Codex guidelines related to use of veterinary drugs and AMR risk analysis

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Codex Guidelines on Veterinary drugs and AMR

- Code of Practice to minimise and contain antimicrobial resistance – CAC/RCP 61-2005.
- Guidelines for the design and implementation of regulatory national food safety assurance programme associated with the use of veterinary drugs in food producing animals – CAC/GL 71-2009.
Code of Practice for fish and Fishery Products

- Section 6: Aquaculture
- 6.3.2 Veterinary drugs
- Gives general guidance on use of veterinary drugs (should be approved), should be based on diagnosis, prescribed by authorised person, follow withdrawal time, maintain records.
Code of Practice to minimise and contain AMR

- Responsibilities of the regulatory authorities
  (quality control, assessment of efficiency, assessment of potential to select resistant microorganisms, establishment of ADI, MRL, withdrawal period, surveillance, control of advertising, training of drug users)

- Responsibilities of the pharmaceutical industry
  (marketing authorisation, marketing and export, training, research)

- Responsibilities of whole sale and retail dealers

- Responsibilities of veterinarians (off-label use, recording, training)

- Responsibilities of the producers
Guidelines for the design and implementation of National Regulatory Food Safety Programme associated with the use of veterinary drugs in food producing animals

1. INTRODUCTION
2. SCOPE
3. GENERAL PRINCIPLES
4. APPROACH BASED ON RISK
5. DEFINITIONS (FOR THE PURPOSE OF THESE GUIDELINES)
6. REGULATORY FRAMEWORK
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   6.2 Approval by competent authority
   6.3 Information on veterinary drugs
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   6.5 Responsibilities of business operators (best practice guidance)
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   11.2 Measures in case of non-compliance: Conduct
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12. **INTERACTION BETWEEN THE CONTROL PROGRAMMES OF TWO COMPETENT AUTHORITIES**

Analytical methods for residue control
General considerations on analytical methods for residue control

13. **INTRODUCTION**

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Attributes of analytical methods for residues of veterinary drugs in foods
Guidelines for risk analysis of foodborne antimicrobial resistance

- **Hazard:** a biological, chemical or physical agent in, or condition of, food with potential to cause an adverse health effect.

- **Risk:** A function of the probability of an adverse effect and the magnitude of that effect, consequential to a hazard(s) in food.

- **Risk Analysis:** A process consisting of three components: risk assessment, risk management and risk communication.
STRUCTURE OF RISK ANALYSIS

Risk Assessment
- Hazard Identification
- Hazard Characterization
- Exposure Assessment
- Risk Characterization

Risk Management
- Risk Evaluation
- Option Assessment
- Option Implementation
- Monitoring & Review

Risk Communication
Figure 2.1. Generic framework for risk management

Preliminary risk management activities
- identify food safety issue
- develop risk profile
- establish goals of risk management
- decide on need for risk assessment
- establish risk assessment policy
- commission risk assessment, if necessary
- consider results of risk assessment
- rank risks, if necessary

Identification and selection of risk management options
- identify possible options
- evaluate options
- select preferred option(s)

Implementation of risk management decision
- validate control(s) where necessary
- implement selected control(s)
- verify implementation

Monitoring and review
- monitor outcomes of control(s)
- review control(s) where indicated
Figure 1: Diagrammatic overview of the microbiological risk management framework (from the Draft Codex Principles and Guidelines for the Conduct of Microbiological Risk Management).
Identification of food safety issue - sources of information

- Surveillance data
- Epidemiological reports
- Case reports
- Studies on interaction of the microorganisms with the environment through food production to consumption continuum
- Studies on dissemination of AMR determinants in the environment
- Science based expert opinion
AMR risk profile

- **Description of AMR food safety issue**
  (AMR hazard of concern, antimicrobial agent to which resistance is expressed, food commodity with which AMR is associated)

- **Information on AMR microorganism(s) and/or determinant(s)**
  (source, transmission route, pathogenicity, virulence, linkage to resistance, growth and survivability, inactivation in foods, distribution, frequency and concentration in food chain;
Characteristics of resistance – mechanism, location, cross-resistance, co-resistance, transferability between microorganisms)
AMR risk profile

