



**Food and Agriculture  
Organization of  
the United Nations**



**World Health  
Organization**

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**Agenda Item 4**

**CX/AMR 10/4/4 Add.1**

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**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 Brazil, Japan, Philippines and the United States of America)*

**BRAZIL**

**General Comments:**

Brazil would like to thank the opportunity to submit comments to the Proposed Draft Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance adopted by 33<sup>a</sup> Session of the Commission in the step 5, recognizing “the good progress made in the Task Force” and also register the excellent work done by the President and all delegations participants of Task Force to the great effort to obtain this result.

Brazilian delegation reaffirms that the document adopted by 33<sup>a</sup> Session of the Commission is more readable; in line to *Codex Alimentarius* language and represents the best approach to *Codex Alimentarius* or national/regional authorities in conducting risk analysis activities related to foodborne antimicrobial resistance.

In the general observations we would like to register that some paragraphs (e.g. 3, 12 and 24) of the document should be harmonized on language meaning by always using the acronym AMR microorganisms and AMR determinants.

**Specific Comments:**

**PARAGRAPH 16: at the end of paragraph add the sentence: “Decision and its motivation should be timely communicated to all interested parties, as well possible results obtained from risk assessment.”**

The paragraph would read: “Consideration of the information given in the risk profile may result in options leading to a range of initial decisions, such as determining that no further action is needed, commissioning a foodborne AMR - risk assessment, establishing additional information gathering pathways or implementing immediate risk mitigation measures. **Decision and its motivation should be timely communicated to all interested parties, as well possible results obtained from risk assessment**”.

*Rationale: to be consistent with what is presented at Figure 1.*

FIGURE 1: Add a title for the Figure. The title should read as: **Figure 1. Overview of the framework for foodborne AMR-risk analysis.**

*Rationale: Figure should be properly identified for easier location.*

FIGURE 1: include the sentence “**establishment of broad risk management goals**” as a new step at Figure 1 between “ranking of the hazard for risk” and “establishment of risk assessment”

*Rationale: to complete the framework for foodborne AMR-risk analysis and be compatible with paragraph 20.*

**PARAGRAPH 26** – merge bullets 8 and 11 or delete bullet 8, as words “use” and “usage” have the same meaning in English.

**PARAGRAPH 26** – insert the word “sound” at the last bullet point.

The bullet point would read: “**Science-based and sound expert opinions**”.

*Rationale: to be consistent with it was previously defined by Task Force (ALINORM 10/33/42, paragraph 71, page 8).*

**PARAGRAPH 33** – insert the word “suggested” before “pre-harvest factors”.

**The paragraph would read:** “Section 2.1 of Appendix 2 includes suggested pre- harvest factors for estimating the likelihood of selection and dissemination of resistance within animal or plant populations. A possible output from the pre-harvest component of exposure assessment is an estimate or probability of the influence of the use of antimicrobial agents on the prevalence of resistance microorganisms in the target animals or crops. Section 2.2 of Appendix 2 considers possible post-harvest factors related to the human exposure to food containing AMR microorganisms and/or antimicrobial resistance determinants. A possible output from the post-harvest component of exposure assessment is an estimate of the likelihood and level of contamination of the food product with resistant microorganisms at the time of consumption”.

*Rationale: to be consistent with Appendix 2 (“Suggested elements for consideration in foodborne AMR-risk assessment”).*

**FIGURE 2: represent Figure 2 in a better readable format.**

**PARAGRAPH 55:** change the last sentence of paragraph to “**minimize the exposure to food containing AMR microorganisms and AMR determinants**”.

**The paragraph would read:** “Table 1 provides examples of RMOs for the control of foodborne AMR risks, inclusive but not exhaustive of existing Codex Codes of Practice, and RMOs specific to foodborne AMR. The table is divided into pre-harvest RMOs, which include measures to reduce the risk related to the selection and dissemination of foodborne AMR microorganisms, and post-harvest RMOs, which include measures to minimize the exposure to food containing contamination of food by AMR microorganisms and AMR determinants”.

*Rationale: to be in accordance with the examples of post-harvest options presented at Table 1.*

**TABLE 1** – Food crop production: delete the words “as supplements” as previously agreed by Task Force and indicated at paragraph 90.

The sentence would read: “Evaluate the safety of viable microorganisms used as supplements in food and feed crop production for their potential to introduce and spread AMR”.

*Rationale: to be in accordance with it was previously defined by Task Force (ALINORM 10/33/42, paragraph 90, page 9).*

**PARAGRAPH 70:** replace “between countries” at the first sentence of paragraph by the text: “taking into account references of international organisms”.

The paragraph would read: “Methodology of surveillance program should be harmonized ~~between countries~~ taking into account references of international organisms. The use of standardized and validated antimicrobial susceptibility testing methods and harmonized interpretive criteria are essential to the ability to use information from such programs”.

