



**JOINT FAO/WHO FOOD STANDARDS PROGRAMME  
AD HOC CODEX INTERGOVERNMENTAL TASK FORCE  
ON ANTIMICROBIAL RESISTANCE**

*Fourth Session*

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**DRAFT GUIDELINES FOR RISK ANALYSIS OF FOODBORNE ANTIMICROBIAL  
RESISTANCE (N01-2008, N02-2008, N03-2008)**

**COMMENTS AT STEP 6**

*(Replies to CL 2009/25-AMR of European Union)*

**EUROPEAN UNION**

The European Union and its Member States (EUMSs) are pleased to submit the following comments in response to CL 2010/25-AMR.

**General Comments:**

The EUMSs consider that there is a need to clarify the use of the terms "antimicrobial resistance" and "antimicrobial resistant" in several parts of the text. In particular, in paragraphs 2, 3, 7, 9, principles 4 and 7, 12, 24, 33, 37, 41 (bullet 6), table 1, 63, 66 (bullets 1 to 5), 67, 69, 72, Appendices 1, 2 and 3, the term "AMR microorganisms" should be replaced by "antimicrobial resistant microorganisms".

**Specific Comments:**

The following specific suggested comments are of **editorial nature** or to **improve clarity of the text**.

**INTRODUCTION**

**Paragraph 2**

*2. In accordance with Codex principles, risk analysis is an essential tool in assessing the overall risk to human health from foodborne AMR microorganisms and determining appropriate risk mitigation strategies to control those risks. Over the past decade, there have been significant developments with respect to the use of risk analysis approaches in addressing AMR. A series of FAO/OIE/WHO expert consultations on AMR have agreed that foodborne AMR microorganisms are possible microbiological food safety hazards .....*

The EUMSs consider that in the first sentence "overall" is not needed and suggest deleting this term. In the third sentence the term possible should be replaced by "potential". The proposed text would read as follows:

*2. In accordance with Codex principles, risk analysis is an essential tool in assessing the overall risk to human health from foodborne AMR microorganisms and determining appropriate risk mitigation strategies to control those risks. Over the past decade, there have been significant developments with respect to the use of risk analysis approaches in addressing AMR. A series of FAO/OIE/WHO expert consultations on AMR have agreed that foodborne AMR microorganisms are possible potential microbiological food safety hazards .....*

**Paragraph 3**

*3. More specifically, these guidelines provide a structured risk analysis framework to address the risks to human health associated with the presence in food and animal feed, including aquaculture,*

*and the transmission through food and animal feed, of AMR microorganisms or antimicrobial resistance determinants linked to non-human use of antimicrobial agents.*

The sentence is unclear; therefore the EUMSs suggest some rewording:

*3. More specifically, these guidelines provide a structured risk analysis framework to address the risks to human health associated with ~~the presence in food and animal feed, including aquaculture, and the transmission through food and animal feed, including aquaculture, of antimicrobial resistant microorganisms~~ or antimicrobial resistance determinants....*

#### **Paragraph 4**

*4. The initial phase of the risk analysis framework consists of a group of tasks collectively referred to as “Preliminary Risk Management Activities”, which are carried out by the risk managers. This allows the risk manager to decide what action to take. This may involve the establishment of a risk assessment policy and the commissioning of a risk assessment or, perhaps, a more appropriate action. If it is decided to commission a risk assessment, the preliminary risk management activities will provide some of the basic information required by risk assessor undertaking this task. ....*

Proposed amendment in the fourth sentence: “...by risk assessor(s)”.

#### **Paragraph 6**

The footnote for the last reference: “OIE Terrestrial Animal Health Code” is missing (it is cited on Page 41).

### **SCOPE**

#### **Paragraph 7**

*7. The scope of these guidelines is to provide science-based guidance on methodology and processes for risk analysis and its application to foodborne AMR related to non-human use of antimicrobial agents. The intent of the guidelines is to assess the risks to human health associated with the presence in food and feed, including aquaculture, and the transmission through food and feed, of AMR microorganisms and antimicrobial resistance determinants, by developing advice on appropriate risk management activities to reduce such risk. The guidelines will further address the risks associated with different areas of use of antimicrobial agents such as veterinary applications, plant protection or food processing.*

The EUMSs suggest replacing the term "reduce" by "minimise" at the end of second sentence.

