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FOOD AND AGRICULTURE
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Agenda Item 5

CX/AMR 08/2/5 Add.1
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME AD HOC CODEX INTERGOVERNMENTAL TASK FORCE ON ANTIMICROBIAL RESISTANCE

Second Session

Seoul, Republic of Korea, 20-24 October 2008

PROPOSED DRAFT GUIDANCE ON CREATING RISK PROFILES FOR ANTIMICROBIAL RESISTANT FOODBORNE MICROORGANISMS FOR SETTING RISK ASSESSMENT AND MANAGEMENT PRIORITIES (REPORT OF THE PHYSICAL WORKING GROUP) (NO3-2008)

(Comments at Step 3)

The following comments have been received from: Argentina, Australia, Brazil, Canada, Costa Rica, Iran, Mexico, New Zealand, Norway, IDF, IFAH

ARGENTINA

Argentina appreciates the opportunity to comment on this document.

General Comments;

Argentina suggests the word term “bacterium” should be replaced with “microorganism” throughout the document.

Specific Comments;

Introduction (p. 6)

In paragraph 2, in connection with the “establishment of broad risk management goals”, we believe that for risk profile analysis, this element exceeds the scope, as the establishment of such “broad risk management goals” would be a more specific activity than risk management. We thus believe this phrase should be deleted.

1. Scope (p. 6)

In paragraph 4, last line, where the areas of use of antimicrobials are described:

- a) *Aquaculture* should be included in veterinary use. It would therefore read as follows: “[...] such as veterinary applications, **aquaculture**, plant protection [...]”)
- b) As for the reference to food processing, we consider it to be confusing and to exceed the scope ad terms of reference of the task force. In this respect, we believe that in order to contain the transmission of antimicrobial resistant microorganisms and resistance determinants through food, consideration of the use of antimicrobials in the food processing industry would exceed the scope of this work, as this element would become human health issue rather than a food safety issue. We therefore propose to delete the phrase “or food processing”.

3. General Principles (p. 7)

These General Principles will be harmonized with those contained in the risk management document. Below are the principles as they should be harmonized.

PRINCIPLE 1: Protection of human health is the primary objective in antimicrobial resistance risk management.

PRINCIPLE 2: Antimicrobial resistance risk management activities should take into account the emergence and dissemination of both resistant foodborne pathogens and resistance determinants through the whole food chain.

PRINCIPLE 3: Antimicrobial resistance risk management activities should focus on clearly defined combinations of food, antimicrobial drug (AM), antimicrobial use and the human pathogens and/or resistance determinants acquired from food.

PRINCIPLE 4: Antimicrobial resistance risk management activities should follow a structured approach⁵.

PRINCIPLE 5: The activities conducted in all phases of antimicrobial resistance risk management should be transparent, timely, consistent, documented and communicated.

PRINCIPLE 6: Risk managers should ensure effective consultations with relevant interested parties⁶.

PRINCIPLE 7: Risk managers and risk assessors should ensure effective interaction.

PRINCIPLE 8: Risk managers should take into account risks resulting from regional differences in human exposure to AMR microorganisms & determinants from the food chain and regional differences in available risk management options.

PRINCIPLE 9: Antimicrobial resistance risk management decisions should be subject to monitoring and review and, if necessary, revision.

PRINCIPLE 10: Risk management activities should take into account recent work by international organizations on antimicrobial resistance.

4.1 Identification of an antimicrobial resistance food safety issue

Paragraph 10 (p. 8)

The concept of “public input” is confusing because of the term and its scope. We thus suggest it be deleted.

4.2, paragraph 13:

Bullet point 3

The word “national” as consideration in national lists of critical antimicrobials is not appropriate in the context of international trade. Only the work undertaken in international reference organizations like OIE and WHO should serve as guidance on critical antimicrobials for human health.

The text would therefore read as follows: “Consideration of critically important microbial lists developed by international groups (e.g. Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials, Rome 2007)”

Bullet point 4

Aquaculture should be included in connection with veterinary use. The final text should read: “[...] *such as veterinary applications, aquaculture, plant protection* [...]”.

As for the reference to “food processing”, we consider it to be confusing and to exceed the scope ad terms of reference of the Task Force. In this respect, we believe that in order to contain the transmission of antimicrobial resistant microorganisms and resistance determinants through food, consideration of the use of antimicrobials in the food processing industry would exceed the scope of this work, as this element would become a human health issue rather than a food safety issue. We therefore propose to delete the phrase “food processing”.

4.3. Rank food safety issues and set priorities for risk assessment and management

Paragraph 17 (p. 9)

Bullet point 1

The inclusion of a subjective variable undermines the scientific criteria that should predominate in risk analysis. The inclusion of “Perceived relative level of risk to consumers” may lead to conclusions and to the adoption of measures that go against the basic principles of risk analysis (transparency, scientific basis). We thus suggest this bullet point should be deleted. Even so, we believe that some clarification or reference could be made in connection with consumer risk, which is completely different from a perception.

Similarly, regarding bullet point 5 “Policy concerns/public demand”, it is considered that a **policy is a public decision** and should, per se, contain the demands from some groups, such as the government, producers and/or consumers, which

⁵ See para. 7 in GL 62-2007.: “The risk analysis should follow a structured approach comprising the three distinct but closely linked components of risk analysis (risk assessment, risk management and risk communication) as defined by the Codex Alimentarius Commission², each component being integral to the overall risk analysis.”

⁶ **For the purpose of the present document, the term “interested parties” refers to “risk assessors, risk managers, consumers, industry, the academic community and, as appropriate, other relevant parties and their representative organizations”.**

may be the case here. For this reason, it is believed that the term “public demand” should be deleted as it does not need to be included.

Paragraph 19

In the framework of the Codex work to ensure food safety, it is considered that “the protection of the health of consumers” as the primary objective of risk managers’ work exceeds the scope of the document. In this respect, we believe that it would not be appropriate to retain this interpretation, so these words should be replaced with “the protection of the health of consumers in relation to food safety”.

The final text would then read as follows: “Risk management goals should have as their primary objective the protection of the health of consumers in relation to food safety”.

4.5. Establish a risk assessment policy

In paragraph 23 (p. 10), line 3, the reference to “all other interested parties” may have too broad an interpretation, so the inclusion of some details is suggested, such as such as academic, research, regulatory and health sectors, and so on. We therefore suggest that the text be redrafted as follows: “[...] and all other interested parties, such as...”

Annex

In paragraph 6 (p. 13), Other risk Profile elements, bullet point 5, the notion of “Public perceptions of the problem and the risk” is considered to be a subjective variable that is not in line with the scientific criteria that should predominate in risk analysis. We thus suggest it be deleted entirely.

In this sense, we believe that some clarification or reference could be included in connection with actual consumer risk, which is completely different from a relative perception.

PROPOSED DRAFT GUIDANCE ON CREATING RISK PROFILES FOR ANTIMICROBIAL RESISTANT FOODBORNE MICROORGANISMS FOR SETTING RISK ASSESSMENT AND MANAGEMENT PRIORITIES.

INTRODUCTION *[to be harmonized]*

1. Antimicrobial resistance resulting from the non-human use of antimicrobials is a recognized food safety concern. Given the complexity surrounding the field of antimicrobial resistance, food safety regulators require a structured approach to manage those concerns. Risk analysis has been implemented as a decisionmaking tool to estimate risks posed by food hazards and to determine appropriate risk mitigation strategies to control those hazards. General frameworks for managing foodborne risks have been developed by international and national authorities to establish principles and guidelines for the conduct of risk analysis.

The Codex *Ad Hoc* Task Force on Antimicrobial Resistance is establishing such a risk management framework; this document is one of three guidance documents that describe those principles and guidelines specific to antimicrobial resistance risk analysis.

2. The initial phase of the risk management framework consists of a group of tasks collectively referred to as preliminary risk management activities. A systematic preliminary risk management process brings the food safety issues into focus and provides a guide for further actions. This document describes the steps to be used by Codex or national/regional authorities in conducting preliminary risk management activities as they relate to antimicrobial resistance. For the purpose of this guidance, preliminary risk management activities are taken to include identification of a food safety problem; development of a risk profile, ranking of the hazard for risk assessment and risk management prioritization; ~~establishment of broad risk management goals~~; establishment of risk assessment policy for the conduct of the risk assessment, commissioning of the risk assessment, and consideration of the results of the risk assessment.

3. This document should be read in close conjunction with the *Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Assessment* and the *Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Management*, documents that are currently under development, as well as the *Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials* (Rome 2007) and the *Working Principles for Risk Analysis for Food Safety for Application by Governments* (CAC/GL 62-2007). In addition, this guidance incorporates the prior work on microbial risk assessment, as described in the Codex documents *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).

