GL xx-xxxx)* and **the** Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance CAC/GL 77-2011. In addition, the Codex Code of Hygienic Practice for Fresh Fruits and Vegetables (CAC/RCP 53-2003) and the Code of Practice on Good Animal Feeding (CAC/RCP 54-2004), and Principles and Guidelines for the Conduct of Microbiological Risk Management (CAC/GL 63-2007) are particularly relevant for use of agricultural chemicals on crops and animal feed, respectively. WHO guidelines on Integrated surveillance of antimicrobial resistance in foodborne bacteria, Application of a One Health Approach (2017) and Critically Important Antimicrobials for Human Medicine (2016) and relevant chapters of the OIE Terrestrial and Aquatic Animal Health Codes and the List of Antimicrobials of Veterinary Importance should also be referenced.]

[3. Where available, national and local guidelines to minimize and contain antimicrobial resistance should be taken into consideration. Best practices and guidelines on the responsible and prudent use of antimicrobials developed by governmental and professional organizations should also be considered.]

~~1.~~ [4.] This document provides ~~additional~~ guidance ~~for~~ [on relevant measures along the food chain to minimize the development and spread of foodborne antimicrobial resistance, including guidance on] the responsible and prudent use of antimicrobials in [the] food [chain]~~-producing animals, and should be read in conjunction with the Recommended International Code of Practice for Control of the Use of Veterinary Drugs CAC/RCP 38-1993~~. It's objectives are [part of a One Health approach] to minimize the potential adverse impact on .**human** [and animal] health resulting from the use of antimicrobial agents in [the] food [chain]~~-producing animals~~, in particular the development of antimicrobial resistance. It is also important to provide for the safe and effective use of ~~veterinary~~ antimicrobial [agents]~~drugs in veterinary medicine~~ by maintaining their efficacy.

This document defines the respective responsibilities of authorities and ~~groups~~[relevant stakeholders] involved in the authorization, production, control, distribution and use of ~~veterinary~~ antimicrobials such as the national regulatory authorities, ~~the veterinary pharmaceutical industry~~[manufacturers], veterinarians [and plant health professionals], [wholesale and retail] distributors[,] ~~and~~ [food] producers[, and consumers] ~~of food-producing animals~~.

~~2.~~ [5.] The marketing authorization procedure has a significant role in establishing the basis for [the responsible and] prudent use of ~~veterinary~~ antimicrobial ~~drugs~~ [agents] ~~in food-producing animals~~ through clear label indications, directions and warning statements.

~~3. A number of codes of practice relating to the use of veterinary antimicrobial drugs and the conditions thereof have been developed by different organisations. These codes were taken into consideration and some elements were included in the elaboration of this Code of Practice to Minimize and Contain Antimicrobial Resistance.~~

~~4.~~ [6.] In keeping with the Codex mission, this Code [of Practice] focuses on antimicrobial use in [the] food~~-producing animals~~[chain]. It is recognized that [the use of antimicrobial agents in the food chain may result in exposure in the environment. As part of a One Health strategy to minimize and contain antimicrobial resistance, **only authorized products should be used** and best practices in the **food** production sector should be followed to minimize the **occurrence/persistence in the environment of antimicrobials and their metabolites from anthropogenic sources, and to minimize the** risks associated with the selection (enhancement) and dissemination of resistant microorganisms and **resistance** determinants **in the environment**.] ~~antimicrobial resistance is also an ecological problem and that management of antimicrobial resistance may require addressing the persistence of resistant microorganisms in the environment. Although this issue is most relevant for CCRVDF with respect to food-producing animals, the same principles apply to companion animals, which also harbor resistant microorganisms.~~

[Scope]

[7. This Code of Practice addresses the risk to human **and animal** health associated with the presence in food**-producing animals, food** and animal feed, and the transmission **by direct contact with food-producing animals and** through food and animal feed, of antimicrobial resistant microorganisms or resistance determinants. It provides [risk-based] guidance on relevant measures along the food chain to minimize **and contain** the development and spread of foodborne antimicrobial resistance, including guidance on good practices in agriculture (crops), **aquaculture** and animal husbandry and guidance on the responsible and prudent use of antimicrobial agents in agriculture (crops), animal husbandry, and aquaculture. Its objectives are to minimise the potential adverse impact on **human and animal** health resulting from the use of antimicrobial agents. **Environmental aspects of AMR should be considered when implementing this Code**. All actors involved in the authorisation, manufacture, sale and supply, prescription and use of antimicrobials in the food chain together with those involved in the handling, preparation, distribution and consumption of food have a role to play in optimizing the use of antimicrobial **agents** and/**or** limiting the spread of resistant microorganisms and **resistance** determinants.]

[8. As there are existing Codex or internationally recognized guidelines, the following areas related to antimicrobial agents or AMR are outside the scope of this document: residues of antimicrobial agents in food; AMR marker genes in recombinant-DNA plants and recombinant DNA microorganisms[1]; nongenetically modified microorganisms (for example, starter cultures) intentionally added to food with a technological purpose[2]; and certain food ingredients, which could potentially carry **antimicrobial resistance determinants**, such as probiotics[3].]

~~**1. Aims and Objectives**~~

~~5. It is imperative that all who are involved in the authorisation, manufacture, sale and supply, prescription and use of antimicrobials in food-producing animals act legally, responsibly and with the utmost care in order to limit the spread of resistant microorganisms among animals so as to protect the health of consumers.~~

~~6. Antimicrobial drugs are powerful tools for the management of infectious diseases in animals and humans. This Code and existing guidelines for the responsible use of antimicrobial drugs in food- producing animals include recommendations intended to prevent or reduce the selection of antimicrobial resistant microorganisms in animals and humans in order to:~~

- ~~Protect consumer health by ensuring the safety of food of animal origin intended for human consumption.~~
- ~~Prevent or reduce as far as possible the direct and indirect transfer of resistant microorganisms or resistance determinants within animal populations and from food- producing animals to humans.~~
- ~~Prevent the contamination of animal derived food with antimicrobial residues which exceed the established MRL.~~
- ~~Comply with the ethical obligation and economic need to maintain animal health.~~

~~7. This Code does not address environmental issues related to antimicrobial resistance from the use of veterinary antimicrobial drugs but it encourages all those involved to consider the ecological aspects when implementing the Code. Efforts should be made to ensure that environmental reservoirs of veterinary antimicrobial drugs, antimicrobial resistant organisms and resistance determinants are kept to a minimum. In particular:~~

- ~~Regulatory authorities should assess the impact of proposed veterinary antimicrobial drug use on the environment in accordance with national guidelines or recognized international guidelines[4]~~
- ~~Research should be conducted on resistant microorganisms in the environment and the magnitude of resistance determinant transfer among microorganisms in the environment.~~

~~8. The responsible use of veterinary antimicrobial drugs in food-producing animals:~~

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[1] [The food safety assessment on the use of antimicrobial resistance marker genes in recombinant-DNA plants is addressed in the *Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants* (CAC/GL 45-2003).]

[2] [The food safety assessment on the use of antimicrobial resistance marker genes in recombinant-DNA microorganisms is addressed in the *Guideline for the Conduct of Food Safety Assessment of Foods Produced Using Recombinant-DNA Microorganisms* (CAC/GL 46-2003).]

[3] [The food safety assessment on the use of probiotics in foods is addressed in a Report of a Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Foods (FAO/WHO, 2002).]