*7.....The intent of the guidelines is to assess the risks to human health associated with the presence in food and feed, including aquaculture, and the transmission through food and feed, of AMR microorganisms and antimicrobial resistance determinants, by developing advice on appropriate risk management activities to ~~reduce~~ minimise such risk.....*

### **DEFINITIONS**

#### **Paragraph 9**

*Food Producing Animals: Animals raised for the purpose of providing food to humans. Most commonly this term refers to poultry, swine, cattle, sheep, fish and crustaceans but it does not exclude other domestically managed animals*

Proposed amendment: “...fish and crustaceans...”

### **GENERAL PRINCIPLES FOR FOODBORNE AMR-RISK ANALYSIS**

#### **Paragraph 10**

*Principle 5: Foodborne AMR-risk analysis should build on Principles and Guidelines for the Conduct of Microbiological Risk Assessment (CAC/GL 30-1999) and Principles and Guidelines for the Conduct of Microbiological Risk Management (CAC/GL 63-2007) and, in addition, needs to consider factors relating to the antimicrobial susceptibility of the microorganism(s) in question and related consequences to treatment of human disease resulting from antimicrobial~~s~~ resistant microorganisms.*

Proposed amendment: “...human disease resulting from antimicrobials resistant microorganisms.”

## DEVELOPMENT OF A FOODBORNE AMR-RISK PROFILE (APPENDIX 1)

### Paragraph 15

*"15. The depth and breadth of the foodborne AMR risk profile may vary depending on the needs of the risk managers and the complexity and urgency of the food safety issue. The fundamental elements that comprise a foodborne AMR risk profile include:*

- *Description of the hazard and public health problem (the AMR food safety issue);*
- *Identification and characterization of the combination of the food commodity, the microorganism/resistance determinants and the antimicrobial agent to which resistance is expressed;*
- *Consideration of critically important antimicrobial lists developed by international organizations and national/regional authorities (e.g., see Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials, Rome 2008);*
- *Description of usage (extent and nature) of the antimicrobial agent(s) in food production, when available (such as veterinary applications, aquaculture, plant protection or food processing);*
- *A list of current control measures; and*
- *Identification of major knowledge gaps."*

The EUMSs consider that paragraph 15 should be reviewed based on the outcome of the discussions on Appendix 1 in order to ensure consistency between the body of the text and Appendix 1.

### Paragraph 17

*17. When there is evidence that a risk to human health exists but scientific data are insufficient or incomplete, it may be appropriate for risk managers to select a provisional decision, while obtaining additional information that may inform and, if necessary, modify the provisional decision. In those instances, the provisional nature of the decision should be communicated to all interested parties and the timeframe or circumstances under which the provisional decision will be reconsidered (e.g., reconsideration after the completion of a risk assessment) should be articulated when the decision is initially communicated.*

The EUMSs consider that the final phrase of the last sentence could be simplified to read:

*17.....the timeframe or circumstances under which the provisional decision will be reconsidered (e.g., reconsideration after the completion of a risk assessment) should be stated articulated when the decision is initially communicated.*

## RANKING OF FOOD SAFETY ISSUES AND SETTING PRIORITIES FOR RISK ASSESSMENT AND MANAGEMENT

### Paragraph 18

*18. Given the potentially high resource costs associated with conducting risk assessments and/or implementing RMOs, the AMR risk profile provides the principal resource that should be used by risk managers in risk ranking or prioritization of this AMR food safety issue among numerous other food safety issues.*

Proposed amendment: "...risk ranking or prioritization of this AMR food safety issue..."

## ESTABLISHMENT OF BROAD RISK MANAGEMENT GOALS

As the text was amended during the last session of the Task Force the heading should be amended accordingly. Therefore, it is suggested to replace the word "**broad**" in the title with "preliminary". The title would read:

Establishment of ~~broad~~ preliminary risk management goals

### Paragraph 20

*20. Following development of the risk profile and the risk ranking/prioritization, risk managers should decide on the preliminary risk management goals that determine the next steps to be taken, if any, to address the identified food safety issue.*

The EUMSs consider that instead of risk ranking/prioritization it should read "**ranking of the hazard for risk assessment/risk management**", this is consistent with Figure 1. The text would read as follows

*20. Following development of the risk profile and the ~~risk ranking/prioritization~~ "**ranking of the hazard for risk assessment/risk management**", risk managers should decide on the preliminary risk management goals that determine the next steps to be taken, if any, to address the identified **AMR** food safety issue.*

#### **ESTABLISHMENT OF RISK ASSESSMENT POLICY**

##### **Paragraph 21**

*21. Following a decision as to the need for a risk assessment, risk assessment policy should be established by risk managers in advance of **undertaking a risk assessment**.....*

Proposed amendment :“... by risk managers in advance of **undertaking a** risk assessment.”