Additional background material with relevant technical information that should be consulted include documents developed by the World Health Organization, the Food and Agriculture Organization and the Codex Alimentarius (e.g., *The Interaction between Assessors and Managers of Microbial Hazards in Food*, Kiel, Germany, March 2000; *Principles and Guidelines for Incorporating Microbiological Risk Assessment in the Development of Food Safety Standards, Guidelines and Related Texts*, Kiel, Germany, March 2002; *The Use of Microbiological Risk Assessment*

Outputs to Develop Practical Risk Management Strategies: Metrics to improve food safety, Kiel, Germany, April 2006; and *Food Safety Risk Analysis, A Guide for National Food Safety Authorities* – FAO Food and Nutrition Paper 87, Rome, 2006).

1. Scope

4. These principles and guidelines are part of an overall framework for the antimicrobial resistance risk analysis process (along with the *Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Assessment* and the *Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Management*, documents that are currently under development). This document is intended for use by Codex and/or national/regional authorities for the conduct of preliminary risk management activities to address the food safety issues associated with the presence of antimicrobial resistant microorganisms and resistance determinants in food and feed, including aquaculture, and the transmission through food and feed of antimicrobial resistant microorganisms and antimicrobial resistance genes. In the course of implementing these preliminary risk management activities, the risk managers should consider the different areas of use of antimicrobials, such as veterinary applications, **aquaculture and plant protection**, or food processing.

2. Definitions [to be harmonized]

5. The definitions of risk analysis terms related to food safety contained in the Procedural Manual of the CAC², shall apply. In particular, see definitions of hazard, risk, risk analysis, risk assessment, risk management, risk communication, risk assessment policy, risk profile, risk estimate, hazard identification, and hazard characterization.

6. Risk manager³ is defined as follows: a national or international governmental organization with responsibility for antimicrobial resistance risk management activities.

3. General Principles

~~PRINCIPLE 1: Protection of human health is the primary objective in antimicrobial resistance risk management.~~

~~PRINCIPLE 2: Antimicrobial resistance risk management activities should take into account the emergence and dissemination of both resistant foodborne pathogens and resistance determinants through the whole food chain.~~

~~PRINCIPLE 3: Antimicrobial resistance risk management activities should focus on clearly defined combinations of the food, antimicrobial drug, antimicrobial use, and foodborne human pathogens and/or resistance determinants.~~

~~PRINCIPLE 4: Antimicrobial resistance risk management activities should follow a structured approach.~~

~~PRINCIPLE 5: The activities conducted in all phases of antimicrobial resistance risk management should be transparent, timely, consistent, fully documented, and openly communicated.~~

~~PRINCIPLE 6: Risk managers should ensure effective consultations with relevant interested parties.~~

~~PRINCIPLE 7: Risk managers and risk assessors should ensure effective interactions.~~

~~PRINCIPLE 8: Risk managers should take into account risks resulting from regional differences in human exposure to foodborne antimicrobial microorganisms and resistant determinants and regional differences in available risk management options.~~

~~PRINCIPLE 9: Antimicrobial resistance risk management decisions should be subject to monitoring and review and, if necessary, revision.~~

~~PRINCIPLE 10: Risk management activities should take into account recent work by international organizations on antimicrobial resistance.~~

² Codex Alimentarius Commission, Procedural Manual.

³ The definition of Risk Manager is derived from the definition for risk management, which may not include all of the individuals who are involved in the implementation phase and related activities associated with managing the risks resulting from antimicrobial resistance; i.e., risk management decisions are largely implemented by industry and other interested parties. The focus of the definition of risk manager in this document is restricted to governmental organizations with authority to decide on the acceptability of risk levels associated with foodborne hazards.

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PRINCIPLE 5: The activities conducted in all phases of antimicrobial resistance risk management should be transparent, timely, consistent, documented and communicated.

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PRINCIPLE 9: Antimicrobial resistance risk management decisions should be subject to monitoring and review and, if necessary, revision.

PRINCIPLE 10: Risk management activities should take into account recent work by international organizations on antimicrobial resistance.

4. Guidelines for Activities

7. These guidelines provide an outline of a series of steps that comprise the preliminary risk management activities, part of the general framework for antimicrobial resistance risk analysis. These activities are conducted by, or under the guidance of, the risk managers.

4.1. Identification of an antimicrobial resistance food safety issue

8. In the context of this document, a potential food safety issue may arise when antimicrobial resistant microorganisms and antimicrobial resistance genes are present in food and feed, including aquaculture, or are transmitted through food and feed. Foodborne exposures to resistant microorganisms or resistance determinants may adversely impact human health by reducing the therapeutic value of antimicrobials used in human medicine because of losses in susceptibility of pathogenic ~~bacteria~~ **microorganisms**. The risk manager initiates the risk management framework to evaluate scope and magnitude of the food safety issue and, where necessary, to commence activities to manage the associated risk.

9. Food safety issues may be identified by the risk manager or be the result of collaboration between different interested parties. Within Codex, a food safety issue may be raised by a member government, or by an intergovernmental or observer organization.

10. Antimicrobial resistance food safety issues may be identified on the basis of information arising from a variety of sources, such as antimicrobial resistance surveillance in animals and in foods of animal origin, food safety monitoring, antimicrobial usage surveys, animal and human surveillance data (including postmarketing surveillance data on approved antimicrobials), epidemiological or clinical studies, laboratory studies, research on resistance transfer, scientific, technological or medical advances, environmental monitoring, recommendations of experts, ~~public input~~, etc. Additional potential sources of information are provided in the *Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005)*

11. To better define the food safety issue, the risk manager may need to pursue information from sources that have specific knowledge pertaining to the issue. An open process, in which the food safety issue is clearly identified and communicated by the risk managers to risk assessors, as well as affected consumers and industry, is essential to promote both an accurate definition and a well-understood and common perception of the issue.

⁵ See para. 7 in GL 62-2007.: “The risk analysis should follow a structured approach comprising the three distinct but closely linked components of risk analysis (risk assessment, risk management and risk communication) as defined by the Codex Alimentarius Commission², each component being integral to the overall risk analysis.”

⁶ For the purpose of the present document, the term “interested parties” refers to “risk assessors, risk managers, consumers, industry, the academic community and, as appropriate, other relevant parties and their representative organizations”.

4.2. Development of an antimicrobial resistance risk profile

12. The antimicrobial resistance risk profile is a description of a food safety problem and its context that presents, in a concise form, the current state of knowledge related to the food safety issue, describes current control measures and risk management options that have been identified to date, if any, and the food safety policy context that will influence further possible actions. The risk profile is usually developed by personnel with specific scientific expertise on the food safety issue of concern and some understanding of antimicrobial resistance risk assessment techniques.

13. The depth and breadth of the antimicrobial resistance risk profile may vary depending on the needs of the risk managers and the complexity of the food safety issue. An extensive list of suggested risk profile elements is provided in the Annex as guidance to risk managers at the national/regional level, and for bringing forward newly proposed work within the Codex process. In certain situations, however, it may be necessary to develop an abbreviated risk profile that could be used as a basis for further preliminary risk management activities, such as prioritizing the development of more comprehensive risk profiles or determining the need for commissioning a risk assessment. The abbreviated risk profile may be particularly useful for resource-challenged countries in determining priorities for further activities. Caution should be exercised in implementing these abbreviated risk profiles, as they may not provide as complete a picture of the food safety issue as needed for effective decision making by the risk managers. The fundamental elements that should comprise an abbreviated risk profile include:

- Description of the public health problem (the antimicrobial resistance food safety issue);
- Identification and characterization of the food commodity + antimicrobial resistant pathogen + antimicrobial use combination;
- Consideration of critically important antimicrobial lists developed by ~~national and~~ international groups (e.g., see *Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials*, Rome 2007);
- Description of usage (extent and nature) of antimicrobials in food production, when available (such as veterinary applications, aquaculture, and plant protection) ~~or food processing~~; and
- Identification of major knowledge gaps.

14. Consideration of the information given in the risk profile may result in a range of initial decisions, such as determining that no further action is needed, commissioning an antimicrobial resistance risk assessment, establishing additional information gathering pathways, or implementing immediate risk mitigation for those food safety issues that require an immediate action⁴ by the risk manager without further scientific consideration (e.g. requiring withdrawal / recall of contaminated products).

15. 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.