[4] ~~VICH (2000). Guidelines on Environmental Impact Assessment for Veterinary Medicinal Products, Phase I. **http://vich.eudra.org/pdf/2000/GI06_st7.pdf**~~

- ~~is controlled by the veterinary profession or other parties with the required expertise~~, **and by the relevant authorities.**
- ~~is part of good veterinary and good animal husbandry practice and takes into consideration disease prevention practices such as the use of vaccination and improvements in husbandry conditions.~~
- ~~aims to limit the use of veterinary antimicrobial drugs according to their approved and intended uses, and takes into consideration on-farm sampling and testing of isolates from food-producing animals during their production, where appropriate, and makes adjustments to treatment when problems become evident.~~
- ~~should be based on the results of resistance surveillance and monitoring (microbial cultures and antimicrobial sensitivity testing), as well as clinical experience.~~
- ~~does not include the use for growth promotion of veterinary antimicrobial drugs that belong to or are able to cause cross resistance to classes of antimicrobial agents used (or submitted for approval) in humans in the absence of a risk analysis. This risk analysis should:~~
    - ~~be undertaken by the appropriate national regulatory authority;~~
    - ~~be based on adequate scientific evidence; and.~~
    - ~~focus on the potential to impact resistance to antimicrobials used in human medicine.~~
- ~~is aimed at all the relevant parties, such as:~~
    - ~~regulatory and scientific authorities;~~
    - ~~the veterinary pharmaceutical industry;~~
    - ~~distributors and others handling veterinary antimicrobial drugs;~~
    - ~~veterinarians, pharmacists and producers of food-producing animals.~~

[Definitions]

[Antimicrobial agent: Any substance of natural, semi-synthetic, or synthetic origin that at *in vivo* concentrations kills or inhibits the growth of microorganisms by interacting with a specific target. The term antimicrobial is a collective for antiviral, antibacterial **(i.e. antibiotics),** antifungal, and antiprotozoal agents.]

[Antimicrobial Resistance (AMR): The ability of a microorganism to multiply or persist in the presence of an increased level of an antimicrobial agent relative to the susceptible counterpart of the same species.]

[Antimicrobial Resistance Determinant: The genetic element(s) encoding for the ability of microorganisms to withstand the effects of an antimicrobial agent. They are located either chromosomally or extra-chromosomally and may be associated with mobile genetic elements such as plasmids, integrons or transposons, thereby enabling horizontal transmission from resistant to susceptible strains.]

[Antibiotic: A naturally derived substance that acts against microorganisms, specifically bacteria.]

[Antibiotic resistance: The ability of a microorganism, specifically bacteria, to multiply or persist in the presence of an increased level of an antibiotic relative to the susceptible counterpart of the same species.]

[Antibacterial: A substance that acts against bacteria. **The term does not include biocides (antiseptics and disinfectants).]**

[Medically important antimicrobials: Antimicrobial agents important for therapeutic use in humans.]

[Infectious diseases-related use [5] **:** Administration of antimicrobial agents for the treatment, control/metaphylaxis and prevention/prophylaxis of disease.]

[Treatment of disease: Administration of antimicrobial agents to infected individuals or populations to resolve clinical signs, infection or illness.]

[Control of disease/metaphylaxis: Administration of antimicrobial agents to populations which contain healthy and infected individuals to minimize or resolve clinical signs, infection or illness.]

[5] **It could be useful to include an explanatory diagram that could further clarify the proposed definitions and distinguish between infectious diseases-related uses and uses not related to infectious diseases.**

[Prevention of disease/prophylaxis: Administration of antimicrobial agents to healthy individuals **in** a population at risk of a specific disease, prior to the onset **of clinical signs,** with appropriate **professional** oversight, dose, and duration.]

Growth promotion: Administration of antimicrobial agents to increase the rate of weight gain and/or the efficiency of feed utilization in animals by other than purely nutritional means. The term does NOT apply to the use of antimicrobials for the specific purpose of treating, controlling, or preventing infectious diseases, even when an incidental growth response may be obtained.

[**Cross-Resistance:** The ability of a microorganism to multiply or persist in the presence of other members of a particular class of antimicrobial agents or across different classes due to a shared mechanism of resistance.]

[**Marketing Authorization:** Process of reviewing and assessing a dossier to support a medicinal product to determine whether to permit its marketing (also called licensing, registration, approval, etc.), finalized by granting of a document also called marketing authorization (MA) (equivalent: product license).]

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

[General Principles to Minimize and Contain Antimicrobial Resistance]

[Principle 1: A One Health approach should be considered, wherever possible and applicable, when identifying, selecting, implementing **and evaluating** AMR risk management options.]

[Principle 2: Good production practices and disease prevention practices such as biosecurity, adequate nutrition, vaccination, improved production practices, and alternatives to antimicrobial agents[6] should **first** be considered to reduce the need for use of antimicrobial agents.]

[Principle 3: Species or sector-specific **guidelines on** responsible and prudent **use of** antimicrobial **agents** should be developed, implemented, and reviewed on a regular basis to maintain their effectiveness in reducing the risk of foodborne antimicrobial resistance. Such guidelines **should be developed on a national or regional level according to the local circumstances of AMR and availability of treatments. These guidelines** could be included as a part of national action plans on antimicrobial resistance with development and dissemination shared among countries and organisations.]

[Principle 4: The WHO list of Critically Important Antimicrobials, the OIE List of Antimicrobials of Veterinary Importance, and national lists, where available, should be used to set priorities for risk assessment and risk management. The lists should be regularly updated **and consolidated.]**

[Principle 5: Responsible and prudent administration in food-producing animals does not include the use for growth promotion of antimicrobial drugs

[Principle 6: Medically important antimicrobial agents should only be used for **infectious diseases-related** purposes (treatment, control/metaphylaxis or prevention/prophylaxis of disease); or in certain circumstances for research and conservation ~~(e.g. skeletal marking in fish)~~.]

[Principle 7: Antimicrobial agents should only be used in well-defined circumstances for the prevention/**prophylaxis and control/metaphylaxis** of a specific disease and follow appropriate **professional** oversight, dose, and duration.]

[Principle 8: Only legally authorized antimicrobial agents should be used and all applicable label directions should be followed; except where specific legal exemptions apply.]

[Principle 9: Foodborne AMR risk management measures should be implemented in a way that is proportionate to the risk and reviewed on a regular basis as described in CAC/GL77. Risk managers should consider potential unintended consequences to human and animal health of recommended risk management measures.]

[6] [Could include ethnoveterinary **and other alternative** approaches, e.g. herbal medicine, **probiotics, prebiotics, competitive exclusion, bacteriophages, immunomodulators, organic acids and teat sealants.]**

[Principle 10: Monitoring and surveillance of the use of antimicrobial agents and the incidence or prevalence, and in particular trends, of foodborne antimicrobial resistant microorganisms and **resistance determinants, with specific consideration being given to temporal trends**, are among the critical factors to consider when **developing risk management measures and** evaluating the effectiveness of implemented risk management measures. Use of medically important antimicrobial drugs in humans, animals **and crops,** and transmission of pathogens and resistance genes between humans, animals, and the environment are additional factors to consider.]

[Principle 11: This document is designed to provide a framework, for the development of measures to mitigate the risk of foodborne AMR, that countries may implement, as part of their national strategy on AMR, in accordance with their capabilities, based on their national situation/capacities, and within a reasonable period of time. A stepwise approach may **be** utilized by some countries to properly implement all of the elements in this document.]

[Principle 12: Medically important antimicrobials should be administered or applied only by veterinarians, plant health professionals or other suitably trained person authorized in accordance with national legislation.]

[Principle 13: Administration of antimicrobial agents should take into consideration sampling and susceptibility testing of isolates from the production setting, where appropriate, and make adjustments to the administration when problems become evident.]

[**Principle 14:** Administration of antimicrobial agents should be based on sound clinical judgement and where feasible on the results of integrated resistance surveillance and monitoring (bacterial cultures and antimicrobial susceptibility testing), as well as relevant experience.]

[**Principle 15:** The reduce, replace and rethink (RRR) strategy should be actively promoted within all sectors.]

[**Principle 16:** On a continuous and stepwise implementation of risk management measures along the food chain to minimize the possible risks associated with foodborne AMR, priority should be given to the most relevant elements as from a public health perspective.]

[Principe 17 (new): Animal health and welfare, and the environment should also be taken into account when considering risk management measures. Efforts should be made to ensure that environmental reservoirs of antimicrobial agents, antimicrobial resistant organisms and resistance determinants are kept to a minimum.]

