

# codex alimentarius commission E



FOOD AND AGRICULTURE  
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**Agenda Item 4**

**CX/AMR 07/1/4**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

AD HOC CODEX INTERGOVERNMENTAL TASK FORCE  
ON ANTIMICROBIAL RESISTANCE

*First Session*

*Seoul, Republic of Korea, 23-26 October 2007*

**CONSIDERATION OF THE ELABORATION OF STANDARDS, GUIDELINES OR  
OTHER TEXTS ON ANTIMICROBIAL RESISTANCE**  
(comments submitted in response to CL 2006/38-AMR)

The following comments have been received from: Canada, Cuba, European Community, Japan, Mexico, Republic of Korea, United States of America, Consumer's International, IFAH and OIE

## **CANADA**

Antimicrobial resistance continues to be a global as well as local public health issue. Various meetings organized in recent years by international bodies (such as World Health Organization [WHO], UN Food and Agricultural Organization [FAO], World Organization for Animal Health [OIE] and CODEX) have addressed many important aspects of antimicrobial resistance related to foodborne bacteria or bacteria of animal origin due to the non-human use of antimicrobial agents. Subsequently, there are a significant number of documents available that demonstrate, in a broad context, the importance and complexity of antimicrobial resistance. However, there is a lack of published work relating to specific methodology for risk assessment, risk profiles, priority setting, and/or risk management advice associated with the non-human use of specific antimicrobial agents, which should particularly include classes of critically important human antimicrobials. Therefore, Canada is proposing new work as included in the two attached Project Documents. These project documents are closely linked; however, they can still be developed either concurrently or independently. Canada anticipates that the new Task Force would address specifically food- or animal-related antimicrobial resistance issues and their impact on public health.

### **Project Document 1**

**Establishment of Principles for the Conduct of Risk Assessments to Assess Risk to Public Health from Antimicrobial Resistance Associated with Foodborne Bacteria and the Non-Human Use of Antimicrobial Agents**

#### **1. Purpose and scope of the proposed work**

The purpose is to develop risk assessment guiding principles that would be used to specifically assess antimicrobial resistance associated with foodborne bacteria and the non-human use of antimicrobial agents. These principles would assist with the development of risk profiles and be applicable to risk assessments associated with the non-human use of antimicrobial agents that are used therapeutically and/or non-therapeutically in animals and are important to human medicine.

## **2. Relevance and timeliness**

This work would be consistent with the proposed activities detailed in Annex 2 of CL 2006/38-AMR as well as the Terms of Reference of the Task Force. It is also consistent with Codex Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005).

## **3. The main aspects to be covered**

Relevant risk assessment principles may be developed or further refined by consideration of Codex's Principles and Guidelines for the Conduct of Microbial Risk Assessment (CAC/GL-30 1999) and OIE's Risk Assessment for Antimicrobial Resistance Arising from the Use of Antimicrobials in Animals (OIE Terrestrial Animal Health Code 2006). It is noted that there are also specific risk assessment reports available in the literature on the use of specific veterinary antimicrobial agents that may be used to compare the new risk assessment working template proposed in this document.

Ideally the information gathered from this guidance would be able to rapidly identify data gaps with suggestions as to whether the data gaps should be filled by expanded surveillance or targeted research, provide guidance as to whether qualitative or quantitative process are appropriate, and potentially link the risk assessment outcome to inform appropriate risk management actions.

## **4. Assessment against the criteria applicable to general subject as contained in the *Criteria for the Establishment of Work Priorities***

***Consumer protection from the point of the view of health and fraudulent practices:*** This new work proposal is consistent with this criterion since it provides guidelines with which antimicrobial resistance risk assessment would be conducted in a consistent, transparent and science-based manner. This would contribute to consumer protection.

***Diversification of national legislation and apparent resultant or potential impediments to international trade:*** In absence of unified guidance document from international standard setting body such as Codex, individual countries have adopted different ways of assessing risks. Many countries (particularly developing countries) may not have guidance on assessing risks from antimicrobial resistant bacteria from food. The elaboration of risk assessment principles will contribute to a more consistent approach to the assessment of risk to public health associated with antimicrobial resistance.

***Scope of the work and establishment of priorities between the various sections of the work:*** This new work proposal provides specific considerations to address the development of a key document needed internationally, although the scope and priorities of the work need to be discussed by the Task Force.