4.3. Rank food safety issues and set priorities for risk assessment and management

16. Given the potentially high resource costs associated with conducting risk assessments and/or implementing risk management goals, a risk ranking or prioritization process is important in placing the risks from a specific food commodity + antimicrobial resistant pathogen + antimicrobial use combination in context with other risk scenarios that require the attention of risk managers. The output from the risk profile provides the principal criteria that should be used by risk managers in this risk ranking or prioritization process.

17. Beyond the description of the food safety issue provided by the risk profile, other criteria may be used for ranking or prioritization; these are generally determined by the risk managers in conjunction with stakeholders, and in consultation with risk assessors on technical aspects of the issues. Such criteria include:

- ~~Perceived relative level of risk to consumers;~~
- Capability to implement effective food safety control measures;
- Potential international trade implications associated with food safety control measures;

⁴ The International Health Regulation (2005) Agreement gives provisions for appropriate measures in case of public health emergencies, including food related events (www.who.int/csr/ihr/ihrwha58_3-en.pdf). The Principles and Guidelines for the Exchange of Information in Food Safety Emergency Situation (CAC/GL 19-1995) defines a food safety emergency as a situation whether accidental or intentional that is identified by a competent authority as constitutes a serious and as yet uncontrolled foodborne risk to public health that requires urgent action. Emergency measures may be part of immediate action.

- Regulatory challenges; and
- Policy concerns / **public demand.**

4.4. Establish broad risk management goals

18. Following development of the risk profile and the conduct of the risk ranking/prioritization steps, risk managers should decide on the broader risk management goals in addressing the food safety issue. Ultimately, the outcome of the preliminary risk management activities and the risk assessment, if conducted, should be combined with the evaluation of available risk management options in order to reach a decision on management of the risk.

19. Risk management goals should have as their primary objective the **food safety and public health protection of the health of consumers**. Other considerations in selecting appropriate risk management goals include the potential impact on trade, as well as the feasibility of implementation, enforcement, and compliance of the risk mitigation measures associated with the goals.

20. The risk management goals may range from more general approaches, such as implementation of codes of practice, to more specific measures, such as the development of regulatory standards and guidelines or the estimation of risks in specific exposure scenarios to inform the risk managers in selecting specific risk mitigation measures. The determination of the need, or the feasibility, of a risk assessment, is often critical in establishing risk management goals. Thus, the risk management goals should be clearly stated prior to commissioning a risk assessment to ensure that the information provided by a risk assessment addresses the risk management goals.

21. The criteria for determining the need for a risk assessment depends on the nature of the risk management goals. Factors that may influence the desirability of a risk assessment include:

- If the nature and magnitude of the risk are not well characterized;
- When risk brings economic, social, cultural and ethical considerations;
- When the risk management goals have major trade implications;
- The availability of resources;
- The urgency of the food safety issue; or
- The availability of scientific information.

22. The establishment of these broad risk management goals should be accomplished as an interactive process between the risk managers, the risk assessors, and external stakeholders. It is imperative that the established goals be developed with full consideration of their ability to address the specific food safety issue of concern. The risk management goals should be clearly communicated to all interested parties.

4.5. Establish a risk assessment policy

23. Determination of risk assessment policy should be included as a specific component of risk management. Risk assessment policy should be established by risk managers in advance of risk assessment, in consultation with risk assessors and **all other interested parties, such as...** This procedure aims at ensuring that the risk assessment is systematic, complete, unbiased and transparent. The mandate given by risk managers to risk assessors should be as clear as possible and provide guidance as to the scope of the risk assessment.

Where necessary, risk managers should ask risk assessors to evaluate the potential changes in risk resulting from different risk management options.

24. For antimicrobial resistance risk assessment policy, risk managers may adopt the General Principles in the Draft Guideline for the Risk Assessment of Foodborne Antimicrobial Resistant Microorganisms (under development) related to non-human use of antimicrobials.

25. Additional elements specific to the food safety issue related to antimicrobial resistance should also be included in order to provide guidelines to risk assessors conducting the risk assessment. For example, the risk assessment policy should provide the risk assessors with guidance on the need to address uncertainty and what assumptions to use when the available data are inconsistent.

4.6. Commission of a risk assessment

26. Based on the established risk management goals, risk managers may commission a risk assessment to provide an objective, systematic evaluation of relevant scientific knowledge to help make an informed decision regarding appropriate risk management activities. The nature and scope of the risk assessment may vary, depending on the food safety issue of concern, but it is important to ensure that a clear mandate is given to risk assessors and that the risk

assessment meets the needs of the risk manager. It is also important that all aspects of the commissioning and conduct of the risk assessment are documented and transparent.

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

- A description of the specific food safety issue (as defined in the risk profile);
- The scope and purpose of the risk assessment;
- The specific questions to be answered by the risk assessment;
- The type (e.g., quantitative, qualitative) of risk assessment to be conducted;
- The expertise and resources required to carry out the risk assessment;
- Timelines for milestones and completion of the risk assessment;
- Criteria to validate the risk model;
- Criteria to assess the scientific and technical adequacy of the risk assessment; and
- Analysis of any future data needs.

28. It is important to ensure that the composition of the risk assessment team is appropriate in terms of expertise and be free of conflicts of interest or bias. The risk managers should also ensure that there are effective and iterative communication pathways between the risk assessors and risk managers during the risk assessment process, and that the risk assessment be adequately reviewed by the scientific community and if appropriate, the public.

29. The risk manager should refer to the Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Assessment (under development).

4.7. Consider the results of the risk assessment

30. The conclusion 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. In reviewing the completeness of the risk assessment, risk managers need to understand the nature, sources and extent of uncertainties and variability of the risk estimates expressed.

ANNEX

Suggested Elements to Include in an Antimicrobial Resistance Risk Profile

A risk profile should present, to the extent possible, information on the following:

1. Definition of the hazard-food commodity combination(s) of concern:

- Hazard(s) of concern – the specific combination of:

o food commodity;

o antimicrobial resistant pathogen; and

o antimicrobial use

- Description of the food commodity and the associated cause for concern (e.g., antimicrobial resistant foodborne illness, trade restrictions) due to the hazard

- Occurrence of the hazard in the food chain.

2. Description of the public health problem (*i.e.*, the adverse human health consequences):

- Characteristics of the resistant microorganism(s) or resistance determinants, including key attributes that are the focus of its public health impact (e.g., cross resistance, co-resistance, horizontal gene transfer);

- Characteristics of the antimicrobial-susceptible infection, illness or disease, including:

o Susceptible populations;

o Annual incidence rate in humans including, if possible, any differences between age and sex;

o Severity of clinical manifestations (e.g., case-fatality rate, rate of hospitalization; and

o Nature and frequency of long-term complications;

- Characteristics of the antimicrobial-resistant infection, illness, or disease:

o Added burden of the infection, illness or disease due to antimicrobial resistance, if readily available (e.g., medical and/or hospital costs; working days lost due to illness, etc.); and

- o Evidence of links between resistance, virulence, and/or fitness of the antimicrobial resistant microorganism
 - Characteristics of treatment of the antimicrobial resistant infection, illness, or disease:
 - o Options for treating the infection, illness, or disease (e.g., importance of antimicrobial drug for treatment of human adverse health effect, possible side effects of alternate treatments);
 - o Extent of human use of the antimicrobial agent for which resistance is the concern;
 - o Availability and nature of treatment; and
 - o Prevalence of resistance in human populations;
3. Description of food commodities associated with the antimicrobial resistant microorganisms or resistance determinants (Post-harvest factors);
- Characteristics of the food commodity (commodities);
 - Food use and handling that influences transmission of the hazard;
 - Frequency and characteristics of foodborne sporadic cases;
 - Epidemiological data from outbreak investigations;
 - Prevalence of resistance on food commodity; and
 - Evidence of a relationship between the presence of the antimicrobial resistant microorganisms or resistance determinants on the food commodity and the occurrence of the adverse health effect in humans.
4. Description of antimicrobial(s) (Pre-harvest factors);
- Chemical, physical and pharmacological properties of the antimicrobial agent;
 - Type of use (treatment/prevention/control/growth promotion);
 - Dose regimen and route of administration;
 - Final product specifications;
 - Specific rules of usage for the country concerned;
 - Frequency or incidence of use of the antimicrobial agent;
 - Factors influencing the persistence of resistance in the pre-harvest production stage;
 - Importance of antimicrobial drug to animal medicine;
 - Associations between usages and development and persistence of resistance;
 - Factors that may affect the dissemination of antimicrobial resistant microorganisms through the food chain;
 - Evidence of a relationship between the use of the antimicrobial and the occurrence of antimicrobial resistant microorganisms, or resistance determinants, in the food commodity of concern;
 - Persistence of the antimicrobial in the environment, and factors affecting the maintenance of antimicrobial resistant microorganisms and/or resistance determinants; and
 - Contribution of alternative (non-foodborne) sources of antimicrobial resistance
5. Antimicrobial resistance genes and resistance determinants:
- Factors that may affect the frequency of transfer of genetic elements through the food chain; and
 - Description of the molecular genetics of the antimicrobial resistance of concern
6. Other Risk Profile Elements:
- Summary of the extent and effectiveness of current risk management practices including food safety production/processing control measures, educational programs, and public health intervention programs (e.g., vaccines);
 - Identification of additional risk mitigation strategies that could be used to control the hazard;
 - The extent of international trade of the food commodity;
 - Existence of regional/international trade agreements and how they may affect public health with respect to the specific hazard-food commodity combination(s);
 - **Public perceptions of the problem and the risk;**