#### **COMMISSION A FOODBORNE AMR-RISK ASSESSMENT**

##### **Paragraph 23**

*23. Information that may be documented in the commissioning of the risk assessment includes:*

- *A description of the specific **AMR** food safety issue (as defined in the risk profile);*

Proposed amendment: “A description of the specific **AMR** food...”

#### **SOURCES OF INFORMATION**

##### **Paragraph 26**

The EUMSs would like to propose the following editorial comments:

##### **Bullet point 2:**

- *Epidemiological investigations of outbreaks and sporadic cases associated with **antimicrobial resistant microorganisms***

Proposed amendment “...cases associated with **antimicrobial** resistant microorganisms.”

##### **Bullet point 5**

- *Studies on interaction between microorganisms and their environment through **the** production to consumption continuum (litter, water, feces and sewage);*

Proposed amendment: “...their environment through **the** production to...”

##### **Bullet point 6**

- *Investigations of the characteristics of **antimicrobial resistant microorganisms and antimicrobial resistance determinants (in vitro and in vivo studies)**;*

Proposed amendment: “...characteristics of **antimicrobial** resistant microorganisms and antimicrobial resistance determinants (**in vitro** and **in vivo**).

##### **Bullet point 7**

- *Research on properties of antimicrobial agents including their resistance selection (**in vitro** and **in vivo**) potential and transfer of genetic elements and the dissemination of resistant microorganisms in the environment;*

Proposed amendment: “...their resistance selection (**in vitro** and **in vitro**) potential and...”

##### **Bullet points 8 and 11**

- *Laboratory and/or field animal/crop trials addressing the linkage of antimicrobial use of antimicrobial agents and resistance (particularly regional data)*
- *Laboratory and/or field animal/crop trials addressing the linkage of antimicrobial usage (particularly regional data) and resistance*

- The same statement is included in bullet points 8 and 11. The EUMSs suggest that bullet point 8 is deleted and bullet point 11 is amended to make it clearer:
- *Laboratory and/or field animal/crop trials addressing the ~~linkage-of-between~~ antimicrobial usage and resistance (~~particularly regional data~~) and resistance (~~particularly regional data~~).*

#### **Bullet point 12:**

- *Science-base ~~and~~ expert opinion*

Proposed amendment: delete "**and**".

#### **HAZARD IDENTIFICATION**

##### **Paragraph 30**

*30. The purpose of hazard identification is to identify the foodborne AMR concern. The food safety issues associated with the hazard may have been identified and prioritised in the preliminary risk management activities. Risk assessors should use this as the starting point for further ~~identifying~~ assessing risks. Risk.....*

Proposed amendment: replacement of the term "identifying" by "**assessing**" in the third sentence.

#### **CONSIDERATION OF THE FOODBORNE AMR-RISK ASSESSMENT RESULTS**

##### **Paragraph 45**

*45. The AMR-risk assessment may also identify areas of research needed to fill key gaps in scientific knowledge on a particular risk or risks associated with a given hazard – combination of food, antimicrobial drug(s), antimicrobial use pattern and resistant foodborne microorganisms/or genetic determinants of resistance.*

According to the report of the last session of the Task Force (para 53) it was agreed to use consistently throughout the text food commodity – microorganism/resistance determinant – antimicrobial agent as the combination of factors to be used to specify the risk analysis. Therefore, the EUMSs consider that paragraph 45 should be amended accordingly:

*45. The AMR-risk assessment may also identify areas of research needed to fill key gaps in scientific knowledge on a particular risk or risks associated with a given hazard – combination of the food commodity, the microorganism/resistance determinants and the antimicrobial agent to which resistance is expressed. ~~antimicrobial drug(s), antimicrobial use pattern and resistant foodborne microorganisms/or genetic determinants of resistance.~~*

#### **Identification of foodborne AMR-RMOs**

**Table 1. Examples of Foodborne AMR Risk Management Options, Pre-harvest options**

**Regulatory controls on conditions of use of veterinary antimicrobial drugs and additives:**

- *Marketing status limitation,*
- *Restrict extra-/off-label use*
- *Extent of use limitation,*
- *Major label restriction, and*
- *Withdrawal of authorization.*