***Work already undertaken by the other international organizations in this field:*** This new work proposal will build upon previous works of various international working groups of WHO, OIE, Codex, VICH with respect to antimicrobial resistance. However, the project document will more specifically address antimicrobial resistance risk assessment and its impact on public health. Codex has already produced Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005) as well as Microbial Risk Assessment (CAC/GL-30 1999). OIE has Terrestrial Animal Health Code 2006, which includes "Risk Assessment for Antimicrobial Resistance Arising from the Use of Antimicrobials in Animals".

## **5. Relevance to Codex Strategic Objectives**

This new work proposal is consistent with Strategic Objective 1, *Promoting Sound Regulatory Frameworks*, and Strategic Objective 2, *Promoting Widest and Consistent Application of Scientific Principles and Risk Analysis*.

## **6. Information on the relation between the proposal and other existing Codex documents**

The proposal would complement but not duplicate Codex Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005) and Codex Principle and Guidelines for the Conduct of Microbial Risk Assessment (CAC/GL 30-1999).

## **7. Identification of any need for technical input for scientific advice**

There is a need for FAO/WHO to establish an expert consultation to provide additional scientific advice. The nature of this advice will be determined by the Task Force at its First Session when specific work proposals have been agreed to.

## **8. Identification of any need for technical input to the standard from external bodies so that this can be planned for**

It is anticipated that OIE will actively participate in the Task Force and contribute to the development of these Principles.

## **9. The proposed time-line for completion of the new work, including the start date, the proposed date for adoption at Step 5, and the proposed date for adoption by the Commission; the time frame for developing a standard should not normally exceed five years**

Envisaging the use of inter-sessional working groups, Canada suggests the following as a possible time-line:

<b>Activity</b>	<b>Step/date</b>
Task Force agrees on the work to be undertaken	October 2007
Commission approves new work	July 2008
Step 5	2010
Adoption by the Commission	2011

## **Project Document 2**

### **To Develop Risk Profiles and/or Risk Assessments of Antimicrobial Resistance Associated with the Non-Human Use of the Selected Antimicrobial Agents that are Critically Important to Human Medicine**

#### **1. Purpose and scope of the proposed work**

The purpose is to develop specific risk profile(s) with respect to antimicrobial resistance associated with the non-human use of selected antimicrobial agents that are critically important to human medicine. The risk profiles would drive more detailed risk assessments that could be utilized by member countries to address the relevant risks. The scope of the work is to limit the risk profiles for those of selected antimicrobials that are critically important to human medicine and that are agreed to by the Task Force.

Patterns of antimicrobial resistance in foodborne or commensal bacteria of food-animal origin have been monitored over the past years by a variety of surveillance programs around the globe such as CIPARS (Canada), DANMAP (Denmark) and NARMS (the USA), etc. Meanwhile, antimicrobial agents have been categorized by several countries (e.g., Australia, Canada and USA) or internationally (i.e., WHO) into different categories based on their importance in human medicine. These data and documents can provide a possible basis for establishment of evidence-based risk profiles associated with the non-human use of antimicrobials that are critically important to human medicine.

#### **2. Relevance and timeliness**

This work would be consistent with the proposed activities detailed in the Annex 2 of CL 2006/38-AMR, as well as the Terms of Reference of the Task Force. It is also consistent with Codex Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005).

#### **3. The main aspects to be covered**

The risk profiles of resistance to specific antimicrobials could be developed using the principles established as proposed in the Project Document 1. However, the establishment of the risk profiles could also be carried out concurrently or independently. Nevertheless, a prioritization process would be needed to determine the individual antimicrobial(s) or its/their class(es) that are to be assessed. It is expected that a prioritization process may consider, but not limit to, the following questions:

- What are the criteria for establishing prioritization process?
- What are the issue(s) or emerging issue(s) that may significantly impact on human medicine or public health?

- What are the agents or classes of antimicrobials, non-human use of which would significantly impact on human medicine due to the development or dissemination of antimicrobial resistance? For the development of the risk profiles, the following points may be considered:
- Importance of the drug in human medicine (indications, extent of use, level of resistance, availability of alternative drugs, resistance mechanisms, etc.).
- Information about the hazard (e.g., the resistant bacteria and the resistance genes) may include: drug resistance in zoonotic/animal pathogens and commensals of public health concern, rate of development of resistance after exposure to the drug in animals and transfer to other animals; transmission of resistant bacteria from animals/animal derived foods to humans; pathogenicity of resistant bacteria derived from food animals in humans; and possible transmission of resistance determinants to human pathogens.
- Information on drug use in various animal species.
- Information about human exposure to hazard including routes of exposure.
- Information on adverse health effects in humans (e.g., dose-response, type and severity of adverse health effects, and at-risk population characteristics).