[Principle 18 (new): Responsible and prudent preventive/prophylactic use of antimicrobials should be limited to exceptional cases, only when the risk of bacterial disease is high and consequences are severe and should be based on veterinarian oversight (or by other suitably trained and authorised person in accordance with national legislation). This use should not be systematic, nor routine, nor applied to compensate for poor hygiene or inadequate animal husbandry/plant production practices, and it should be prescribed only for a limited duration to cover the period of risk. It should always be based on epidemiological and clinical knowledge, with documented justification. When considering preventive use in populations; it should be focused on subsets at highest risk. Preventive use of antibiotics should be limited to individual animals only. Preventive use should always represent a very small proportion of total infectious disease-related use.]

[Principle 19 (new): Responsible and prudent control/metaphylactic use should not be systematic, nor routine, nor applied to compensate for poor hygiene or inadequate animal husbandry/plant production practices. The decision to administer antimicrobials metaphylactically should be based on a diagnosis and prescribed by or on the order of a veterinarian or other suitably trained person authorised in accordance with national legislation, with documented justification. It should be based on epidemiological and clinical knowledge, an understanding of risk factors associated with the group, and in accordance with pre-established criteria (where available) for initiation of administration of antimicrobials.]

Responsibilities of the Regulatory Authorities

9. The ~~national~~ regulatory authorities, which are responsible for granting the marketing authorisation for antimicrobials for use in ~~food-producing animals~~[the food chain], have a significant role in specifying the terms of this authorisation and in providing the appropriate information to the veterinarian [and plant health professionals] through product labelling and/or by other means, in support of [the responsible and] prudent use of ~~veterinary~~ antimicrobial ~~drugs~~[agents] in ~~food-producing animals~~ [the food chain]. It is the responsibility of regulatory authorities to develop up-to-date guidelines on data requirements for evaluation of ~~veterinary~~ antimicrobial ~~drug~~[agent] applications. National governments in cooperation with animal [plant,] and public health professionals should adopt a ~~proactive~~[One Health] approach to promote [the responsible and] prudent use of antimicrobials in ~~food-producing animals~~[the food chain] as an element of a national strategy for the containment of antimicrobial resistance. Other elements of the national strategy should include good animal husbandry [and **plant** production] practices, vaccination [and biosecurity] policies and development of animal [and plant] health care at the farm level, all of which should contribute to reduce the prevalence of animal [and plant] disease requiring antimicrobial treatment. ~~Use of veterinary antimicrobial drugs for growth promotion that belong to classes of antimicrobial agents used (or submitted for approval) in humans and animals should be terminated or phased out in the absence of risk-analysis, as described in Paragraph 8~~.

~~10. It is the responsibility of the pharmaceutical company or sponsor[7] to submit the data requested by the regulatory authorities for granting marketing authorisation.~~

~~11. The use of antimicrobial agents in food-producing animals requires a marketing authorisation, granted by the competent authorities when the criteria of safety, quality and efficacy are met.~~

- ~~The examination of dossiers/drug applications should include an assessment of the risks to both animals and humans resulting from the use of antimicrobial agents in food- producing animals. The evaluation should focus on each individual veterinary antimicrobial drug but take into consideration the class of antimicrobials to which the particular active principle belongs.~~
- ~~The safety evaluation should include consideration of the potential impact of the proposed use in food-producing animals on human health, including the human health impact of antimicrobial resistance developing in microorganisms found in food- producing animals and their environment associated with the use of veterinary antimicrobial drugs.~~

~~12.~~ [10.]. If dose ranges or different durations of treatment are indicated, the national **regulatory** authorities should give guidance on the approved product labelling regarding the conditions that will minimize the development of resistance **in target pathogens, and minimize the exposure to the antimicrobial of other microorganisms that might be of public health relevance**, when this information is available.

[11. For more information on antimicrobial drugs for food-producing animals see the OIE Aquatic Animal Health Code Chapter 6.2.4- Responsibilities of competent authorities and **the OIE** Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 1. Marketing authorization, **and other Sections.]**

~~13. The relevant authorities should make sure that all the antimicrobial agents used in food- producing animals are prescribed by a veterinarian or other suitably trained person authorized in accordance with national legislation or used under conditions stipulated in the national legislation. (See OIE Guidelines for Antimicrobial Resistance: Responsible and Prudent Use of Antimicrobial Agents in Veterinary Medicine (Terrestrial Animal Health Code, Appendix 3.9.3)~~

~~14. No veterinary antimicrobial drug should be administered to animals unless it has been evaluated and authorized for such use by the relevant authorities or the use is allowed through off-label guidance or legislation. Regulatory authorities should, where possible, expedite the market approval process of new veterinary antimicrobial drug formulations considered to have the potential to make an important contribution in the control of antimicrobial resistance.~~

~~15. Countries without the necessary resources to implement an efficient authorisation procedure for veterinary antimicrobial drugs and whose supply of veterinary antimicrobial drugs mostly depends on imports from foreign countries should:~~

- ~~ensure the efficacy of their administrative controls on the import of these veterinary antimicrobial drugs,~~
- ~~seek information on authorizations valid in other countries, and~~

~~[7] As defined in the VICH Good Clinical Practice Guideline, http://vich.eudra.org/pdf/2000/Gl09_st7.pdf~~

- develop the necessary technical cooperation with experienced authorities to check the quality of imported veterinary antimicrobial drugs as well as the validity of the recommended conditions of use. Alternatively, a national authority could delegate a competent institution to provide quality certification of veterinary antimicrobial drugs.

16. All countries should make every effort to actively combat the manufacture, advertisement, trade, distribution and use of illegal and/or counterfeit bulk active pharmaceutical ingredients and products. Regulatory authorities of importing countries could request the pharmaceutical industry to provide quality certificates or, where feasible, certificates of Good Manufacturing Practices prepared by the exporting country's national regulatory authority.

QUALITY CONTROL OF ANTIMICROBIAL AGENTS

17.[12. Regulatory authorities should ensure that quality controls are carried out in accordance with international guidance and in compliance with the provisions of good manufacturing practices., in particular:

- to ensure that the quality and concentration (stability) of veterinary antimicrobial drugs in the marketed dosage form(s) is maintained and properly stored up to the expiry date, established under the recommended storage conditions.
- to ensure the stability of veterinary antimicrobial drugs when they are mixed with feed or drinking water.
- to ensure that all veterinary antimicrobial drugs are manufactured to the appropriate quality and purity.

[13. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 2. Quality control of antimicrobial agents and VMP containing medically important antimicrobial agents.] **Relevant Chapters of the OIE Aquatic Animal Health should be quoted**.

ASSESSMENT OF EFFICACY

[14. Assessment of efficacy is important to assure adequate response to the administration of antimicrobials.]

[15. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 3. Assessment of therapeutic efficacy.] **Relevant Chapters of the OIE Aquatic Animal Health should be quoted.**

18. Preclinical data should be generated to establish an appropriate dosage regimen necessary to ensure the efficacy of the veterinary antimicrobial drug and limit the selection of microbial resistant microorganisms. Such preclinical trials should, where applicable, include pharmacokinetic and pharmacodynamic studies to guide the development of the most appropriate dosage regimen.

19. Important pharmacodynamic information may include:

- mode of action;
- the spectrum of antimicrobial activity of the substance;
- identification of bacterial species that are naturally resistant relevant to the use of the veterinary antimicrobial drugs;
- antimicrobial minimum inhibitory and/or bactericidal concentrations;
- determination of whether the antimicrobial exhibits time or concentration-dependent activity or co-dependency,
- evaluation of activity at the site of infection.

20. Important pharmacokinetic information may include:

- bio-availability according to the route of administration;
- concentration of the veterinary antimicrobial drug at the site of infection and its distribution in the treated animal;
- metabolism which may lead to the inactivation of veterinary antimicrobial drugs;
- excretion routes.

21. The use of fixed combinations of veterinary antimicrobial drugs should be justified taking into account:

- pharmacodynamic (additive or synergistic effects towards the target microorganism);

- pharmacokinetics (maintenance of the concentrations of associated antimicrobials responsible for additive or synergistic effects at the site of infection throughout the treatment period).

22. Clinical data should be generated to confirm the validity of the claimed indications and dosage regimens established during the preclinical phase.