Taking into account that no references or definitions are provided for some of the terms used in the bullet points above, the EUMSs would like to propose replacing the bullets above in order to improve clarity:

- **Restrictions of the marketing authorisation,**
- **Conditions for sale (marketing status),**
- **Conditions for extent of use by e.g. restricting extra-/off-label use,**
- **Withdraw the right to commercialise the antimicrobial (withdrawal of authorization).**

## FOODBORNE RISK COMMUNICATION AS A RISK MANAGEMENT TOOL

### Paragraphs 79-81

The EUMSs consider that paragraphs 79 to 82 are drafted in a rather prescriptive way without stating who is responsible for implementation. The following amendments for clarity are proposed:

*79. ~~Industry (pharmaceutical, food producer, food processor, etc.) associations should be encouraged to develop and provide~~ Guideline documents, training programs, technical bulletins and other information that assists developed by industry (pharmaceutical, food producer, food processor, etc.) associations may assist to decrease foodborne AMR.*

*80. ~~Training should be undertaken involving all the relevant professional organizations, regulatory authorities, the pharmaceutical industry, veterinary schools, research institutes, professional associations and other approved users is of importance to ensure the safety to the consumer of animal derived food and, therefore, the protection of public health. Training should~~ involve all the relevant professional organizations, regulatory authorities, the pharmaceutical industry, veterinary schools, research institutes, professional associations and other approved users –this part of the sentence is moved to the first sentence]*

*81. ~~Consumers can enhance both their personal and the public's~~ limit their health risks by being responsible for keeping aware of and following food safety-related instructions. Multiple means of providing this information to consumers, should be undertaken, such as Public education programs, appropriate labelling and public interest messages are important tools to inform consumers. Consumer organizations can play a significant role in providing getting this information to consumers. Information to promote food safety should be disseminated.*

### APPENDIX 1 SUGGESTED ELEMENTS TO INCLUDE IN A FOODBORNE AMR RISK PROFILE

The EUMSs support the inclusion of an appendix on "suggested elements to include in a foodborne risk profile" and therefore, the EUMS consider that the square brackets should be removed.

The EUMSs would like to make the following comments in relation to the text in Appendix I.

This sort of information is included as Annex 1 to the Principles and Guidelines for the Conduct of Microbiological Risk Management (MRM) CAC/GL-63 (2007) and a cross reference should be added.

#### Point 4: Information on the antimicrobial agent to which resistance is expressed

##### Third bullet, second sub-bullet

- *What pathways may have led to the presence of resistance to the antimicrobial agent?*
- *Were related antimicrobial agents used in food production (potential role of cross-resistance or co-resistance)?*

The EUMSs consider that the wording "related antimicrobials" may be too restrictive since there is evidence of cross- or co-resistance between antimicrobial agents that come from different classes. There are also studies suggesting that other agents like zinc oxide may play a role in the development of antimicrobial resistance. Therefore, if this needs to be covered too the sentence could read as follows:

- *Were ~~related other antimicrobial or other agents which may have an effect on emergence and spread of AMR used in production of food (potential role of cross-resistance or co-resistance)?~~*

#### Point 6: Other Relevant Information

##### Second and third bullet points

- *What is the evidence of a relationship between the use of the antimicrobial agent and the occurrence of*
- *AMR microorganisms, or antimicrobial resistance determinants, in the food commodity of concern?*

The two bullets should be merged to improve clarity. Therefore, the proposed final text would read as follows:

- *What is the evidence of a relationship between ~~the~~ any use of the antimicrobial agent and the occurrence of ~~an~~—AMR microorganisms, or antimicrobial resistance determinants, in the food commodity of concern?*

### **APPENDIX 3: EXAMPLES OF QUALITATIVE FOODBORNE AMR-RISK ASSESSMENT**

#### **Example 2**

#### **Illustrative Exposure Assessment Scoring**

*9. The rankings of “Negligible,” “Low,” “Medium,” “High,” and “Not Assessable” may be used for qualitative determination of the probability of human exposure to a given foodborne resistant microorganisms in a given food or feed commodity, animal species, or plant. ....:*

Proposed amendment “...foodborne resistant microorganisms in a given food or feed...”