#### **4. Assessment against the criteria applicable to general subject as contained in the *Criteria for the Establishment of Work Priorities***

***Consumer protection from the point of the view of health and fraudulent practices:*** This new work would contribute to enhance consumer protection since it provides specific guidelines about potential risk profiles associated with resistance to specific antimicrobials.

***Diversification of national legislation and apparent resultant or potential impediments to international trade:*** This new work would lead to development of appropriate internationally-recognized risk profiles, which the member countries could utilize consistently to establish their own standards or accordingly to develop relevant policy in order to manage the potential antimicrobial resistance risk. Therefore, the new work would contribute to minimizing potential impediments to international trade.

***Scope of the work and establishment of priorities between the various sections of the work:*** This new work proposal deals with the establishment of specific risk profiles associated with non-human use of selected antimicrobials critically important to human medicine. However, the scope, the priorities of the work including priority setting techniques need to be further defined by the Task Force. For instance, the targeted antimicrobial agent(s) should be considered among the critical important antimicrobials for human medicine (during the initial phase in developing risk profiles) and decided by the Task Force.

***Work already undertaken by the other international organizations in this field:*** Currently no specific risk profiles associated with the non-human use of selected antimicrobials are available. Thus, this new work proposal does not duplicate work undertaken by other international organizations. It is noted that some risk assessments conducted by regulatory bodies or academia are available in literature.

#### **5. Relevance to Codex Strategic Objectives**

This new work proposal is consistent with Strategic Objective 1, *Promoting Sound Regulatory Frameworks*, and Strategic Objective 2, *Promoting Widest and Consistent Application of Scientific Principles and Risk Analysis*.

#### **6. Information on the relation between the proposal and other existing Codex documents**

The proposal would complement but not duplicate Codex Code of Practice to Minimize and Contain Antimicrobial Resistance (CAC/RCP 61-2005) and Codex Principle and Guidelines for the Conduct of Microbial Risk Assessment (CAC/GL 30-1999).

#### **7. Identification of any need for technical input for scientific advice**

There is a need for FAO/WHO to establish an expert consultation to provide additional scientific advice. The nature of this advice will be determined by the Task Force at its First Session when specific work proposals have been agreed to.

### 8. Identification of any need for technical input to the standard from external bodies so that this can be planned for

Involvement of OIE and/or other national/international veterinary organizations is encouraged.

### 9. The proposed time-line for completion of the new work, including the start data, the proposed date for adoption at Step 5, and the proposed date for adoption by the Commission; the time frame for developing a standard should not normally exceed five years

It is expected that the work could be completed within a four-year period for the Task Force. Envisaging the use of inter-sessional working groups, Canada suggests the following as a possible time-line:

Activity	Step/date
Task Force agrees on the work to be undertaken	October 2007
Commission approves new work	July 2008
Step 5	2010
Adoption by the Commission	2011

## CUBA

The following proposals are the result of a wide distribution and analysis of Circular Letter CL 2006/38-AMR among institutions dealing with the subject antimicrobial resistance in the country.

As a result of this consultation we are proposing the following:

- Elaboration of project documents for the following:
  - Guidelines on the application, evaluation and management of risks of antimicrobials used in human and veterinary medicine;
  - Analytical methods used for the evaluation of susceptibility to antimicrobials
  - Methodology for the establishment of antimicrobial resistance surveillance programmes of food with the purpose of:
    - a) Determine resistant bacteria in food as part of risk analysis in relation to food safety to ensure human health protection.
    - b) Observe the change of antimicrobial resistance in bacteria which can be transmitted through food.
    - c) Detect the appearance of new mechanisms of antimicrobial resistance.
    - d) Supply data which can be used as a reference for the elaboration of policies on the use of antimicrobial drugs in both human and animals.
    - e) Identify the entry into the country of strains resistant or multi resistant to antimicrobials of clinical importance from imported foods, for example *Salmonella typhimurium* DT104.
    - f) Analysis of the susceptibility of pathogenic bacteria in foods to antimicrobials according to established techniques.
    - g) Analysis of food safety microbial indicators.
    - h) Surveys based on scientific criteria (the program WHONET developed for this type of study is recommended).
- Special attention should be given to bacteria present in foods of animal origin sampled at different steps of the food chain, including those at processing, packaging, distribution and retail because of the possible transfer of resistant bacteria from animals to humans, or of genes transferring genetic

information which encode resistance of bacteria from animal to humans, for instance *Salmonella* and *Escherichia coli* which can constitute an important risk to animal and human health.