- Initial assessment of the need and benefits to be gained from requesting an antimicrobial resistance risk assessment, and the feasibility that such an assessment could be accomplished within the required time frame; and
- If a risk assessment is identified as being needed, recommended questions that should be posed to the risk assessor;

7. Assessment of available information and major knowledge gaps:

- Existing antimicrobial resistance risk assessments on the food commodity + antimicrobial resistant pathogen + antimicrobial use combination(s) including, if possible;
- Other relevant scientific knowledge and data that would facilitate risk management activities including, if warranted, the conduct of a risk assessment;
- Existing Codex guidance documents (including existing Codes of Hygienic Practice and/or Codes of Practice);
- International and/or national governmental and/or industry codes of hygienic practice and related information; and
- Areas where major absences of information exist that could hamper risk management activities, including, if warranted, the conduct of a risk assessment.

AUSTRALIA

Australia is pleased to provide the below comments in response to Agenda Item 5: Proposed Draft Guidance on Creating Risk Profiles for Antimicrobial Resistant Foodborne Microorganisms for Setting Risk Assessment and Management Priorities at Step 3 (CX/AMR 08/2/5).

General comments;

Australia commends the Working Group led by the US Codex delegation for developing the draft Guidance on Creating Risk Profiles for Antimicrobial Resistant Foodborne Microorganisms for Setting Risk Assessment and Management Priorities broadly consistent with the Codex document Principles and Guidelines for the Conduct of Microbiological Risk Management (CAC/GL 63-2007). The draft document provides useful guidance on preliminary risk management activities related to antimicrobial resistance.

Specific comments;

Page	Section/Paragraph	Comment
7	Section 3. General Principles	Section 3 needs to be harmonised with the general principles in the risk management guideline. Specific examples may aid understanding. It would be valuable to add to the principles the concepts of “strength and quality of evidence” and “weight of evidence” (see also Agenda item 4).
7	PRINCIPLE 8: Risk managers should take into account risks resulting from regional differences in human exposure to foodborne antimicrobial microorganisms and resistant determinants and regional differences in available risk management options.	There may also be regional differences in antimicrobial use patterns that may significantly impact the risk profile.

BRAZIL

General comments:

1. Brazil supports the suggestion made by the Working Group regarding the unification of the three documents.
2. Brazil believes that the antimicrobial use in agriculture should be more emphasized in the document CX/AMR 08/02/06 jun.08. So, we consider that it may be necessary to ask to IPCC for some advice.

Specific Comments;

PRINCIPLE 10:

Brazil suggests replacing the word “recent” by the word “relevant”.

Risk management activities should take into account relevant work by international organizations on antimicrobial resistance.

Paragraph 21

Brazil does not understand the meaning of the expression “ethical considerations” in the context of the second bullet. If it is to be maintained, we would like to have some clarification in the text and/or to mention an example.

CANADA

Canada would like to thank the United States for revising the draft guidance on “Creating risk profiles for antimicrobial resistance foodborne microorganisms for setting risk assessment and management priorities” taking into account the comments provided during the working group meeting in Brussels. Canada appreciates the opportunity to review and provide the following comments on the revised draft:

General Comments;

Canada notes that there is a difference between the title of the document and the actual content of the document. We note that the content covers the preliminary risk management activities of which risk profiling is only a single component. In view of the desire to ensure consistency with Codex Working Principles for Risk Analysis we would support the title of the document to be modified to reflect the content of the document as it provides valuable guidance. Maintaining the broadened scope we believe will facilitate the eventual merger of the three documents.

The document introduces the term “Establishing Broad Risk Management Goals”- we note that this term is taken from the FAO Food and Nutrition Paper #87 (Food Safety Risk Analysis). However, in the FAO document, there is a clearer link between the use of this term and subsequent identification and selection of risk management options. Furthermore, use of this term creates an inconsistency with the preliminary risk management activities as defined in the Codex Procedural Manual and the Codex Working Principles on Risk Analysis and creates confusion with risk management options as the relationship between them is not clear. Canada is of the view that the Task Force needs to consider how it will address this inconsistency

Specific Comments:

1. General Principles: Canada recommends the following general principles be considered for risk profiling.

Principle 1: AMR risk profiling activities should clearly describe the AMR food safety problem, its public health context, and the availability of pertinent scientific information,

Principle 2: AMR risk profiling should give consideration to all relevant international documents (for example recommendations of the “Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials”) for setting priorities for further risk assessment and/or risk management activities.

Principle 3: AMR risk profiling activities should focus on clearly defined combinations of the food, antimicrobial drug(s), antimicrobial use practice, and resistant foodborne microorganisms/or genetic determinants of resistance.

Principle 4: AMR risk profile should provide as much information as possible to risk managers to facilitate decision-making.

Identification of an antimicrobial resistance food safety issue:

2. Paragraph 8: The second sentence “Foodborne exposures to resistant microorganisms or resistance determinants may adversely impact human health by reducing the therapeutic value of antimicrobials used in human medicine because of losses in susceptibility of pathogenic bacteria.” needs to be expanded to highlight other potential adverse effects of resistance. It may include amongst others: loss of treatment options and increased severity of infection (prolonged duration of illness, increased frequency of bloodstream infections, increased hospitalization, and increased mortality) as reflected in the risk assessment guidance document.

3. Paragraph 10: Canada recommends that this section should also highlight plant production and food processing related information that may be useful to identify food safety issues.

4. Paragraph 13, bullet 2: Suggest replacing “antimicrobial resistant pathogen” with “antimicrobial resistant microorganisms”. Similar phrasing should be used throughout the document for consistency (e.g., in Section 4.3, paragraph 16).

Establish broad risk management goals

5. There is some confusion in this section between risk management goals and risk management options. Paragraph 20 provides examples of risk management options that risk managers could consider after a risk assessment yet they are identified as “risk management goals”. This is an example of the confusion created by the use of undefined terms not found in the Codex Working Principles for Risk Analysis. Please also refer to the second paragraph under General Comments.

6. Paragraph 21: Canada suggests to delete bullets 2 and 3 since these are factors to be taken into consideration in selecting risk management options and are not relevant to deciding whether a risk assessment is required. These points are better suited in the risk management section.

Establish a risk assessment policy:

7. Paragraph 23: It is suggested this paragraph also include text indicating that risk manager(s) should consider the outcome of risk profile in formulating the risk assessment policy.

Commission of a risk assessment:

8. Paragraph 27: It is suggested to delete bullets 7, 8 and 9 since they should be part of the risk assessment portion of the guidance and not part of the preliminary risk management activity.

Consider the results of the risk assessment:

9. Section 4.7: Canada recommends expanding this section to highlight the fact that risk managers should consider the risk estimate and the possible available risk management options that can be implemented to address the specific antimicrobial resistance food safety issue. Furthermore, it would be important to link/delineate the activities that are conducted as part of preliminary risk management process and those conducted afterwards.

Annex:

10. Point 1: Hazard of concern: Canada suggests that “antimicrobial resistant pathogen” should be expanded to include “antimicrobial resistant microorganism/resistance determinants”.

11. Point 2, bullet 3: Characteristics of the antimicrobial resistant infection, illness, or disease: Added burden of the infection, illness or disease should also list potential adverse effects of resistant infections listed in comment #5 above.

12. Point 4 should be expanded as “Description of antimicrobial(s) use associated factors (Pre-harvest factors)” (suggested addition underlined).

13. Point 6, last bullet should be deleted as this is not an element of a risk profile. The risk profile can facilitate the development of appropriate questions to be posed to risk assessors but the profile would not, itself, recommend questions.