*Rationale: the harmonization would be more feasible and the obtained information more consistent and standardized.*

**PARAGRAPH 80** – amend the first sentence of paragraph to include the words “and plant” (“animal and plant derived food”).

**The paragraph would read:** “Training should be undertaken to ensure the safety to the consumer of animal and plant 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”.

**Rationale: to obtain consistency with other parts of the document.**

## **JAPAN**

### **General Comments:**

Japan is of the view that the Draft GLs should be consistent, as much as possible, with the *Working Principles for Risk Analysis for Food Safety for Application by Government* (CAC/GL 62-2007) in the context of Section on “GENERAL PRINCIPLES FOR FOODBORNE AMR-RISK ANALYSIS” in the Draft GLs. Japan believes that the following specific comments may help the Task Force resolving discrepancies between the *Working Principles* and the document and refining the document.

### **Specific Comments:**

#### **Reorganization of subsections and paragraphs**

According to footnote 4 of paragraph 31 in CAC/GL 62-2007, consideration of the result of the risk assessment is a part of risk management, but not risk assessment. Therefore the current sub-section on “Consideration of the foodborne AMR-risk assessment results” should be placed in the Section on “FOODBORNE AMR-RISK MANAGEMENT”.

In this regard, Japan proposes to reorganize some texts in paragraphs 44 - 50 in the sub-section on “Consideration of the foodborne-AMR-risk assessment results” and the Section on “FOODBORNE AMR-RISK MANAGEMENT”, presented as follows:

#### **FOODBORNE AMR-RISK ASSESSMENT**

##### **Risk Characterization**

##### **Presentation of the foodborne AMR-risk assessment results (New sub-section)**

43-bis. The conclusions of the risk assessment including a risk estimate, if available, should be presented in a readily understandable and useful form to risk managers and made available to other risk assessors and interested parties so that they can review the assessment. <<Displacement of 1<sup>st</sup> sentence in para.44>>

##### **~~Consideration of the foodborne AMR-risk assessment results~~**

~~44. The conclusions of the risk assessment including a risk estimate, if available, should be presented in a readily understandable and useful form to risk managers and made available to other risk assessors and interested parties so that they can review the assessment. <<Become 43 bis. above>> The responsibility for resolving the impact of uncertainties described in the risk assessment on RMOs lies with the risk manager and not with the risk assessors.<<Moved to para. 48>>.~~

~~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.<<Moved to after para.50>>~~

#### **FOODBORNE AMR-RISK MANAGEMENT**

46. [No change]

47. [No change]

48. Once a decision has been made to take action, RMOs should be identified, evaluated, selected, implemented, monitored and reviewed, with adjustments made when necessary. The decision should be based on AMR-risk assessment and should be proportionate to the assessed risk.<<reproduced of paragraph 32 in CAC/GL62 2007>>. The responsibility for resolving the impact of uncertainties on described in the risk management decision assessment on RMOs lies with the risk manager and not with the risk assessors.<<Displacement of the second sentence in para. 44 with some modifications to be consistent with paragraph 32 of CAC/GL 62 2007)>>

49. [No change, except a minor correction as follows: *Code of Hygienic Practice for Eggs and Eggs Products* (CAC/RCP ~~1561-1976~~<sup>2005</sup>)]

50. [No change]

**Consideration of the foodborne AMR-risk assessment results**

50-bis. The AMR-risk assessment should clearly and fully answer the questions asked by the risk managers as far as possible given the availability of data and should identify and quantify sources of uncertainties in risk estimates, where appropriate. <<New text from 1<sup>st</sup> sentence of 2.4.7. Step 7: Consider the results of the risk assessment in the Food Safety Risk Analysis (FAO Food and Nutrition Paper No.87) >>

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.<<displacement of paragraph 45>>

As consequent to the changes proposed above, “**Table of Contents**” should also be amended accordingly.

**Other specific comments:**

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

**Para.10.**

Reference to “*Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005)*” should be added in Principle 5, as follows, because Foodborne AMR-risk analysis should consider not only microorganisms but also antimicrobials.

**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 *Code of Practice to Minimize and Contain Antimicrobial Resistance* (CAC/RCP 61-2005) 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 antimicrobials resistant microorganisms.

**PRELIMINARY FOODBORNE AMR-RISK MANAGEMENT ACTIVITIES**

**Establishment of broad risk management goals**

**Para. 20.**

This whole sentence including its subsection title “Establishment of broad risk management goals” should be deleted because it is not possible to establish risk management goals in the absence of risk assessment output, prior to conducting AMR-risk assessment.

Consequently, in Table of Contents, reference to “Establishment of broad risk management goals” should be removed.