- It is also of interest to collect incidence data on bacteria in vegetables, mainly those that are consumed raw or with minimal processing, because the different types of plants and vegetables may be exposed to manure or agriculture run-off and be contaminated with resistant bacteria of animal origin. The use of water contaminated from sewage or drain system in agriculture is also a risk in the transfer of resistant bacteria.

Taking into consideration the consequences of ingesting a food with bacteria resistant to antimicrobials, from a food safety perspective, it should be necessary to assess the condition in which it is consumed, if there is a need for a treatment before consumption which ensure the elimination of the bacteria or if it is ready for the consumption and assess the risk. Another important aspect is if the food is domestically produced or it is imported, for the reasons above mentioned with reference to the introduction into the country of resistant strains.

Activities undertaken in Cuba

Because of the interest in this subject a National Group has been established within the Technical Committee of Food Hygiene Standardization to consider studies focusing on Risk Analysis of antimicrobial resistance with the primary objective of evaluating the national situation.

Taking into consideration the importance of knowing the behaviour of antimicrobial resistance in bacteria isolated in food a research project, led by the Instituto de Nutrición e Higiene de los Alimentos (INHA), is ongoing since 2004 on resistance patterns of *Escherichia coli* and *Salmonella*. The study has determined at least 100 resistant strains with a percentage of moderate- intermediate resistance and showing a wide diversity of patterns of resistance for one, two and three antibiotics.

## EUROPEAN COMMUNITY

We can support the document in general and restate that we welcome that Codex Alimentarius addresses the issue of antimicrobial resistance in more detail.

We have comments on the documents and proposals for future work.

The European Community and its Member States support the approach decided by the Codex Alimentarius Commission as regards antimicrobial resistance and are strongly in favour of activities aimed at preventing the development of antimicrobial resistance in a balanced way in all relevant areas: human medicine, veterinary medicine related in particular to food production, and plant protection. We wish however to provide some general comments on the terms of reference of the Task Force and suggest that it could maintain a general discussion on its own terms of reference before embarking on work on concrete proposals.

The European Community and its Member States are also pleased to submit two proposals for new work presented in the form of project documents.

### 1. Comments on the document:

#### a) Comments on the terms of reference

On “Objectives”: We find it important that the risk presented by the use/misuse of antimicrobials used in animals and by the use/misuse of antimicrobials in humans in particular are put in perspective. This is because there is the possibility that the impact of the use of antimicrobials in animals is overestimated. An overestimation could trigger measures that are out of proportion. We therefore suggest adding the following to the text under the heading “objectives”: “The Task Force should attempt to put into perspective the risk of increase of antimicrobial resistance in human beings and animals generated by different areas of use such as human medicine, veterinary applications, plant protection or food-processing”.

We also suggest modifying the text under “Terms of reference” as follows “To develop guidance on the methodology for the assessment of the risk that antimicrobial resistance in humans and animals increases due to the use of antimicrobials in humans, animals, plants and food processing. The methodology should be described so that it can be applied by FAO/WHO through JEMRA in close co-operation with JECFA and OIE with subsequent consideration....”