23. Criteria to be considered include:

- parameters for qualitatively and quantitatively assessing efficacy;
- diversity of the clinical cases met when carrying out clinical trials;
- compliance of the protocols of clinical trials with good clinical practice, such as VICH guidelines[8];
- eligibility of the studied clinical cases based on appropriate clinical and microbiological criteria.

ASSESSMENT OF THE POTENTIAL OF VETERINARY ANTIMICROBIAL DRUGS[AGENTS] TO SELECT FOR RESISTANT MICROORGANISMS

[16. The competent authority should assess the potential of medically important antimicrobial drugs to select for resistant microorganisms taking into account CAC/GL77.]

[17. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 4. Assessment of the potential of antimicrobial agents to select for resistance and Chapter 6.10 Risk Analysis for Antimicrobial Resistance Arising from the Use of Antimicrobial Agents in Animals.] **Relevant Chapters of the OIE Aquatic Animal Health should be quoted.**

24. Where applicable, data from preclinical or clinical trials should be used to evaluate the potential for target microorganisms, foodborne and/or commensal microorganisms to develop or acquire resistance.

25. Appropriate information should be provided to support an adequate assessment of the safety of veterinary antimicrobial drugs being considered for authorisation in food-producing animals. The regulatory authorities should develop criteria for conducting such assessments and interpreting their results. Existing guidelines for antimicrobial resistance risk assessment, such as the OIE Guideline[9] may be used for more comprehensive information. The type of information to be evaluated in these assessments may include, but is not limited to, the following:

- the route and level of human exposure to food-borne or other resistant microorganisms;
- the degree of cross resistance within the class of antimicrobials and between classes of antimicrobials;
- the pre-existing level of resistance, if available, in pathogens causing gastrointestinal infections in humans (baseline determination);
- the concentration of active compound in the gut of the animal at the defined dosage level.

ESTABLISHMENT OF ADIS (ACCEPTABLE DAILY INTAKE), MRLS (MAXIMUM RESIDUE LIMIT), AND WITHDRAWAL PERIODS FOR VETERINARY ANTIMICROBIAL DRUGS

26. When setting ADIs and MRLs for veterinary antimicrobial drugs, the safety evaluation is carried out in accordance with international guidelines and should include the determination of microbiological effects (e.g., the potential biological effects on the human intestinal flora) as well as toxicological and pharmacological effects.

27. An acceptable daily intake (ADI) and a maximum residue limit (MRL) for appropriate food stuffs (i.e., meat, milk, eggs, fish and honey) should be established for each antimicrobial agent. MRLs are necessary in order that officially recognised control laboratories can monitor that the veterinary antimicrobial drugs are being used as approved. Withdrawal periods should be established for each veterinary antimicrobial drug, which make it possible to produce food in compliance with the MRLs.

28. Withdrawal periods have to be established for each veterinary antimicrobial drug by taking into account:

- the MRLs established for the considered veterinary antimicrobial drug;
- the pharmaceutical form;
- the target animal species;

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[8] VICH Good Clinical Practice Guideline , http://vich.eudra.org/pdf/2000/GI09_st7.pdf

[9] Antimicrobial resistance: risk analysis methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin, http://www.oie.int/eng/publicat/rt/2003a_r20314.htm

- ~~the dosage regimen and the duration of treatment;~~
- ~~the route of administration.~~

[ASSESSMENT OF ENVIRONMENTAL IMPACT]

[18. Regulatory authorities should assess the impact of proposed ~~veterinary~~ antimicrobial ~~drug~~[agent~~]~~ use on the environment in accordance with national guidelines or recognized international guidelines.]

[19. For more information on antimicrobial drugs for food-producing animals see the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products guidelines[10].]

[20. Regulatory authorities should consider **addressing** the environmental aspects of AMR (e.g. pollution from pharmaceutical manufacture, impacts of reusing waste water for irrigation and using manure for soil fertilization, harmonized monitoring and establishment of maximum admissible levels, etc.]

ESTABLISHMENT OF A SUMMARY OF PRODUCT CHARACTERISTICS FOR EACH VETERINARY ANTIMICROBIAL DRUG FOR FOOD-PRODUCING ANIMALS

[21. Regulatory authorities should establish a Summary of Product Characteristics that can be utilized in labelling and as a package insert.]

[22. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 7. Establishment of a summary of product characteristics for each VMP containing antimicrobial agents.] **Relevant Chapters of the OIE Aquatic Animal Health should be quoted**.

~~29. The summary of product characteristics contains the information necessary for the appropriate use of veterinary antimicrobial drugs. It constitutes, for each veterinary antimicrobial drug, the official reference of the content of its labelling and package insert. This summary contains the following items:~~

- ~~pharmacological properties;~~
- ~~target animal species;~~
- ~~indications;~~
- ~~target microorganisms;~~
- ~~dosage and administration route;~~
- ~~withdrawal periods;~~
- ~~incompatibilities;~~
- ~~shelf-life;~~
- ~~operator safety;~~
- ~~particular precautions before use;~~
- ~~instructions for the return or proper disposal of un-used or out-of-date products;~~
- ~~any information on conditions of use relevant to the potential for selection of resistance should be included, for the purpose of guidance on prudent use;~~
- ~~class and active ingredient of the veterinary antimicrobial drug.~~

SURVEILLANCE **AND MONITORING** PROGRAMMES

[23. Regulatory authorities should establish systems for the surveillance and monitoring of antimicrobial resistance and antimicrobial use following the Codex *Proposed Draft Guidelines on Integrated Surveillance (CAC/GL xx-xxxx)*, taking into consideration relevant sections of Guidelines for Foodborne Antimicrobial Resistance CAC/GL 77-2011; WHO guidelines on Integrated surveillance of antimicrobial resistance in foodborne bacteria, Application of a One Health Approach (2017); and OIE Terrestrial Animal Health Code Chapter 6.7 Harmonisation of national antimicrobial resistance surveillance and monitoring programmes and Chapter 6.8 Monitoring of the quantities and usage patterns of antimicrobial agents used in food-producing animals.] **Relevant Chapters of the OIE Aquatic Animal Health should be quoted.**

[10] [VICH (2000). Guidelines on Environmental Impact Assessment for Veterinary Medicinal Products, Phase I. **http://vich.eudra.org/pdf/2000/GI06_st7.pdf]**

[24. The surveillance and monitoring of **antimicrobial** resistant **microorganisms** in different production sectors and in different products is necessary for understanding the development and dissemination of **antimicrobial** resistance, providing relevant risk assessment data, and assessing the effectiveness of interventions. Surveillance **and monitoring** programmes involve specific and continuous data collection, analysis and reporting that quantitatively monitor temporal trends in the occurrence **and/or prevalence** and distribution of resistance to **antimicrobial agents**; it also allows the identification of emerging or specific patterns **of multiple resistance**.]

~~30. The relevant authorities should develop a structured approach to the investigation and reporting of the incidence and prevalence of antimicrobial resistance. For the purposes of this Code, priority should be given to the evaluation of antimicrobial resistance in foodborne microorganisms.~~

~~For reasons of efficiency, the methods used to establish such programmes (laboratory techniques, sampling, choice of veterinary antimicrobial drug(s) and microorganism(s)) should be harmonized as much as possible at the international level (e.g. OIE documents on "Harmonisation of National Antimicrobial Resistance Monitoring and Surveillance Programmes in Animals and Animal Derived Food" http://www.oie.int/eng/publicat/rt/2003/a_r20318.htm and "Standardisation and Harmonisation of Laboratory Methodologies Used for the Detection and Quantification of Antimicrobial Resistance" http://www.oie.int/eng/publicat/rt/2003/a_r20317.htm).~~

~~31. Preferably, epidemiological surveillance of antimicrobial resistance should be accompanied by data on the amounts of veterinary antimicrobial drugs used by veterinarians and other authorized users in food-producing animals. These data could be collected using one or more of the following sources:~~

- ~~production data from manufacturers;~~
- ~~importers and exporters;~~
- ~~if possible, data on intended and actual usage from manufacturers, wholesale and retail distributors including feed mills, and veterinary prescription records;~~
- ~~surveys of veterinarians, farmers and producers of food-producing animals.~~
- ~~32. Regulatory authorities should have in place a pharmacovigilance programme for the monitoring and reporting of adverse reactions to veterinary antimicrobial drugs, including lack of the expected efficacy related to microbial resistance. The information collected through the pharmacovigilance programme should form part of the comprehensive strategy to minimize microbial resistance.~~

~~33. In cases, where the assessment of data collected from pharmacovigilance and from other post-authorization surveillance including, if available, targeted surveillance of antimicrobial resistance, suggests that the conditions of use of the given veterinary antimicrobial drug should be reviewed, regulatory authorities shall endeavour to achieve this re-evaluation~~.