**- Commissioning a foodborne AMR-risk assessment**

**Para. 22.**

In the first sentence, the text “risk management goals” should be replaced with “risk assessment policy”. Risk assessment should be carried out by following a risk assessment policy, but not risk management goals.

**Identification of foodborne AMR –RMOs**

**Para 55, Table 1 (Examples of Foodborne AMR Risk Management Options) be slightly amended as follows:**

Table 1. Examples of Foodborne AMR Risk Management Options	
PRE-HARVEST OPTIONS	
Animal feed production	[No amendment]

Food animal production	[No amendment]
Food and feed crop production	[No amendment]
Waste management	Implement control measures to limit the spread of AMR microorganisms and antimicrobial resistance determinants <del>of microorganisms</del> through other sources of contamination, by assuring the appropriate use of human and animal waste (biosolids, manure, other natural fertilizers ) in fields for food and animal feed production:
POST-HARVEST OPTIONS	
[No amendment]	

### Selection of foodborne AMR-RMOs

#### Para. 62.

The text should be amended as follows to correctly explain that ALOP or public health goal should be determined at first, but not desired. In addition, the last sentence should be moved to a new footnote, because it provides only a source of relevant information, but not specific guidance.

62. In order to select the best RMO or combination of RMOs to address an AMR food safety issue, if necessary, risk managers should first determine an ALOP or public health goal. Once the level/ goal is established, information obtained from the evaluation of RMOs (relative to the specific combination of the food commodity, the AMR microorganism/antimicrobial resistance determinants and the antimicrobial agent to which resistance is expressed) can be used to determine the most efficient approach to achieving the ~~desired~~ determined level/goal. For AMR, an example of an ALOP might be a specific target for the incidence of cases of resistant foodborne infectious diseases<sup>22</sup>. ~~A variety of approaches to setting ALOPs or public health goals are described in FAO Food and Nutrition Paper 87 “Food Safety risk analysis – A guide for national food safety authorities”.~~

#### Foot note 22

22 A variety of approaches to setting ALOPs or public health goals are described in FAO Food and Nutrition Paper 87 “Food Safety risk analysis – A guide for national food safety authorities”.

### Implementation of foodborne AMR-RMOs

#### Para. 65.

Paragraph 65 should be deleted, because the current proposed text explains what food producers and processors currently perform, but does not provide any specific guidance related to AMR food safety issue.

### Monitoring and review of foodborne AMR-RMOs

#### Para. 66.

In order to provide more specific guidance, the end of 1<sup>st</sup> sentence should be amended as follows:

.....properly implemented and achieve predetermined ALOP or public health goal.

### SURVEILLANCE OF USE OF ANTIMICROBIAL AGENT AND AMR MICROORGANISM AND ANTIMICROBIAL RESISTANCE DETERMINANTS

#### Para. 69.

In the second sentence, the text “and data from human” should be inserted after the text “other natural fertilizers” because human data should be a part of surveillance.

### FOODBORNE AMR-RISK COMMUNICATION

#### Paras 74 and 75

The first sentence of paragraph 74 should be deleted because this sentence is not appropriate and reference to “risk communication decision makers” is not understandable. Then these two paragraphs should be merged as follows:

Communication with all interested parties should be integrated into all phases of a risk analysis, and promotes better understanding of risks and acceptance of risk management approach (see Figure 1).

## **PHILIPPINES**

The Philippines commends the work of the Task force on AMR for developing the Proposed Draft Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance to step 5. The Philippines does not have any further comments on the document and thus would like to propose for elevation of the guidelines to step 8.

## **UNITED STATES OF AMERICA**

### **General comment:**

There are inconsistent uses of “and,” “or,” and “and/or” between the phrases of “antimicrobial resistant microorganisms” and “resistance determinants” throughout the document. For example, under the Scope section (at paragraphs 7-8), “and” is used. In paragraph 12, “or” is used; while in paragraph 24, “and/or” is used. It is anticipated that the Task Force will be able to come to consensus on what conjunctions are preferred and appropriate and that the conjunctions will be used in a consistent manner.

### **Specific comments:**

#### **1. Paragraph 9, Definition for “cross-resistance”**

It is the view of the United States that “cross-resistance” is incorrectly defined, even though it is referenced from the Rome consultation. We suggest revision of the first and third sentences and deletion of the second sentence.

The new definition would read:

**A resistance mechanism in a microorganism that confers the ability to survive in the presence of related members of a particular antimicrobial class, or across certain classes due to a related mechanism of resistance. Cross-resistance is often used to imply selection pressure exists when any of the affected antimicrobials are used.**

*Rationale: Improves clarity of the first and third sentence and reduces confusion created by the second sentence. As written, the second sentence is technically incorrect because the intrinsic activity of an antimicrobial agent is not correlated to a “level of resistance.” Potency has nothing to do with cross-resistance.*

#### **2. Paragraph 10, Principle 6**

Co-resistance is used here alone. However, co- and cross-resistance are used jointly throughout the draft guidelines. The U.S. suggests that Principle 6 should be modified to read “Co-and Cross-resistance should be considered...” This should also be followed throughout the document.