#### b) Comments on Annex 2

We are aware that Annex 2 (extract of CAV 29/LIM 18 “REPORT OF THE IN-SESSION WORKING GROUP TO ANALYZE COMMENTS RECEIVED AND TO PREPARE PROPOSALS FOR THE TITLE OBJECTIVES, TERMS OF REFERENCE AND THE FRAME FOR THE PROPOSED TASK FORCE”) is part of a document submitted at the last Codex Commission meeting representing the report of an intra-session working group. We are thus aware that the document cannot be modified retrospectively. Nevertheless we would like to make some comments on the document in order to increase common understanding of the issues mentioned there:

- Bullet point two would more precisely address the issue by saying: “development of a risk assessment methodology and risk assessment policy concerning the risk that antimicrobial resistance in humans and animals increases due to the use of antimicrobials in human medicine, veterinary applications, plant protection or food-processing”.
- Bullet point three: To our knowledge the specific consideration of apiculture is important due to the particular nature of honey production.
- Bullet point four addresses two different issues: public health and animal health. Animal health relates to the need to treat animals to foster their health and to avoid unnecessary suffering. This could have been more clearly stated. To avoid misunderstanding, we would like to stress that at the same time other uses such as for growth promotion also need to be addressed by the Task Force.
- Bullet point six describes in a complicated manner that it is necessary to identify risk management options in order to select measures suitable to reduce resistance to antimicrobials.
- Point 6 under “Activities”: To our understanding it is crucial to implement a dialogue between Codex and other departments of WHO that deal with public health and the use of antimicrobials in humans.

This will assist in putting different risks associated with the use of antimicrobials into perspective and thus ensure that risk management measures are proportionate to the risk represented by each area of use. We reiterate earlier comments emphasizing that the European Community and its Member States strongly support activities aimed at preventing the development of antimicrobial resistance, in a balanced way in all relevant areas: human medicine, veterinary medicine related in particular to food production, and plant protection.

#### 2. Proposals for activities

The European Community and its 27 Member States wish to submit two project proposals for areas of work previously identified. These are:

- 1) Proposal for guidelines on a risk assessment methodology for antimicrobial resistance to be used by FAO and WHO. (Annex I)
- 2) Identification of risk management measures designed to contribute to the containment of antimicrobial resistance. (Annex II)

ANNEX I

### **Project Document 1**

#### **Proposal for guidelines on a risk assessment methodology for antimicrobial resistance to be used by FAO and WHO**

##### **1. Purpose and scope of the proposed work**

The purpose is to identify and describe a risk assessment methodology that can be used by risk assessors in order to qualify and, if possible, quantify the risk to human health from the use of antimicrobials in animal production, food and feed production and processing.

## 2. Relevance and timeliness

Antimicrobial agents are essential for human and animal health and welfare. Antimicrobial agents are widely used in humans, animals (food producing animals and companion animals), horticulture and food processing to treat or prevent disease, as a production aid (growth promotion) or as a preservative.

On the one hand, the increasing antimicrobial resistance of important human pathogenic bacteria is increasingly perceived as a threat to public health. Any use of antimicrobials, whether in humans, animals, horticulture or food-processing, may potentially lead to bacterial resistance. On the other hand, it must be highlighted however that antimicrobials administered to animals play also a major role in preventing food borne diseases.

Increasing international travel and international trade may spread resistance world-wide. Antimicrobial resistance is thus a global public and animal health concern that is impacted by both human and non-human antimicrobial usage.

In consequence, the human, animal, horticulture and food processing sectors have a shared responsibility and role in efforts to prevent and minimize antimicrobial resistance selection pressures for both human and non-human use of antimicrobials.

The types of antimicrobials used for each purpose are frequently the same, or closely related to each other. In order to manage the risk to human health from antimicrobial resistance of food borne origin, it is therefore necessary to develop an internationally recognised risk assessment methodology and policy to evaluate these risks. This will need to consider particular antimicrobial agents or groups of antimicrobials and associated use patterns in a holistic manner considering use and risks in all relevant areas of human medicine, veterinary applications, horticulture or food-processing.

This work is intended to supplement the Working Principles for Risk Analysis for Application in the Framework of Codex Alimentarius<sup>1</sup> and to provide FAO, WHO and Codex members with guidance on how to evaluate the risk from the development of antimicrobial resistance deriving from particular antimicrobial agents or groups of antimicrobials and associated use patterns.

## 3. The main aspects to be covered

The completed guideline would describe an appropriate evaluation procedure which should:

- attempt to establish risk profiles of antimicrobials used in feed and food production and processing with respect to the development of antimicrobial resistance in food borne bacteria and consequent impact on the containment of antimicrobial resistance in animal and public health;
- be a sequence of evaluation steps, each one solving one well-defined evaluation problem (i.e. the likelihood of transfer of resistant bacteria from animals to humans via food);
- provide techniques to solve the evaluation problem at each step, using the appropriate data input to that step. This input needs to be identified.
- integrate the steps into the Codex risk assessment system, i.e. hazard identification, dose-response assessment, exposure assessment, and risk characterization;
- provide techniques to combine all steps into an integrated evaluation methodology, enabling the output of one step to be used as the input for the next step (e.g. flow charts, decision trees);
- include a documentation method to keep track of all the evaluation results (decisions) and models developed during the evaluation;
- include a tiered approach to the decision on whether qualitative or quantitative risk assessment is necessary.