DISTRIBUTION OF ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~[AGENTS] ~~IN VETERINARY MEDICINE~~

[25. Regulatory authorities should make sure antimicrobial agents are distributed through appropriate distribution systems in accordance with national legislation and medically important antimicrobials are distributed to appropriately credentialed veterinarians, plant health professionals, or other suitably trained person authorized in accordance with national legislation.]

[26. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 9. Supply and administration of the VMP containing antimicrobial agents.] **Relevant Chapters of the OIE Aquatic Animal Health should be mentioned.**

~~34. The relevant authorities should make sure that all veterinary antimicrobial drugs used in food- producing animals are, to the extent possible:~~

- ~~prescribed by a veterinarian or other suitably trained person authorized in accordance with national legislation or used under conditions stipulated in the national legislation;~~
- ~~supplied only through licensed/authorized distribution systems;~~
- ~~administered to animals by a veterinarian or, under the supervision of a veterinarian or other suitably trained person authorized in accordance with national legislation; and that~~
- ~~proper records are kept of their administration (see Paragraph 58, Responsibilities of Veterinarians: Recording section).~~

[27. **D**istribution and use **should be** regularly controlled by the competent authorities, **and** targeted checks **should** be carried out, where appropriate, on prescribers with high levels or concerning patterns of prescriptions.]

CONTROL OF ADVERTISING

[28. Regulatory authorities should assure that advertising of antimicrobial agents is done in accordance to national legislation.]

[29. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 10. Control of advertising.] **Relevant Chapters of the OIE Aquatic Animal Health should be mentioned.**

~~35.~~[30.] Advertising of ~~veterinary~~ antimicrobial ~~drugs~~[agents] should be done in a manner consistent with prudent use guidelines and any other specific regulatory recommendation for the product.

All advertising of ~~veterinary~~ antimicrobial ~~drugs~~[agents] should be controlled by the relevant authorities.

- The authorities should ensure that advertising of ~~veterinary~~ antimicrobial ~~drugs~~[agents]:
    - complies with the marketing authorisation granted, in particular with the content of the summary of product characteristics; and
    - complies with each country's national legislation.

TRAINING OF USERS OF ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~[AGENTS]

~~36.~~[31.] ~~Training should be undertaken to assure the safety to the consumer of animal derived food and therefore the protection of public health.~~ Training should involve all the relevant professional organisations, regulatory authorities, ~~the pharmaceutical industry~~[marketing authorization holders], ~~veterinary~~ schools, research institutes, professional associations[, trade associations] and other approved users such as farmers and producers ~~of food animals~~ and should focus on:

- information on disease prevention and management strategies to reduce the need to use ~~veterinary~~ antimicrobial ~~drugs~~[agents];
- relevant ~~pharmacokinetic and pharmacodynamic~~ information to enable the veterinarian [and plant health professionals] to use ~~veterinary~~ antimicrobial ~~drugs~~[agents] **responsibly and** prudently;
- the ability of ~~veterinary~~ antimicrobial ~~drugs~~[agents] to select for resistant microorganisms ~~in food-producing animals~~ that may contribute to animal[, plant], human health **and environmental** problems; and
- the need to observe responsible **and prudent** use recommendations and using ~~veterinary~~ antimicrobial ~~drugs~~[agents] in ~~animal husbandry~~[production settings] in agreement with the provisions of the marketing authorisations and ~~veterinary~~[professional] advice.

[32. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.3 - Responsible and prudent use of antimicrobial agents in veterinary medicine section 11. Training on the usage of antimicrobial agents.] **Relevant Chapters of the OIE Aquatic Animal Health should be mentioned.**

DEVELOPMENT OF RESEARCH

~~37.~~[33.] The relevant authorities should encourage public and private research to:

- improve the knowledge about the mechanisms of action of antimicrobials in order to optimise the dosage regimens and their efficacy;
- improve the knowledge about the mechanisms of selection, emergence and dissemination of resistance determinants;
- develop practical models for applying the concept of risk analysis to assess the public health concern precipitated by the development of resistance;
- further develop protocols to predict, during the authorisation process, the impact of the proposed use of the ~~veterinary~~ antimicrobial ~~drugs~~[agents] on the rate and extent of resistance development; and
- develop and encourage [good animal husbandry **and plant production** practices and] alternative methods to prevent [and treat] infectious diseases [that would reduce the need to use antimicrobials]

- [develop alternatives to antimicrobials, new antimicrobials, rapid diagnostics, and vaccines, including autogenous vaccines.]
- [determine the potential transfer to fresh produce and other crops of resistant microorganisms and determinants from animal manures used as fertilizer.]

[34. Research should be conducted, as resources permit, on **antimicrobials, their metabolites, resistant microorganisms and resistance determinants** in the environment, and if feasible, factors affecting and the magnitude of resistance determinant transfer among microorganisms in the environment.]

COLLECTION AND DESTRUCTION OF ~~UNUSED~~ **OR** [OUT-OF-DATE] ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~[AGENTS]

~~38.~~[35. The relevant authorities should develop effective [and compulsory] procedures for the safe collection and destruction of unused or out-of-date ~~veterinary~~ antimicrobial ~~drugs~~[agents].

Responsibilities of ~~the Veterinary Pharmaceutical Industry~~[Manufacturers]

MARKETING AUTHORISATION OF ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~ [AGENTS] ~~FOR FOOD-PRODUCING ANIMALS~~

~~39.~~[36. It is the responsibility of the ~~veterinary pharmaceutical industry~~ antimicrobial agent marketing authorization holders:

- to supply all of the information requested by the national regulatory authority in order to establish objectively the quality, safety and efficacy of ~~veterinary~~ antimicrobial ~~drugs~~[agents]; and
- to ensure the quality of this information on the basis of the implementation of procedures, tests and trials in compliance with the provisions of good manufacturing, good laboratory and good clinical practices.

MARKETING AND EXPORT OF ~~VETERINARY~~ ANTIMICROBIAL ~~DRUGS~~[AGENTS]

~~40.~~[37.] Only officially licensed/authorized ~~veterinary~~ antimicrobial ~~drugs~~[agents] should be marketed, and then only through approved distribution systems.

- Only ~~veterinary~~ antimicrobial ~~drugs~~[agents] meeting the quality standards of the importing country should be exported from a country in which the products were produced;
- The information necessary to evaluate the amount of ~~veterinary~~ antimicrobial ~~drugs~~[agents] marketed should be provided to the national regulatory authority.

[38. Package size and the strength of antimicrobial formulations should be adapted as far as possible to the approved indications of use (**in order to** avoid improper dosing, overuse and leftovers).]

ADVERTISING

~~41.~~[39.] It is the responsibility of the ~~veterinary pharmaceutical industry~~[marketing authorization holders] to advertise ~~veterinary~~ [medically important] antimicrobial[s] ~~drugs~~ in accordance with the provisions of Paragraph**s** ~~35~~[**28**-30] on the Responsibilities of the Regulatory Authorities, Control of Advertising and to not ~~inappropriately~~ advertise [medically important] antimicrobials ~~directly~~ to the ~~food animal~~ producer. [Advertising should only be allowed to persons permitted to prescribe or supply antimicrobial drugs. Promotional campaigns involving economic or material benefits for prescribers or suppliers of antimicrobials should be prohibited.]

TRAINING

~~42.~~[40.] It is the responsibility of the ~~veterinary pharmaceutical industry~~[marketing authorization holders] to participate in the training of users of ~~veterinary~~ antimicrobial ~~drugs~~[agents] as defined in Paragraph ~~36~~[31].