#### **3. Paragraph 15 and Appendix 1**

The United States anticipates that paragraph 15, which describes fundamental elements that comprise a food borne AMR risk profile, will need to be aligned with the revised Appendix 1 during the working group meeting that is scheduled to be held prior to the fourth Task Force meeting.

#### **4. Paragraph 20**

The title of this section is “Establishment of Broad Risk Management Goals,” while the contents of this paragraph make reference to “preliminary risk management goals.” Because there is inconsistency in the title of this section and its contents, it is suggested that the text in the paragraph be amended by replacing the word “preliminary” with “broad.”

#### **5. Paragraphs 27 and 28**

Paragraphs 27 and 28 should be combined.

## 7. Paragraphs 32 and 36; Figure 2

To clarify the processes of Exposure and Hazard Characterization, the United States suggests that the respective parts of Figure 2 be separated.

1. The exposure assessment component of Figure 2 should be placed under paragraph 32 as the new Figure 2 and re-titled, “Examples of approaches in food borne antimicrobial resistance exposure assessment.”
2. The hazard characterization component of the current Figure 2 should be placed after paragraph 36 as a new Figure 3 and titled, “Examples of approaches for food borne antimicrobial resistance hazard characterization.”
3. “Figures 2 and 3” should replace the two places in the text of paragraph 36 where “Figure 2” is mentioned so that the last two sentences in paragraph 36 would read:

**“Figure 3 includes examples of different types of approaches (e.g., qualitative mapping, semi-quantitative and quantitative models) that could be used to link exposure to adverse health effects. Figures 2 and 3 also include a depiction of selected inputs to the exposure assessment and hazard characterization processes, which are listed in detail in Appendix 2.”**

## 6. Paragraph 41 (linked with addition to Paragraph 26)

Bullet 2: We believe it is more appropriate to refer to “non-scientists” rather than “non-mathematicians.”

We suggest revision of Bullet 4 for clarity purposes so that it will read:

**“Quantitative uncertainty analysis is preferred; however, it may be arrived at through use of professional and/or expert judgment.”**

Bullet 5—“existing microbial and AMR-risk assessments”—appears to be misplaced with the other elements to consider in association with risk characterization. It is suggested that this bullet be slightly modified to read: “Existing relevant microbial and AMR-risk analyses” and moved to the end of Paragraph 26.

## 10. Table 1 (middle section) Food Animal Production

It is suggested that the first three sentences under “Non-regulatory controls on condition of use of veterinary antimicrobial drugs and additives” be rewritten for clarity and the U.S. offers the following alternative language:

**“Develop and implement national or regional treatment guidelines<sup>18</sup> targeting a specific AMR problem.**

**Develop and regularly update antimicrobial responsible use guidelines<sup>19</sup> written by professional bodies and other internationally recognized entities, such as OIE.**

**Improve availability, speed, and accuracy of diagnostic microbiological tests.**

**Disseminate and use international standards for:**

- **Bacterial culture and antimicrobial susceptibility testing<sup>20</sup>; and**
- **Interpretive criteria.”**

Under Bullet 2 of this section, we suggest “species specific” be removed as a qualifier of responsible use guidelines in the second bullet. *Rationale: some responsible use guidelines are not species-specific (e.g., those from OIE), and to reduce confusion with national treatment guidelines that address a species-specific AMR problem.*

We also suggest deleting “clinical practice guideline” from footnote 19 to clarify the distinction between national treatment guidelines and responsible use guidelines.

## 11. Title of Surveillance section (at paragraph 69)

We suggest rewording the current title of this section to read: **“Surveillance of AMR food borne pathogens, AMR resistance determinants, and antimicrobial use”**.

*Rationale: For clarity.*

## 12. Paragraph 77

The United States feels that this paragraph is somewhat confusing as written and offers the following alternative language:

**“Information on food animal and food crop production antimicrobial products that is considered essential by the national or regional authority to ensure their safe and effective use should be made available by the relevant industry in the form of labeling, data sheets, or leaflets”.**

## 13. Appendix 1

To be consistent with the rest of the text “determinant” should be made plural throughout Appendix 1.

Under #6:

For clarity, we suggest moving bullet 1 from # 6 to the end of #5 where adverse effects are discussed.

Bullets 2 and 3 seem to be the result of a typographical error and should be combined into a single bullet to read:

**“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?”**

This new combined bullet 2/3 could be moved to the end of #4 where antibiotic use is discussed.