The following issues should be considered when developing the methodology:

- the necessity to develop a specific methodology for different purposes;

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<sup>1</sup> see Codex Procedural Manual, 15<sup>th</sup> edition page 101-107



- the consideration of scenarios which lead to the development of antimicrobial resistance in humans and animals. These exposure pathways are generally considered to be composed of the following elements (with examples):
  - 1) source (humans, animals, plants);
  - 2) transport media (water, air);
  - 3) exposure point (public places, hospitals, farm, stable etc, etc.);
  - 4) route of exposure (ingestion, inhalation);
  - 5) receptor population (e.g. children, adults, elderly people, companion animals, farm animals, wild animals).

Exposure pathways are very complex and are constantly changing. In most cases, there are multiple exposure pathways present which may affect a number of different populations.

- the necessity to evaluate scenarios based on existing routes through which animals and humans can be exposed to resistant bacteria and the need to design resistance development models;
- the necessity to identify respective model input evaluation in order to perform a resistance exposure pathway assessment;
- the need to address the range of potential human and animal health impacts and the cumulative effects of resistance;
- the need to use the available information on currently marketed antimicrobials used in different areas with respect to antimicrobial resistance development as examples;
- the necessity to consider the need to control bias and to thoroughly document uncertainties;
- the possible impact on current evaluation procedures as performed by JEMRA, JECFA and JMPR.

#### **4. Assessment against the criteria applicable to the subject as contained in the Criteria for the establishment of work priorities.**

Consumer protection from the point of view of health and fraudulent practices: This new work proposal is consistent with this criterion as it provides additional guidance with which to undertake scientific safety assessments for antimicrobials

Diversification of national legislations and apparent resultant or potential impediments to international trade: This proposal is consistent with this criterion as it intends to provide scientific guidance which JEMRA (JECFA;JMPR) and Codex members may utilize to establish their national /regional guidance.

Scope of work and establishment of priorities between the various section of work: The terms of reference of this proposal provide sufficient guidance to indicate the general scope and nature of the intended work to permit the Task Force to discuss and determine the final scope of the project.

Work already undertaken by other organizations in this field:

- Second Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Management options 15–18 March 2004 Oslo, Norway (report available at: <http://www.who.int/foodsafety/publications/micro/mar04/en/index.html>)
- First Joint FAO/OIE/WHO Expert Workshop on Non-human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment, Geneva, 1-5 December 2003 (report available at: <http://www.who.int/foodsafety/publications/micro/nov2003/en/index.html>)
- OIE List of Antimicrobials of Veterinary Importance, RESOLUTION No. XXXIII available at [http://www.oie.int/download/SG/2006/A\\_RF\\_2006\\_WEBPUB.pdf](http://www.oie.int/download/SG/2006/A_RF_2006_WEBPUB.pdf) p.152
- Critically important antibacterial agents or human medicine for risk management of non-human use. Report of a WHO working group consultation 15 - 18 February 2005, Canberra, Australia (available at: [http://www.who.int/foodborne\\_disease/resistance/FBD\\_CanberraAntibacterial\\_FEB2005.pdf](http://www.who.int/foodborne_disease/resistance/FBD_CanberraAntibacterial_FEB2005.pdf))

- Report of a Joint FAO/OIE/WHO Expert Consultation on Antimicrobial Use in Aquaculture and Antimicrobial Resistance Seoul, Republic of Korea, 13–16 June 2006  
[http://www.fao.org/ag/agn/food/risk\\_antimicrobial\\_en.stm](http://www.fao.org/ag/agn/food/risk_antimicrobial_en.stm)
- OIE Terrestrial code – Chapter 3.9. Antimicrobial resistance  
[http://www.oie.int/eng/normes/mcode/en\\_titre\\_3.9.htm](http://www.oie.int/eng/normes/mcode/en_titre_3.9.htm) ;
  - 1) Guidelines for the harmonisation of national antimicrobial resistance surveillance and monitoring programmes
  - 2) Guidelines for the monitoring of the quantities of antimicrobials used in animal husbandry
  - 3) Guidelines for the responsible and prudent use of antimicrobial agents in veterinary medicine
  - 4) Risk assessment for antimicrobial resistance arising from the use of antimicrobials in animals