- Information on the antimicrobial agent(s) to which resistance is expressed
  (Class, non-human uses, purpose, sector, routes of administration, frequency, potential for extra-label use, potential role of cross- and co-resistance on food production, trends in use, trends in relation between use and occurrence of AMR)

- Information on food commodities
  (source-domestic, imported, volume of production, frequency and volume of consumption, description of food production to consumption continuum, characteristics of food that may impact risk management – pH, $a_w$, cooking)
AMR risk profile

- Information on adverse public health effect
  (Characteristics of the disease, frequency, severity, susceptible population, risk factors, epidemiological patterns, regional, seasonal, ethnic differences, consequences of AMR on disease outcome, loss of treatment options, increased frequency, severity of infection, prolonged duration, hospitalisation requirement)
AMR risk profile

- Risk management information
  (identification of management options to reduce AMR hazard in food production to consumption continuum, measures to reduce the risk of selection and dissemination of AMR, measures to minimise contamination, cross-contamination with AMR microorganism, effectiveness of current management practices based on surveillance or other data)

- Evaluation of available information and major knowledge gaps
  (uncertainty in available information, identification of knowledge gaps)
Next steps after development of risk profile

- Ranking of food safety issue and setting priorities for risk assessment and management
- Establishment of preliminary risk management goals
- Establishment of risk assessment policy
- Commissioning risk assessment
Risk Assessment - components

Hazard identification

Hazard characterization

Exposure assessment

Risk characterization
# Hazard Identification

## MICROORGANISMS AND RESISTANCE
- Potential human pathogens likely to acquired resistance
- Commensals with AMR determinants
- Mechanisms of AMR, frequency of transfer and prevalence
- Co- and cross-resistance and importance of other antimicrobial agents
- Pathogenicity, virulence and their linkage to resistance

## ANTIMICROBIAL AGENTS
- Description antimicrobial agent
- Class
- Mode of action
- Pharmacokinetics
- Potential human and non-human uses of the antimicrobial agent
Hazard Characterization

Human host and adverse health effects
• Nature of the infection, disease
• Diagnostic aspects
• Epidemiological pattern (outbreak or sporadic)
• Antimicrobial therapy and hospitalization
• Increased frequency of infections and treatment failures
• Persistence of hazards in humans
HAZARD Characterisation

- Food matrix related factors that can influence the survival of the microorganisms while passing through the gastrointestinal tract
- Dose-response relationship: mathematical relationship between the exposure and probability of adverse outcome (e.g. infection, disease and treatment failure)
The objective is to arrive at an estimate of the adverse health effects related to resistance conditional on disease and infection with an AMRM.
Exposure Assessment

Antimicrobial use selecting for AMRM/AMRD

Animal/crop and microbial factors affecting dissemination of AMRM/AMRD

Other possible sources of AMRM/AMRD for target animal/crop

Selection and dissemination of AMRM/AMRD

Frequency and concentration of AMRM/AMRD at harvest

Food processing factors affecting frequency and concentration of microorganism

Consumer factors affecting frequency/concentration of microorganism, and food consumption rate

Microbial factors affecting transfer and maintenance of resistance

Exposure to AMRM/AMRD via consumption of food
Exposure Assessment Scoring

• Qualitative Risk assessment

Negligible (0) – Virtually no probability that exposure to the hazard can occur;

Moderate (1) – Some probability for exposure to occur;

High (2) – Significant probability for exposure to occur.
Risk characterization

• Number of people falling ill
• Microorganisms attributable to a foodborne source
• Frequency of infections, treatment failures
• Duration of infectious disease
• Deaths
• Therapeutic alternatives
• Comparison of public health burden before and after interventions
Risk Characterization Scoring

No Additional Risk: Value of 0
Some Additional Risk: Value between 1 and 2
High Additional Risk: Value between 3 and 4
Very High Additional Risk: Value between 5 and 6
Risk management options

- **Animal production:**
  - Implementation of GAP, biosecurity
  - Support disease diagnosis and susceptibility testing
  - Dissemination of prudent use guidelines
  - Restrict extra-label use
  - Implement surveillance
  - Promote use of alternatives for disease control

- **Animal feed:** Implement programmes to minimise use of feed or ingredients that could be source of AMR
Risk management options

- Waste treatment
- Ensure far, sewage and waste treatment
- Postharvest measures
- Reprocessing
- Recall procedures
THANK YOU