RESEARCH

~~43.~~[41.] It is the responsibility of the ~~veterinary pharmaceutical industry~~[marketing authorization holders] to contribute to the development of research as defined in Paragraph ~~37~~[33]. [**including r**esearch on the development of alternatives to the use of antimicrobials, new antimicrobials, rapid diagnostics and vaccines]

Responsibilities of Wholesale and Retail Distributors

~~44.~~[42.] Retailers distributing ~~veterinary~~ [medically important] antimicrobial[s] ~~drugs~~ should only do so on the prescription of a veterinarian, [plant health professional] or other suitably trained person authorized in accordance with national legislation and all products should be appropriately labelled.

~~45.~~[43.] Distributors should encourage compliance with the national guidelines on the responsible use of ~~veterinary~~ [medically important] antimicrobial[s] ~~drugs~~ and should keep detailed records of all [medically important] antimicrobials supplied according to the national regulations including:

- date of supply
- name of prescribing veterinarian [, plant health professional, or other suitably trained and authorized person **in accordance with national legislation**]
- name of user
- name of medicinal product
- batch number
- quantity supplied

~~46.~~[44.] Distributors should participate in the training of users of ~~veterinary~~ antimicrobial ~~drugs~~[agents] as defined in Paragraph ~~36~~[30].

Responsibilities of Veterinarians[11] **[and Plant Health Professionals]**

~~47.~~[45.] The veterinarian ~~is~~[and plant health professionals are] responsible for identifying recurrent disease problems and developing alternative strategies to prevent or treat infectious disease. These may include ~~changes in husbandry conditions and vaccination programs where vaccines are available~~[biosecurity, improved production practices, and alternatives to antimicrobials **including vaccinations where applicable/available**].

[46. For more information on antimicrobial drugs for food-producing animals see the OIE Terrestrial Animal Health Code Chapter 6.9.6 – Responsibilities of veterinarians.] **Relevant Chapters of the OIE Aquatic Animal Health should be mentioned**.

~~48. Veterinary antimicrobial drugs should only be prescribed for animals under his/her care, which means that:~~

- ~~the veterinarian has been given responsibility for the health of the animal or herd/flock by the producer or the producer's agent;~~
- ~~that responsibility is real and not merely nominal;~~
- ~~that the animal(s) or herd/flock have been seen immediately before the prescription and supply, or~~
- ~~recently enough for the veterinarian to have personal knowledge of the condition of the animal(s) or current health status of the herd or flock to make a diagnosis and prescribe; and~~
- ~~the veterinarian should maintain clinical records of the animal(s) or the herd/flock.~~

~~49.~~[47.] It is recommended that ~~veterinary~~ professional organizations develop for their members ~~species-specific clinical practice guidelines on the responsible use of veterinary antimicrobial drugs~~[species or sector-specific **guidelines for** responsible and prudent use **of antimicrobial agents**].

[Within the national action plans, which countries are developing under the Global Action Plan, there should be the recommendation to develop **sector and** species-specific clinical practice guidelines on the responsible use of veterinary antimicrobial agents. These guidelines would be created by the sector specific veterinary professional organizations **depending on local AMR circumstances and availability of treatment**]

~~50.~~[48.] ~~Veterinary a~~[A]ntimicrobial ~~drugs~~[agents] should only be used when necessary and in an appropriate manner:

- A prescription [or order for application] for ~~veterinary~~[medically important] antimicrobial[s] ~~drugs~~ must precisely indicate the treatment regimen, the dose, the dosage intervals, the duration of the treatment, the withdrawal period[, when appropriate,] and the amount of antimicrobial to be delivered depending on the dosage, ~~the number, and the weight of the animals~~[and the characteristics of the individual or population] to be treated;
- [The delivered amount should be limited only for the treatment concerned. **Prescriptions** should also indicate the animal keeper/owner and the identification of the animal(s) **or plants** to be treated;]
- All ~~veterinary [medically important]~~ antimicrobial[s] ~~drugs~~ should be prescribed [or applied] and used according to [label directions and] the conditions stipulated in the national legislation.

[11] Under some circumstances, this may refer to a suitably trained person authorized in accordance with national legislation.

~~51.~~[49.] [For food-producing animals, the]~~The~~ appropriate use of ~~veterinary~~ [medically important] antimicrobial[s] ~~drugs~~ in practice is a clinical decision which should be based on the experience and local expertise of the prescribing veterinarian, and the accurate diagnosis, based on adequate diagnostic procedures. There will be occasions when a group of animals, which may have been exposed to pathogens, may need to be treated without recourse to an accurate diagnosis and antimicrobial susceptibility testing in order to prevent the development of clinical disease and for reasons of animal welfare.

~~52.~~[50.] Determination of the choice of a ~~veterinary~~ antimicrobial [agents] ~~drug~~ by:

- The expected efficacy of the treatment based on:
    - the ~~clinical~~ experience of the veterinarian [, plant health professional or suitably trained and authorized person **in accordance with national legislation**];
    - the spectrum of the antimicrobial activity towards the pathogens involved;
    - the ~~epidemiological~~ history of the ~~rearing~~[production] unit particularly in regards to the antimicrobial resistance profiles of the pathogens involved. ~~Ideally~~[Whenever possible], the antimicrobial profiles should be established before the commencement of treatment. [If this is not possible, samples should nevertheless be taken before start of the treatment to allow, if necessary, for adjustment of therapy based on sensitivity testing.] Should a first antimicrobial treatment fail or should the disease recur, the use of a second ~~veterinary~~ antimicrobial ~~drug~~[agent] should be based on the results of microbiological/**susceptibility** tests;
    - the appropriate route of administration;
    - results of initial treatment;
    - [previous published scientific information on the treatment of the specific disease;]
    - ~~known pharmacokinetics/tissue distribution to ensure that the selected veterinary antimicrobial drug is active at the site of infection;~~
    - ~~prognosis~~[the likely course of the disease].
- The need to minimize the adverse health impact from the development of **anti**microbial resistance based on:
    - the choice of the activity spectrum of the ~~veterinary~~ antimicrobial ~~drug~~[agent] [(narrow-spectrum antimicrobials should be preferred whenever possible/appropriate)];
    - the targeting of specific microorganism;
    - known or predictable susceptibilities using antimicrobial susceptibility testing;
    - optimized dosing regimens;
    - the use of effective combinations of ~~veterinary~~ antimicrobial ~~drugs~~[agents];
    - the importance of the antimicrobial drugs to veterinary and human medicine; and,
    - the route of administration.

~~53. If the label conditions allow for some flexibility, the veterinarian should consider a dosage regimen that is long enough to allow an effective recovery of the animal but is short enough to limit the selection of resistance in foodborne and/or commensal microorganisms.~~

OFF-LABEL USE

~~54.~~[51.] [For food-producing animals, the]~~The~~ off-label use of a veterinary antimicrobial drug may be permitted in appropriate [(exceptional)] circumstances and should be in agreement with the national legislation in force including the administrative withdrawal periods to be used. It is the veterinarian's responsibility to define the conditions of responsible use in such a case including the therapeutic regimen, the route of administration, the duration of the treatment **and the withdrawal period.** Off-label use of [medically important] antimicrobial **for** growth promot**ion purposes** should not be permitted.

[Human health risk related to foodborne antimicrobial resistance should be an important factor when considering the off-label use of veterinary antimicrobial agents.]

RECORDING

~~55.~~[52.] [For food-producing animals, records]~~Records~~ on veterinary antimicrobial drugs should be kept in conformity with national legislation. Veterinarians may refer to recording information as covered in the relevant national legislation.~~12~~

In particular, for investigation of antimicrobial resistance, veterinarians should:

- record the antimicrobial susceptibility testing results;
- **record the antimicrobial used, the dosage regimen and the duration**;
- investigate adverse reactions to veterinary antimicrobial drugs, including lack of expected efficacy due to antimicrobial resistance, and report it, as appropriate, to the regulatory authorities [(through a pharmacovigilance system)].

~~56.~~[53.] [For food-producing animals, veterinarians]~~Veterinarians~~ should also periodically review farm records on the use of veterinary antimicrobial drugs to ensure compliance with their directions.