## **5. Relevance to Codex Strategic Objectives**

This work is consistent with Codex objectives in particular:

- Protection of consumer health,
- Facilitation of fair practices in food trade,
- Promotion of the application of scientific principles and risk analysis,
- Development of horizontal provisions which would provide methodological consistency.

## **6. Information on the relation between the proposal and other existing Codex documents.**

The proposal would supplement but not duplicate relevant existing Codex, OIE or WHO guidance on risk assessment.

## **7. Identification of any need for technical inputs for scientific advice.**

JEMRA and others experienced in microbiological risk assessment particularly in relation to antimicrobial agents.

## **8. Identification of any need for technical input to the standard from external bodies that this can be planned for.**

To be identified

## **9. The proposed timeline for completion of the new work, including the start date, the proposed date for adoption at Step 5 and the proposed date for adoption by the Commission; the timeframe for developing a standard should not normally exceed 5 years.**

If agreed, to be by the Task Force at its first meeting, a draft would be presented to the Task Force at its second meeting (possibly 2008) for consideration at Step 3. It is expected that the work can be completed within the four-year timeframe for the Task Force.

ANNEX 2

## **Project Document 2**

### **on a proposal for guidelines for risk management measures designed to contribute to the prevention of antimicrobial resistance in with respect to different areas of use**

#### **1. Purpose and scope of the proposed work**

The purpose is to identify risk management measures that can be implemented by Codex members in order to contain and minimise the transmission of food borne antimicrobial resistant microorganisms to consumers through food.

The scope of the work would include identifying the criteria for monitoring the impact of risk management measures on consumer health.

## **2. Relevance and timeliness**

Antimicrobial agents are essential for human and animal health and welfare. Antimicrobial agents are widely used in humans, animals (food producing animals and companion animals), horticulture and food processing to treat or prevent disease, as a production aid (growth promotion) or as a preservative.

On the one hand, the increasing antimicrobial resistance of important human pathogenic bacteria is increasingly perceived as a threat to public health. Any use of antimicrobials, whether in humans, animals, horticulture or food-processing, may potentially lead to bacterial resistance. On the other hand, it must be highlighted however that antimicrobials administered to animals play also a major role in preventing food borne diseases.

Increasing international travel and international trade may spread resistance world-wide. Antimicrobial resistance is thus a global public and animal health concern that is impacted by both human and non-human antimicrobial usage.

In consequence, the human, animal, horticulture and food processing sectors have a shared responsibility and role in efforts to prevent and minimize antimicrobial resistance selection pressures for both human and non-human use of antimicrobials.

The types of antimicrobials used for each purpose are frequently the same, or closely related to each other. In order to manage the risk to human health from antimicrobial resistance of food borne origin it is therefore necessary to develop an internationally recognised risk assessment methodology and policy to evaluate these risks. This will need to consider particular antimicrobial agents or groups of antimicrobials and associated use patterns in a holistic manner considering use and risks in all relevant areas of human medicine, veterinary applications, horticulture or food-processing.

This work is intended to provide Codex members with guidance on what risk management measures are the most appropriate to implement with a view to protecting the health of consumers while ensuring production of safe food and fair trade.

## **3. The main aspects to be covered**

Develop guidelines for the management of the risk of development and transmission of antimicrobial resistant micro-organisms via the food chain.

Different risk management approaches should be evaluated for their efficiency in containing antimicrobial resistance globally and minimising antimicrobial resistance spread through the food chain.