COSTA RICA

Costa Rica is grateful for the opportunity to express its comments and wishes is to state the following:

1. Costa Rica agrees that the three documents should be integrated (Guidance on Creating Risk Profiles for Antimicrobial Resistant Foodborne Microorganisms for Setting Risk Assessment and Management Priorities, Item 5; Science-based Risk Assessment Guidance Regarding Foodborne Antimicrobial Resistant Microorganisms, Item 4; and Risk Management Guidance to Contain Foodborne Antimicrobial Resistant Microorganisms, Item 6) and proposes the above order for their discussion in logical sequence.

2. Costa Rica also considers that “plants” should be included in the document, where appropriate, because the scope also refers to plant protection.

3. The document should stress that the risk profile should be case-by-case. Also with regard to Section 4.1, Costa Rica considers that there should be broader discussion of the risk posed by the presence of antibiotic-resistance genes (free DNA).

4. We suggest including “antibiotic residues” under Item 3 on page 12 [*Translator’s note: page 14 in the Spanish text*].

5. The word “debe” should replace “debería” throughout the text. [*T.N. This concerns the Spanish text only*].

6. In the Annex, Item 1, non-pathogen resistant organisms should also be considered alongside antimicrobial resistant pathogens, so the text should read “antimicrobial resistant microorganisms”.

IRAN

The Iranian committee for Antimicrobial Resistance has reviewed the drafts and consensus has been made on the following comments:

General comments;

1. Antimicrobial resistance is not just a national problem and all of countries and national authorities should work together to solve the problem. An international agreement on antimicrobial usage that enforces the parties to work together and take their decisions and measures mutually under the agreement is a powerful tool. As a future plan, the Task Force may organize for preparing such a protocol in the international and regional levels.

2. Risk communication is one of the important steps in risk analysis. A data bank or a clearing house working under protocol or Task Force can facilitate the exchange of scientific, technical and legal information on antimicrobials and resistant microorganisms as well as the decisions and measures taken on risk assessments and risk managements.

Such a bank serves as a means through which required information (including the national strategic plans for antimicrobial usage) is made available for the purpose of risk assessment and profiling process. If any database for antimicrobials exists, it can be improved and adopted for risk profiling and assessment as well.

3. Risk assessment and further actions for risk management on antimicrobial resistance are complex cases that need skilled and trained personnel. International or regional workshops or capacity building programs by FAO/WHO could help the countries which are less skilled in this field to implement legal actions. It is strongly recommended the Task Force coordinate for strengthening of human resources and institutional capacities for appropriate actions in developing countries (e.g. developing the strategic plans, tracing antimicrobials in food by standard test methods and assessing risks of antimicrobials and resistant microorganisms in food).

4. It is recommended that the titles as well as the method of numbering and bulleting in the three documents to be harmonized.

5. Since in many cases the term of “pathogen” does not cover the meaning of the text, it is suggested “Foodborne pathogens” to be substituted by “Foodborne microorganisms”.

6. “Foodborne” is a more familiar term rather than “acquired from food” which contains all of microorganisms transmitted via food and has been used commonly in food microbiology texts.

7. “Organisms”, “bacteria”, or any other term that means microorganism, should be replaced with “microorganisms”, in order to make harmonization in the whole of the texts.

Specific Comments;

Page 7:

- Definitions:

The explanation of Risk Managers described in the footnote is preferred to be included in the definition of Risk Managers in the main text. It would be more influential if stated in the definition that national authorities or governmental organizations are responsible for risk management activities.

Page 7:

- General principles:

Principle 8:

It should be read as following:

.... To foodborne antimicrobial resistant microorganisms and resistance determinants and

Page 8:

Due to the importance and correlation between using antimicrobials in human cases and veterinary applications, it is suggested that the following phrase (in bold) to be added to:

- Identification of major gaps (including data resulted from clinical studies such as identifying resistant microorganisms to certain antimicrobials and data related to the usage of antimicrobials in human cases)

Page 13:

The following expressions (in bold) are recommended to be added:

- Suggested Elements to Include in an Antimicrobial Resistance Risk Profile

4 Description of antimicrobial(s) (Pre-harvest factors);

- Chemical, physical and pharmacological properties of the antimicrobial agent;
- Type of use (treatment/prevention/control/growth promotion / use as additives or preservatives);
- Dose regimen and route of administration; as well as the time of administration (withdrawal period/time between administration and milking or slaughtering);

The following elements and information are also recommended to be considered:

6 Other Risk Profile Elements

- If a risk assessment is identified (including results derived from medical cases) as being needed, recommended questions that should be posed to the risk assessor;
- The regional/international databases or information in data banks (if available)

- the National authorities or regional/international institutions should provide training programs for those who are involved in risk assessment and risk management in order to improving their abilities and bringing them up to date.

7 Assessment of available information and major knowledge gaps

- Existence of the regional/international databases or data banks

MEXICO

Mexico congratulates the Working Group in structure and layout of the document.

Given that the document considers microorganisms in general without distinguishing between those that are pathogenic and those that are not, we suggest replacing the term “pathogens” with “microorganisms” and harmonizing this term in the documents CX/AMR 08/2/4, CX/AMR 08/2/5 and CX/AMR 08/2/6.

NEW ZEALAND

New Zealand is pleased to offer the following comments in response to the above:

New Zealand congratulates the United States and the physical Working Group on producing a most useful reworked proposed draft.

New Zealand has withheld its comments until the meeting of Task Force. This is because we support the working recommendation of one integrated guidance document. This approach will probably resolve some issues we have identified as regards risk management overall and the relationship of both risk profiles and risk assessment to it within an AMR risk management framework so we will reserve our comments until the Task Force’s deliberation of and response to the recommendation.

NORWAY

General Comments;

Norway takes the opportunity to thank the representatives from Canada, USA and Denmark/France (EC) for successful development of the draft guidance documents.

1. Terms and definition

In the title, objectives and terms of reference (TOR) for the TFAMR, the terms antimicrobial resistance, microorganisms and antimicrobials are applied. Furthermore, in CX/AMR 08/2/4 (Agenda Item 4), page 17, the following definition of antimicrobials (antimicrobial agents) is applied: Any substance of natural, semi-synthetic, or synthetic origin that at in vivo concentrations kills or inhibits the growth of microorganism by interacting with a specific target.

The term microorganisms includes bacteria, virus and fungi and the expression antimicrobial agents (consequently) includes antibacterial, antiviral and antifungal drugs. In modern text books in pharmacology the term antibacterial drugs is applied for natural, semi-synthetic and synthetic medicinal substances that kills or inhibits the growth of bacteria (see e.g. Rang and Dale’s Pharmacology, 6th edition, 2007, Elsevier Limited). Unless antimicrobial agents in general are to be included in the TFAMR, the term antibacterial drugs should be applied throughout the document. However, when such substances are used for plant protection or as growth promoter, the term antibacterial agents have to be applied because such use is not included in the common definition of drugs. It should be noted that the expression antibacterial drug is applied by e.g. U.S. Food and Drug Administration and the European Medicine Evaluation Agency (EMA). Furthermore, in the proposed draft guidance documents CX/AMR 08/2/4, CX/AMR 08/2/5 and CX/AMR 08/2/6 the term antimicrobial, leaving agent, is often applied. As antimicrobial (or antibacterial) is not a noun, but an adjective, the wording should be antibacterial drugs and antibacterial agents, respectively.

E.g. CX/AMR 08/2/4 includes a list of definitions. Norway is in favour of only including in this list terms/words that are defined differently in the literature, as those who are performing risk assessment or risk profiling in the field of antibacterial drug resistance should be expected to be familiar with terms such as cross-resistance and co-resistance.

Specific Comments;

The definition of risk profile included in the Procedural Manual of the CAC should be included point 2. Definitions in the document, i.e.: The description of the food safety problem and its context

The guidance document would benefit from including tables on possible data requirement to be collected/applied in the various steps of a risk profiling. This would also make it easier to the reader to distinguish risk assessment from risk profiling.

In point 1 in the Appendix to the RP document antimicrobial suggests antibacterial drug use to be included in the definition of the hazard-food combination of concern. As the resistant bacteria/determinants are not causing the hazard,

but are the hazards in themselves; the description of antibacterial drug usage etc have to be moved to a separate section, e.g. included in section 4. In point 4 in description antibacterial drugs is “defined” as pre-harvest factors. Norway is of the opinion that pre-harvest factors should describe the hazard (the antibacterial resistance and/or resistance determinants) contained in the animals or crop. Therefore, Pre-harvest factors should be deleted from the heading in point 4 in the Appendix to CX/AMR 08/2/5.