TRAINING

~~57.~~[54.] ~~Veterinary~~ ~~p~~[P]rofessional organizations should participate in the training of users of ~~veterinary~~ antimicrobial ~~drugs~~[agents] as defined in Paragraph ~~36~~[31].

Responsibilities of [Food] Producers

~~58.~~[55.] Producers are responsible for preventing disease outbreaks and implementing health and welfare programmes on their farms. They ~~may, as appropriate,~~ [should] call on the assistance of ~~their~~ veterinarian[, plant health professional] or other suitably trained person authorized in accordance with national legislation. All people involved with ~~food-producing animals~~[the food chain] have an important part to play in [preventing disease and] ensuring the responsible [and prudent] use of ~~veterinary~~ antimicrobial ~~drugs~~[agents].

~~59.~~[56.] Producers ~~of food-producing animals~~ have the following responsibilities:

- to use ~~veterinary~~ antimicrobial ~~drugs~~[agents] only when necessary and not as a replacement for good management and farm hygiene, or other disease prevention methods such as vaccination;
- to implement a health plan in cooperation with the veterinarian [, plant health professional, or other suitably trained person authorized in accordance with national legislation] ~~in charge of the animals~~ that outlines preventative measures ~~(e.g. mastitis plan, worming and vaccination programmes, etc.)~~;
- to use ~~veterinary~~ antimicrobial ~~drugs~~[agents] in the species, for the uses and at the doses on the approved labels and in accordance with the prescription, product label instructions or the advice of a veterinarian [, plant health professional or other suitably trained person authorized in accordance with national legislation] familiar with the animals ~~and~~[or] the production site;
- ~~to isolate sick animals and dispose of dead or dying animals promptly under conditions approved by relevant authorities;~~
- to comply with the storage conditions of ~~veterinary~~ antimicrobial ~~drugs~~[agents] according to the approved product labelling;
- to address hygienic conditions regarding contacts between people (veterinarians, [plant health professionals,] breeders, owners, children) and the ~~animals~~[populations] treated;
- to comply with the recommended withdrawal periods to ensure that residue levels in ~~animal derived~~[the] food do not present a risk for the consumer;
- to not use out-of-date ~~veterinary~~ antimicrobial ~~drugs~~[agents] and to dispose of all unused ~~veterinary~~ antimicrobial ~~drugs~~[agents] in accordance with the provisions on the product labels [and national legislation];
- to inform the veterinarian[, plant health professional, or other suitably trained person authorized in accordance with national legislation] in charge of the [production] unit of recurrent disease problems;

~~12 Veterinarians can also refer to the "Recommended International Code of Practice for Control of the Use of Veterinary Drugs CAC/RCP 38-1993."~~

- to maintain all clinical and laboratory records of microbiological and susceptibility tests ~~if required by the national regulatory authority~~. These data should be made available to the ~~veterinarian~~[professional] in charge of ~~treating the animals~~[treatment] in order to optimize the use of ~~veterinary~~ antimicrobial ~~drugs~~[agents].
- to keep adequate records of all ~~veterinary~~ antimicrobial ~~drugs~~[agents] used, including the following:
    - name of the ~~veterinary~~ antimicrobial ~~drug~~[agent]/active substance and batch number;
    - name of supplier;
    - date of administration;
    - identification of the ~~animal or group of animals~~[production unit] to which the ~~veterinary~~ antimicrobial ~~drug~~[agent] was administered;
    - ~~clinical conditions~~[disease] treated;
    - quantity and duration of the antimicrobial agent administered;
    - withdrawal periods;
    - result of laboratory tests;
    - result of treatment;
    - name of the prescribing veterinarian [, plant health professional] or other suitably trained person authorized in accordance with national legislation.
- To ensure sound management of ~~animal~~ wastes and other materials to ~~avoid~~ [minimize] dissemination of antimicrobial agents and resistance determinants into the environment;
- To prevent the unnecessary contact with and transmission of resistant bacteria to all personnel, including farm workers;
- To assist the relevant authorities in surveillance programs related to antimicrobial resistance.

[57. The responsible and prudent use of antimicrobials must be supported by continuous efforts in disease prevention to minimise infection during production and decrease the volume of antibiotics used. Efforts should aim to improve health, thereby reducing the need for antibiotics. This can be achieved by improving hygiene, biosecurity and health management on farms, and implementing national or international good animal husbandry, aquaculture, or agricultural practices. Disease prevention through the use of vaccines and other measures such as probiotics (beneficial bacteria found in various foods), prebiotics (non-digestible foods that help probiotic bacteria grow and flourish) or competitive exclusion products (intestinal bacterial flora that limit the colonisation of some bacterial pathogens) should be considered and applied wherever appropriate and available.]

[58. Concerted efforts of all stakeholders within the entire food chain is required to minimize and contain foodborne antimicrobial resistance. While such efforts mainly focus on **responsible and** prudent use of antimicrobial agents in primary production at the farm level, the later phase of the food chain also plays a significant role in preventing transmission and spread of resistant bacteria and resistance determinants.

Food processing industry, food retailers and consumers should take necessary action in accordance with the Principles and Guidelines for the Conduct of Microbiological Risk Management (CAC/GL 63-2007).

Food retailers should favor food produced in accordance with quality schemes and systems of production and supply that apply principles of prudent use i.e. that minimize the use of antimicrobials (and, in case of food producing animals, promote high standards of animal health and welfare).]

[Responsibilities of Consumers]

[59. Consumers have an important role to play to minimize and control antimicrobial resistance. By practicing safe food handling techniques, following health recommendations, and maintaining awareness of antimicrobial resistance information, consumers can minimize the risk of contracting and spreading infectious bacteria thereby further reducing the need for antibacterials. Consumer should:

- Take antibiotics only when needed **in accordance with medical prescription**;
- Use a food thermometer to ensure that foods are cooked to a safe internal temperature: 145°F (63°C) for whole beef, pork, lamb, and veal (allowing the meat to rest for 3 minutes before carving or consuming), 160°F (71°C) for ground meats, and 165°F (74°C) for all poultry, including ground chicken and ground turkey;

- Wash hands after touching raw meat, poultry, and seafood. Also wash work surfaces, cutting boards, utensils, and grill before and after cooking;
- Keep food below 40°F and refrigerating foods within 2 hours of cooking (1 hour during the summer heat);
- Separate raw meat, poultry, seafood and eggs from fresh produce and ready-to-eat foods to avoid cross contamination. Use different cutting boards to prepare raw meat or poultry and any food that will be eaten without cooking;
- Wash hands after contact with feces, animals or animal environments;
- Report suspected outbreaks of illness from food to local health department; and
- Review Competent Authority's traveler's health recommendations when preparing to travel to a foreign country.

[Responsibilities of feed business operators]

Reference should be made to chapter 6.9 Article 6.9.8 of the OIE Animal Health Code

[Advocacy and Communication]

[60. The successful control of antimicrobial resistance along the food chain requires the involvement and cooperation of all parties along the food chain. These include the relevant authorities and stakeholders such as the manufacturers, veterinarians and plant health professionals, wholesale and retail distributors, producers, and consumers who are involved in the authorisation, production, control, importation, exportation, distribution and use of antimicrobial agents.]

[61. Advocacy and communication strategies should identify relevant target audiences, such as policy makers, health, veterinary and agricultural professionals, farmers, players in the food industry, the media and the general public, who all have a responsibility in minimising antimicrobial resistance along the food chain.]

[62. Advocacy and communication efforts at the international and national levels should aim to raise awareness of the importance of antimicrobials in treating bacterial infections and the public health challenges of antimicrobial resistance, including within a food safety perspective.]

[63. Advocacy campaigns should be tailored to the specific stakeholder groups. Campaigns targeted at the agriculture **and aquaculture** sectors should include good animal husbandry, **aquaculture** or agricultural practices and the **responsible and** prudent use of antimicrobials. Those at the food industries should reinforce prevention of contamination and food hygiene practices. National guidelines and education programmes should promote best practices, including correct treatment, measures to prevent and reduce the transmission of pathogens, infection control and hygiene measures. **Campaigns may also be targeted at consumers to encourage them to demand food that is produced in accordance with standards which require responsible use of antimicrobials i.e. where the amounts used are kept as low as possible (and, in case of food producing animals, where high standards of animal health and welfare are promoted)**.]