IDF

General comments;

IDF would like to congratulate to Chairs of the three TFAMR physical Working Groups for the excellent work done as is reflected in the resulting Codex documents CX/AMR 08/2/4, CX/AMR 08/2/5 and CX/AMR 08/2/06.

IDF supports the proposal to merge the 3 documents into one with the objective of providing coherent and harmonized Codex guidance on the risk analysis process with regard to foodborne antimicrobial resistant microorganisms. IDF would like to propose using the wording that can be found in CX/AMR 08/2/4, para. 3 (section “Background”) as a common introduction to explain the purpose and scope of the document.

Specific comments;

Page 6, **SECTION INTRODUCTION**

In order to be consistent with the other documents a general sentence should be inserted as can be found in CX/AMR 08/2/4, page 15, first para. of SECTION 1. INTRODUCTION:

AMR is inherently related to antimicrobial use in any environment including human and non-human uses. IDF would like to propose using the paragraph that currently appears in CX/AMR 08/2/4, page 15, first para. of SECTION 1. INTRODUCTION , at the beginning of the section INTRODUCTION of a merged document.

Page 7, 3. **General principles**

IDF proposes to insert an additional bullet point referring to aspects related to animal health and welfare, which are important to be taken into account by risk managers. It could read as follows:

PRINCIPLE XX Risk managers should take into account the need to protect animal health and welfare.

Page 8, 4.2. **Development of an antimicrobial resistance risk profile**, para. 12, last sentence

IDF is of the view that stakeholders who are familiar with the relevant production chain should be consulted in the process of development of an antimicrobial risk profile. The following additional sentence should be added to the end of the respective paragraph:

The risk profile is usually developed by personnel with specific scientific expertise on the food safety issues of concern and some understanding of antimicrobial risk assessment techniques. Stakeholders who are familiar with the relevant production chain and related production techniques should be consulted.

Page 9, 4.1 **Identification of an antimicrobial resistance food safety issue**, para.15

This paragraph provides the precautionary approach to be used by the ‘risk managers’ during selection of risk management options. Therefore, this is misplaced in this subsection, which deals with development of risk profiles. The text in this paragraph should be transferred to the Section 4.4 Establish broad risk management goals.

Page10, 4.4. **Establish broad risk management goals**, para. 21, second bullet point

IDF would like to propose to expand on the present text for the bullet point to read:

- When the risk brings is connected to economic, social, cultural and ethical considerations including consequences for animal health and welfare;

IFAH

IFAH is pleased to provide the following suggestions for revision and comments on specific sections as requested by the Working Group on Risk Profiles. IFAH has used brackets [] to indicate a bullet point or section which has been edited or commented upon, and providing some rationale for the action.

General Comments;

- Within the Codex Risk Analysis procedure, Risk Profiles are considered as Preliminary Risk Management activities.
- Risk Prioritization is the appropriate step at which national authorities take into account both the WHO and OIE Antimicrobial Categorization lists

- The Risk Profile leads to prioritization for commissioning of Risk Assessments.
- In exceptional situations, provisional risk management decisions may be implemented by national authorities on the basis of the outcome of the Risk Profile.

Specific Comments;

[IFAH recommends using the actual title that will appear in the harmonized document] ~~DEVELOPMENT OF GUIDANCE ON CREATING RISK PROFILES FOR ANTIMICROBIAL RESISTANT FOODBORNE MICROORGANISMS FOR SETTING RISK ASSESSMENT AND MANAGEMENT PRIORITIES~~

(at Step 3 of the Elaboration Procedure)

INTRODUCTION [to be harmonized]

1. [IFAH suggests using this paragraph in a harmonized document and deleting it here] ~~Antimicrobial resistance resulting from the non-human use of antimicrobials is a recognized food safety concern. Given the complexity surrounding the field of antimicrobial resistance, food safety regulators require a structured approach to manage those concerns. Risk analysis has been implemented as a decision-making tool to estimate risks posed by food hazards and to determine appropriate risk mitigation strategies to control those hazards. General frameworks for managing foodborne risks have been developed by international and national authorities to establish principles and guidelines for the conduct of risk analysis. The Codex Ad Hoc Task Force on Antimicrobial Resistance is establishing such a risk management framework; this document is one of three guidance documents that describe those principles and guidelines specific to antimicrobial resistance risk analysis.~~

2. [IFAH adds the following edits to improve clarity] The initial phase of the risk management framework consists of a group of tasks collectively referred to as preliminary risk management activities. A systematic preliminary risk management process brings the food safety issues into focus and provides a guide for further actions. This document describes the steps to be used by ~~Codex~~ JEMRA or national/regional authorities in conducting preliminary risk management activities as they relate to antimicrobial resistance. ~~For the purpose of this guidance, preliminary risk management activities are taken to include identification of a food safety problem; development of a risk profile, ranking of the hazard for risk assessment and risk management prioritization; establishment of broad risk management goals; establishment of risk assessment policy for the conduct of the risk assessment, commissioning of the risk assessment, and consideration of the results of the risk assessment.~~

3. [IFAH suggests deleting the line referencing the other two project documents since there will only be different sections in a harmonized version in the next iteration] This document should be read in close conjunction with ~~the Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Assessment and the Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Management, documents that are currently under development, as well as the Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials (Rome 2007) and the Working Principles for Risk Analysis for Food Safety for Application by Governments (CAC/GL 62-2007).~~ In addition, this guidance incorporates the prior work on microbial risk assessment, as described in the Codex documents 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). Additional background material with relevant technical information that should be consulted include documents developed by the World Health Organization, the Food and Agriculture Organization and the Codex Alimentarius (e.g., The Interaction between Assessors and Managers of Microbial Hazards in Food, Kiel, Germany, March 2000; Principles and Guidelines for Incorporating Microbiological Risk Assessment in the Development of Food Safety Standards, Guidelines and Related Texts, Kiel, Germany, March 2002; The Use of Microbiological Risk Assessment Outputs to Develop Practical Risk Management Strategies: Metrics to improve food safety, Kiel, Germany, April 2006; and Food Safety Risk Analysis, A Guide for National Food Safety Authorities – FAO Food and Nutrition Paper 87, Rome, 2006).

[IFAH suggests that the Purpose (from Seoul Project Document, Annex V, be included here, as moved from Bullet # 2 above] Purpose and Scope

4. The Purpose of this guidance is to describe the process of identifying food safety issues associated with antimicrobial resistance, the data needed for risk profiles, and setting priorities for risk assessment with respect to antimicrobial resistant foodborne microorganisms and/or resistance determinants in food or feed, including aquaculture.

The Scope of this guidance includes: preliminary risk management activities are taken to include identification of a food safety problem; development of a risk profile, ranking of the hazard for risk assessment and risk management prioritization; establishment of broad risk management goals; establishment of risk assessment policy for the conduct of the risk assessment, commissioning of the risk assessment, and consideration of the results of the risk assessment.

[IFAH views the following sentences as redundant to those above and proposes deletion for clarity] ~~These principles and guidelines are part of an overall framework for the antimicrobial resistance risk analysis process (along with the Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Assessment and the Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Management, documents that are currently under~~

development). This document is intended for use by Codex and/or national/regional authorities for the conduct of preliminary risk management activities to address the food safety issues associated with the presence of antimicrobial resistant microorganisms and resistance determinants in food and feed, including aquaculture, and the transmission through food and feed of antimicrobial resistant microorganisms and antimicrobial resistance genes. In the course of implementing these preliminary risk management activities, the risk managers should consider the different areas of use of antimicrobials, such as veterinary applications, plant protection or food processing.

2. Definitions [to be harmonized]

5. The definitions of risk analysis terms related to food safety contained in the Procedural Manual of the CAC¹, shall apply. In particular, see definitions of hazard, risk, risk analysis, risk assessment, risk management, risk communication, risk assessment policy, risk profile, risk estimate, hazard identification, and hazard characterization.

6. Risk manager² is defined as follows: a national or international governmental organization with responsibility for antimicrobial resistance risk management activities.

3. General Principles [IFAH suggests alignment of Principles among all 3 documents]

- PRINCIPLE 1: Protection of human health is the primary objective in antimicrobial resistance risk management. Animal health should also be considered when evaluating risk management options, to the greatest extent possible.
- PRINCIPLE 2: [IFAH suggests the following Principle be deleted for clarity because it is redundant with Principle 3 below] ~~Antimicrobial resistance risk management activities should take into account the emergence and dissemination of both resistant foodborne pathogens and resistance determinants through the whole food chain.~~
- PRINCIPLE 3: Antimicrobial resistance risk management activities should focus on clearly defined combinations of the food animal species, food, antimicrobial drug, antimicrobial use, and the human zoonotic pathogens and/or resistance determinants.
- PRINCIPLE 4: Antimicrobial resistance risk management activities should follow a structured approach.
- PRINCIPLE 5: The activities conducted in all phases of antimicrobial resistance risk management should be transparent, timely, consistent, fully documented, and openly communicated.
- PRINCIPLE 6: Risk managers should ensure effective consultations with relevant interested parties.
- PRINCIPLE 7: Risk managers and risk assessors should ensure effective interactions.
- PRINCIPLE 8: Risk managers should take into account risks resulting from regional differences in human exposure to foodborne antimicrobial microorganisms and resistant determinants and regional differences in available risk management options.
- PRINCIPLE 9: Antimicrobial resistance risk management decisions should be subject to monitoring and review and, if necessary, revision.
- PRINCIPLE 10: [IFAH recommends the following change for clarity] National authorities should implement, as much as possible, the Codex Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC-RCP 61-2005), the relevant sections of the OIE Terrestrial Animal Health Code (2007)³, the Codex Code of Food Hygiene (CAC/RCP 1-1969, Rev. 4 (2003)) and relevant WHO documents/guidelines on containment of antimicrobial resistance in food animals

4. Guidelines for Activities

7. These guidelines provide an outline of a series of steps that comprise the preliminary risk management activities, part of the general framework for antimicrobial resistance risk analysis. These activities are conducted by, or under the guidance of, the risk managers.

4.1 Identification of an antimicrobial resistance food safety issue

8. [IFAH recommends the following changed for clarity] In the context of this document, a potential food safety issue may arise when antimicrobial resistant microorganisms and antimicrobial resistance genes are present in food and

¹ Codex Alimentarius Commission, Procedural Manual.

² The definition of Risk Manager is derived from the definition for risk management, which may not include all of the individuals who are involved in the implementation phase and related activities associated with managing the risks resulting from antimicrobial resistance; i.e., risk management decisions are largely implemented by industry and other interested parties. The focus of the definition of risk manager in this document is restricted to governmental organizations with authority to decide on the acceptability of risk levels associated with foodborne hazards.

³ http://www.oie.int/eng/normes/Mcode/en_sommaire.htm

feed, including aquaculture, or are transmitted through food and animal feed. Foodborne exposures to resistant microorganisms or resistance determinants may adversely impact human health by reducing the therapeutic response value of antimicrobials used to treat in human zoonotic foodborne disease medicine because of decreased losses in susceptibility of these pathogenic bacteria. The risk manager initiates the risk management process framework to evaluate the scope and magnitude of the food safety issue and, where necessary, to commence activities to manage the identified associated risk.

9. Food safety issues may be identified by the risk manager or be the result of collaboration between different interested parties. Within Codex, a food safety issue may be raised by a member government, or by an intergovernmental or observer organization.

10. Antimicrobial resistance food safety issues may be identified on the basis of information arising from a variety of sources, such as antimicrobial resistance surveillance in animals and in foods of animal origin, food safety monitoring, antimicrobial usage surveys, animal and human surveillance data (including post-marketing surveillance data on approved antimicrobials), epidemiological or clinical studies, laboratory studies, research on resistance transfer, scientific, technological or medical advances, environmental monitoring, recommendations of experts, public input, etc. Additional potential sources of information are provided in the Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005)

11. To better define the food safety issue, the risk manager may need to pursue information from sources that have specific knowledge pertaining to the issue. An open process, in which the food safety issue is clearly identified and communicated by the risk managers to risk assessors, as well as affected consumers and industry, is essential to promote both an accurate definition and a well-understood and common perception of the issue.

4.2. Development of an antimicrobial resistance risk profile

12. The antimicrobial resistance risk profile is a description of a food safety problem and its context that presents, in a concise form, the current state of knowledge related to the food safety issue, describes current control measures and risk management options that have been identified to date, if any, and the food safety policy context that will influence further possible actions. The risk profile is usually developed by personnel with specific scientific expertise on the food safety issue of concern and some understanding of antimicrobial resistance risk assessment techniques.

13. [IFAH proposes the following change for clarity]The depth and breadth of the antimicrobial resistance risk profile may vary depending on the needs of the risk managers and the complexity of the food safety issue. An extensive list of suggested risk profile elements is provided in the Annex as guidance to risk managers at the national/regional level, and for bringing forward newly proposed work within the Codex process. In certain situations, however, it may be necessary to develop an abbreviated risk profile that could be used as a basis for further preliminary risk management activities, such as prioritizing the development of more comprehensive risk profiles or determining the need for commissioning a risk assessment. The abbreviated risk profile may be particularly useful for resource-challenged countries in determining priorities for further assessment activities. Caution should be exercised in implementing these abbreviated risk profiles, as they may not provide as complete a picture of the food safety issue as needed for effective decision making by the risk managers. The fundamental elements that should comprise an abbreviated risk profile include:[IFAH comments that readers of the document may find it is difficult to match this short list with specific line items in the Annex. It is suggested to mark the information needed in the annex with a symbol which relates to the information needed in the abbreviated risk profile]

- Description of the public health problem (the antimicrobial resistance food safety issue);
- Identification and characterization of the food commodity + antimicrobial resistant pathogen + antimicrobial use combination;
- Consideration of critically important antimicrobial lists developed by national and international groups (e.g., see Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials, Rome 2007);
- Description of usage (extent and nature) of antimicrobials in food production, when available (such as veterinary applications, plant protection or food processing); and
- Identification of major knowledge gaps.

14. Consideration of the information given in the risk profile may result in a range of initial decisions, such as determining that no further action is needed, commissioning an antimicrobial resistance risk assessment, establishing additional information gathering pathways, or implementing immediate risk mitigation for those food safety issues that

require an immediate action⁴ by the risk manager without further scientific consideration (e.g. requiring withdrawal / recall of contaminated products).

15. 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.

4.3. Rank food safety issues and set priorities for risk assessment and management

16. Given the potentially high resource costs associated with conducting risk assessments and/or implementing risk management goals, a risk ranking or prioritization process is important in placing the risks from a specific food commodity + antimicrobial resistant pathogen + antimicrobial use combination in context with other risk scenarios that require the attention of risk managers. The output from the risk profile provides the principal criteria that should be used by risk managers in this risk ranking or prioritization process.

17. Beyond the description of the food safety issue provided by the risk profile, other criteria may be used for ranking or prioritization; these are generally determined by the risk managers in conjunction with stakeholders, and in consultation with risk assessors on technical aspects of the issues. Such criteria include:

- Perceived relative level of risk to consumers;
- Capability to implement effective food safety control measures;
- Potential international trade implications associated with food safety control measures;
- Regulatory challenges; and
- Policy concerns/public demand.

4.4. Establish broad risk management goals

18. Following development of the risk profile and the conduct of the risk ranking/prioritization steps, risk managers should decide on the broader risk management goals in addressing the food safety issue. Ultimately, the outcome of the preliminary risk management activities and the risk assessment, if conducted, should be combined with the evaluation of available risk management options in order to reach a decision on management of the risk.

19. Risk management goals should have as their primary objective the protection of the health of consumers. Other considerations in selecting appropriate risk management goals include the potential impact on trade, as well as the feasibility of implementation, enforcement, and compliance of the risk mitigation measures associated with the goals.

20. The risk management goals may range from more general approaches, such as implementation of codes of practice, to more specific measures, such as the development of regulatory standards and guidelines or the estimation of risks in specific exposure scenarios to inform the risk managers in selecting specific risk mitigation measures. The determination of the need, or the feasibility, of a risk assessment, is often critical in establishing risk management goals. Thus, the risk management goals should be clearly stated prior to commissioning a risk assessment to ensure that the information provided by a risk assessment addresses the risk management goals.

21. The criteria for determining the need for a risk assessment depends on the nature of the risk management goals. Factors that may influence the desirability of a risk assessment include:

- If the nature and magnitude of the risk are not well characterized;
- When risk brings economic, social, cultural and ethical considerations;
- When the risk management goals have major trade implications;
- The availability of resources;
- The urgency of the food safety issue; or

⁴ The International Health Regulation (2005) Agreement gives provisions for appropriate measures in case of public health emergencies, including food related events (www.who.int/csr/ihr/ihrwha58_3-en.pdf). The Principles and Guidelines for the Exchange of Information in Food Safety Emergency Situation (CAC/GL 19-1995) defines a food safety emergency as a situation whether accidental or intentional that is identified by a competent authority as constitutes a serious and as yet uncontrolled foodborne risk to public health that requires urgent action. Emergency measures may be part of immediate action.