[64. The engagement and consultation of stakeholders prior to enforcement or introduction of prudent use policies or measures are critical for successful implementation. Regulatory authorities should engage all relevant stakeholder groups.]

[65. Establishment of an Adhoc scientific AMR Newsletter with the objective of collection of recent advances in AMR specially in the field of the tripartite organizations (FAO, WHO and OIE), Codex **Alimentarius**, universities and institutions; with relevance to the development and transmission of food-borne antimicrobial resistance in the food chain (with special emphasis on the genera of Enterobacteriaceae (**STEC**, *Salmonella, Shigella, Campylobacter* and *Vibrio*).

~~**Conclusions**~~

~~60. Veterinary antimicrobial drugs are very important tools for controlling a great number of infectious diseases in both animals and humans. It is vital that all countries put in place the appropriate systems to ensure that veterinary antimicrobial drugs are manufactured, marketed, distributed, prescribed and used responsibly, and that these systems are adequately audited.~~

~~61. This document is designed to provide the framework that countries may implement in accordance with their capabilities but within a reasonable period of time. A stepwise approach may be appropriate for a number of countries to properly implement all of the elements in this document.~~

62. The continued availability of veterinary antimicrobial drugs, which are essential for animal welfare and animal health and consequently human health, will ultimately depend on the responsible use of these products by all those involved in the authorisation, production, control, distribution and use of antimicrobials in food-producing animals.

End Notes

[1]A. Franklin, J. Acar, F. Anthony, R. Gupta †T. Nicholls, Y. Tamura, S. Thompson, E.J. Threlfall, D. Vose, M. van Vuuren, D.G. White, H. C. Wegener & M.L. Costarrica. Antimicrobial resistance: harmonization of national antimicrobial resistance monitoring and surveillance programmes in animals and in animal-derived food. Rev. sci. tech. Off. Int. Epiz., 20 (3), 859-870. http://www.oie.int/eng/publicat/rt/2003/a_r20318.htm

[2]D.G. White, J. Acar, F. Anthony, A. Franklin, R. Gupta, †T. Nicholls, Y. Tamura, S. Thompson, E.J. Threlfall, D. Vose, M. van Vuuren, H. C. Wegener & M.L. Costarrica. Antimicrobial resistance: standardization and harmonization of laboratory methodologies for the detection and quantification of antimicrobial resistance. Rev. sci. tech. Off. Int. Epiz., 2001, 20 (3), 849-858. http://www.oie.int/eng/publicat/rt/2003/a_r20317.htm

List of Abbreviations [Acronyms] Used in this Code

ADI – Acceptable Daily Intake

CAC – Codex Alimentarius Commission

CAC/RCP – Codex Alimentarius Commission/Recommended Code of Practice CCRVDF Codex Committee on Residues of Veterinary Drugs in Foods – FAO Food and Agriculture Organization of the United Nations

MRL – Maximum Residue Limit

OIE – Office International des epizooties/International Office of Epizooties

VICH International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products

WHO World Health Organization

Glossary of Definitions and Terms

Veterinary Antimicrobial Drug

Veterinary antimicrobial drug(s) refers to naturally occurring, semi-synthetic or synthetic substances that exhibit antimicrobial activity (kill or inhibit the growth of microorganisms). Where anticoccidial products have antibacterial activity, they should be considered as veterinary antimicrobial drugs, except where this is precluded by national legislation.

Disease Treatment/Therapeutic Use

Treatment/Therapeutic Use refers to use of an antimicrobial(s) for the specific purpose of treating an animal(s) with a clinically diagnosed infectious disease or illness.

Disease Prevention/Prophylactic Use

Prevention/Prophylactic Use refers to use of an antimicrobial(s) in healthy animals considered to be at risk of infection or prior to the onset of clinical infectious disease. This treatment includes:

- control of the dissemination of a clinically diagnosed infectious disease identified within a group of animals, and
- prevention of an infectious disease that has not yet been clinically diagnosed.

Growth Promotion

Growth Promotion refers to the use of antimicrobial substances to increase the rate of weight gain and/or the efficiency of feed utilization in animals by other than purely nutritional means. The term does NOT apply to the use of antimicrobials for the specific purpose of treating, controlling, or preventing infectious diseases, even when an incidental growth response may be obtained.

AGENDA ITEM 5 PROPOSED DRAFT GUIDELINES ON INTEGRATED SURVEILLANCE OF ANTIMICROBIAL RESISTANCE

Mixed Competence

European Union Vote

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 **establish or** improve national systems of monitoring and surveillance of antimicrobial resistance and antimicrobials **use** (**AMU**)[13].

A monitoring and surveillance programme for tracking changes in the AMR of bacteria throughout the food chain, combined with epidemiological information from humans and **animals and** data on the use of antimicrobials (AM) in humans, animals **and plants**, 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 counties and sectors.

Monitoring and surveillance information on **foodborne** AMR **and AMU** 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 (**risk assessment, risk management and risk communication)**
- Assessing trends in occurrence of food borne AMR and **resistance** 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

The**se** guidel**ines** will contribute to **the** design and implementation of National Action Plans (NAP**s** 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 **foodborne AMR and AMU**.

[13] Note that monitoring the use of antimicrobials is implicit in these guidelines for monitoring and surveillance of AMR

3. Use of these guidelines

Application of these guidelines should be in conjunction with the *Code of Practice to Minimize and Contain Antimicrobial Resistance* (CAC/RCP 61-2005)[14]. 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 **OIE** 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 **in all relevant sectors** 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.

The microorganisms covered by these guidelines are those of public health relevance.

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

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,

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

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.

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[15].

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[14] Currently under review

[15] Critically important antimicrobials for human medicine – 5th rev. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO

Hazard:

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

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**n [**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 AM**U in all relevant sectors** 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 **to** human **health;**
- 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 **human** health perspective (e.g. combinations of bacterial species/ **range of antimicrobials** / 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 **antimicrobials.** 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, **plant health professionals**, 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[16] and reporting options of OIE Guidance for the collection of data on antimicrobial agents used in animals[17]).

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[18]) 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 **and for ~~plants~~ crops** 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.

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16 http://apps.who.int/iris/bitstream/10665/255747/1/9789241512411-eng.pdf?ua=1

17 http://www.oie.int/fileadmin/Home/fr/Our_scientific_expertise/docs/pdf/AMR/Survey_on_monitoring_antimicrobial_agents_Dec2016.pdf

18 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 **and for ~~plants~~ crops** 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 **and for ~~plants~~ crops** 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 Surveillance Collection of national and regional AM sales/use by type of use and species group, and route of administration	Based on risk profile Alignment of methodologies across sectors 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	Co-ordinated and systematic analysis and reporting of data from along the food chain Integration of data from human sources in co-ordinated analysis and reporting

10. Design of monitoring and surveillance programmes

Many options are available in regard to design of integrated monitoring and surveillance programmes for AMR **and AMU**. 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 (CI antimicrobials
- Emerging foodborne AMR threats
- Changing antimicrobial use patterns
- Epidemiology of potential transmission of resistance form 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.), **other edible tissues (liver, kidney, etc**.), fish, dairy product, , 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[19].

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.

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:

[19] Guidance on sampling methods is provided by the Codex documents CCFH and CCMAS

- 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 accreditated 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 ant**imicrobial** 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 particulars patterns of resistance.

Suggested panel of antimicrobials by bacteria for inclusion for **susceptibility testing** 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/use 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 [20] 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 anti**microbials** (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

[20] OIE Annual report on the use of antimicrobial agents in animals

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 **transport and storage** to analysis.

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.

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 **programme** 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), **susceptibility testing** 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 **prudent and responsible** use of antimicrobials.

Information provided from monitoring and surveillance of AMR **and AMU** 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 monitoring and surveillance **of AMR and AMU** 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 **data on AMU** in humans and animals and **data on AMR** 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 veterinary medicinal products **containing** 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.