- The availability of scientific information.

22. The establishment of these broad risk management goals should be accomplished as an interactive process between the risk managers, the risk assessors, and external stakeholders. It is imperative that the established goals be developed with full consideration of their ability to address the specific food safety issue of concern. The risk management goals should be clearly communicated to all interested parties.

4.5. Establish a risk assessment policy

23. Determination of risk assessment policy should be included as a specific component of risk management. Risk assessment policy should be established by risk managers in advance of risk assessment, in consultation with risk assessors and all other interested parties. This procedure aims at ensuring that the risk assessment is systematic, complete, unbiased and transparent. The mandate given by risk managers to risk assessors should be as clear as possible and provide guidance as to the scope of the risk assessment. Where necessary, risk managers should ask risk assessors to evaluate the potential changes in risk resulting from different risk management options.

24. [IFAH proposes the following change for clarity] For antimicrobial resistance risk assessment policy, risk managers may consult ~~adopt the General Principles in the Draft Guideline for the Risk Assessment portion of the guidance or relevant Codex or FAO documents. of Foodborne Antimicrobial Resistant Microorganisms (under development) related to non-human use of antimicrobials.~~

25. Additional elements specific to the food safety issue related to antimicrobial resistance should also be included in order to provide guidelines to risk assessors conducting the risk assessment. For example, the risk assessment policy should provide the risk assessors with guidance on the need to address uncertainty and what assumptions to use when the available data are inconsistent.

4.6. Commission of a risk assessment [IFAH comments that this section may need to be better coordinated with the Risk Assessment guidance draft in terms of ensuring that Risk Assessment is done to guide the selection of Risk Management options, and not just to derive “risk estimates”.]

26. [IFAH suggests the following change for clarity] Based on the established risk management goals, risk managers may commission a risk assessment to provide an objective, systematic evaluation of relevant scientific knowledge to help make an informed decision regarding implementation of the most appropriate risk management options activities. The nature and scope of the risk assessment may vary, depending on the food safety issue of concern, but it is important to ensure that a clear mandate is given to risk assessors and that the risk assessment meets the needs of the risk manager. It is also important that all aspects of the commissioning and conduct of the risk assessment are documented and transparent.

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

- A description of the specific food safety issue (as defined in the risk profile);
- The scope and purpose of the risk assessment;
- The specific questions to be answered by the risk assessment;
- The type (e.g., quantitative, qualitative) of risk assessment to be conducted;
- The expertise and resources required to carry out the risk assessment;
- Timelines for milestones and completion of the risk assessment;
- Criteria to validate the risk model;
- Criteria to assess the scientific and technical adequacy of the risk assessment; and
- Analysis of any future data needs.

28. It is important to ensure that the composition of the risk assessment team is appropriate in terms of expertise and be free of conflicts of interest or bias. The risk managers should also ensure that there are effective and iterative communication pathways between the risk assessors and risk managers during the risk assessment process, and that the risk assessment be adequately reviewed by the scientific community and if appropriate, the public.

29. The risk manager should refer to the Principles and Guidelines for the Conduct of Antimicrobial Resistance Risk Assessment (under development).

4.7. Consider the results of the risk assessment [IFAH recommends that this section be coordinated with the Risk Management Evaluation and Selection sections to ensure continuity and alignment]

30. [IFAH suggests the following change for clarity] The conclusion 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. In reviewing the completeness of the risk assessment, risk managers need to understand the nature, sources and extent of uncertainties and variability of the risk estimates expressed. The risk management decisions will be made with the outcome of the Risk Assessment. Post-implementation review of the risk management options for effectiveness should follow the same process.

ANNEX

Suggested Elements to Include in an Antimicrobial Resistance Risk Profile

[IFAH recommends alignment of these elements with the abbreviated risk profile approach in Section 13 by means of symbols to denote the key elements.]

A risk profile should present, to the extent possible, information on the following:

Definition of the hazard-food commodity combination(s) of concern:

- Hazard(s) of concern – the specific combination of:
 - food commodity;
 - antimicrobial resistant pathogen; and
 - antimicrobial use
- Description of the food commodity and the associated cause for concern (e.g., antimicrobial resistant foodborne illness, trade restrictions) due to the hazard
- Occurrence of the hazard in the food chain.

Description of the public health problem (i.e., the adverse human health consequences):

- Characteristics of the resistant microorganism(s) or resistance determinants, including key attributes that are the focus of its public health impact (e.g., cross resistance, co-resistance, horizontal gene transfer);
- Characteristics of the antimicrobial-susceptible infection, illness or disease, including:
 - Susceptible populations;
 - Annual incidence rate in humans including, if possible, any differences between age and sex;
 - Severity of clinical manifestations (e.g., case-fatality rate, rate of hospitalization; and
 - Nature and frequency of long-term complications;
- Characteristics of the antimicrobial-resistant infection, illness, or disease:
 - Added burden of the infection, illness or disease due to antimicrobial resistance, if readily available (e.g., medical and/or hospital costs; working days lost due to illness, etc.); and
 - Evidence of links between resistance, virulence, and/or fitness of the antimicrobial resistant microorganism
- Characteristics of treatment of the antimicrobial resistant infection, illness, or disease:
 - Options for treating the infection, illness, or disease (e.g., importance of antimicrobial drug for treatment of human adverse health effect per WHO Critically Important Antimicrobial Agent list, possible side effects of alternate treatments);
 - Extent of human use of the antimicrobial agent for which resistance is the concern;
 - Availability and nature of treatment; and
 - Prevalence of resistance in human populations;

Description of food commodities associated with the antimicrobial resistant microorganisms or resistance determinants (Post-harvest factors);

- Characteristics of the food commodity (commodities);
- Food use and handling that influences transmission of the hazard;
- Frequency and characteristics of foodborne sporadic cases;
- Epidemiological data from outbreak investigations;
- Prevalence of resistance on food commodity; and
- Evidence of a relationship between the presence of the antimicrobial resistant microorganisms or resistance determinants on the food commodity and the occurrence of the adverse health effect in humans.

Description of antimicrobial(s) (Pre-harvest factors);

- Chemical, physical and pharmacological properties of the antimicrobial agent;

- Type of use (treatment/prevention/control/growth promotion);
- Dose regimen and route of administration;
- Final product specifications;
- Specific rules of usage for the country concerned;
- Frequency or incidence of use of the antimicrobial agent;
- Factors influencing the persistence of resistance in the pre-harvest production stage;
- Importance of antimicrobial drug to animal medicine per OIE Critically Important List;
- Associations between usages and development and persistence of resistance;
- Factors that may affect the dissemination of antimicrobial resistant microorganisms through the food chain;
- Evidence of a relationship between the use of the antimicrobial and the occurrence of antimicrobial resistant microorganisms, or resistance determinants, in the food commodity of concern;
- Persistence of the antimicrobial in the environment, and factors affecting the maintenance of antimicrobial resistant microorganisms and/or resistance determinants; and
- Contribution of alternative (non-foodborne) sources of antimicrobial resistance

Antimicrobial resistance genes and resistance determinants:

- Factors that may affect the frequency of transfer of genetic elements through the food chain; and
- Description of the molecular genetics of the antimicrobial resistance of concern

Other Risk Profile Elements:

- Summary of the extent and effectiveness of current risk management practices including food safety production/processing control measures, educational programs, and public health intervention programs (e.g., vaccines);
- Identification of additional risk mitigation strategies that could be used to control the hazard;
- The extent of international trade of the food commodity;
- Existence of regional/international trade agreements and how they may affect public health with respect to the specific hazard-food commodity combination(s);
- Public perceptions of the problem and the risk;
- Initial assessment of the need and benefits to be gained from requesting an antimicrobial resistance risk assessment, and the feasibility that such an assessment could be accomplished within the required time frame; and
- If a risk assessment is identified as being needed, recommended questions that should be posed to the risk assessor;

Assessment of available information and major knowledge gaps:

- Existing antimicrobial resistance risk assessments on the food commodity + antimicrobial resistant pathogen + antimicrobial use combination(s) including, if possible;
- Other relevant scientific knowledge and data that would facilitate risk management activities including, if warranted, the conduct of a risk assessment;
- Existing Codex guidance documents (including existing Codes of Hygienic Practice and/or Codes of Practice);
- International and/or national governmental and/or industry codes of hygienic practice and related information; and
- Areas where major absences of information exist that could hamper risk management activities, including, if warranted, the conduct of a risk assessment.