Risk management measures employed, envisaged or suggested by Codex members and observers should be considered, these may include:

- collection of data on consumption of antimicrobial agents (humans, animals, plants);
- increase antimicrobial resistance information related to the marketing of products containing antimicrobial agents;
- support educational campaigns directed at professionals and the general public to avoid overuse and misuse of antimicrobials;
- apply restricted distribution schemes for products containing antibacterial substances (e.g. prescription only);
- propose to prohibit the use of certain antimicrobials for certain purposes;
- promote appropriate use of antimicrobials in animals;
- promote prevention programmes (e.g. immunisation)
- implementation of monitoring systems in food (including methods of analysis, sanction and reporting systems);
- consideration of GMOs which contain genes expressing resistance to antibiotics;
- programmes encouraging the development of new antimicrobial agents;
- programmes encouraging the development of alternative treatments and vaccines;

- programmes supporting the development of rapid and reliable diagnostic and susceptibility tests;
- co-operation, co-ordination and partnership at international level;
- support of developing countries to identify and implement the appropriate measures;
- establishment of co-ordinated and coherent surveillance networks at regional or international level and encourage the participation of other institution and structures (including links between established surveillance networks in human and veterinary medicines).

In a second step, the task force may wish to consider criteria for drafting a resolution to call on other areas to contribute to the prevention of antimicrobial resistance in a similar manner.

#### **4. Assessment against the criteria applicable to the subject as contained in the Criteria for the establishment of work priorities.**

Consumer protection from the point of view of health and fraudulent practices: The proposal is consistent with this criterion as it provides additional guidance on the selection of appropriate risk management measures for antimicrobials used in animals, plants or food-processing with a view to protecting the health of consumers.

Diversification of national legislations and apparent resultant or potential impediments to international trade: The new work proposal is consistent with this criterion as it will provide technical guidance which countries may utilize to establish their own national/regional guidance on risk assessment and prioritization of work.

Scope of work and establishment of priorities between the various section of work: While the precise scope of this work proposal will need to be defined by the Task Force, this proposal provides sufficient guidance to indicate the general scope and nature of the intended work to permit the Task Force to discuss and determine the final scope of the project.

Work already undertaken by other organizations in this field:

- Codex Code of practise to minimise and contain antimicrobial resistance (CAC/RCP 61/2005) (available at: [http://www.codexalimentarius.net/web/standard\\_list.do?lang=en](http://www.codexalimentarius.net/web/standard_list.do?lang=en))
- Second Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Management options 15–18 March 2004 Oslo, Norway (report available at: <http://www.who.int/foodsafety/publications/micro/mar04/en/index.html>)
- First Joint FAO/OIE/WHO Expert Workshop on Non-human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment, Geneva, 1-5 December 2003 (report available at: <http://www.who.int/foodsafety/publications/micro/nov2003/en/index.html>)
- OIE List of Antimicrobials of Veterinary Importance, RESOLUTION No. XXXIII available at [http://www.oie.int/download/SG/2006/A\\_RF\\_2006\\_WEBPUB.pdf](http://www.oie.int/download/SG/2006/A_RF_2006_WEBPUB.pdf) p.152
- Critically important antibacterial agents or human medicine for risk management of non-human use. Report of a WHO working group consultation 15 - 18 February 2005, Canberra, Australia (available at: [http://www.who.int/foodborne\\_disease/resistance/FBD\\_CanberraAntibacterial\\_FEB2005.pdf](http://www.who.int/foodborne_disease/resistance/FBD_CanberraAntibacterial_FEB2005.pdf))
- Report of a Joint FAO/OIE/WHO Expert Consultation on Antimicrobial Use in Aquaculture and Antimicrobial Resistance Seoul, Republic of Korea, 13–16 June 2006 [http://www.fao.org/ag/agn/food/risk\\_antimicrobial\\_en.stm](http://www.fao.org/ag/agn/food/risk_antimicrobial_en.stm)
- OIE Terrestrial code – Chapter 3.9. Antimicrobial resistance [http://www.oie.int/eng/normes/mcode/en\\_titre\\_3.9.htm](http://www.oie.int/eng/normes/mcode/en_titre_3.9.htm);
  - 1) Guidelines for the harmonisation of national antimicrobial resistance surveillance and monitoring programmes
  - 2) Guidelines for the monitoring of the quantities of antimicrobials used in animal husbandry
  - 3) Guidelines for the responsible and prudent use of antimicrobial agents in veterinary medicine
  - 4) Risk assessment for antimicrobial resistance arising from the use of antimicrobials in animals

Moreover in the European Community a number of guidance document have been established<sup>2</sup>

## 5. Relevance to Codex Strategic Objectives

This work is consistent with Codex objectives in particular:

- Protection of the health of consumers,
- Promotion of fair practices in the food trade,
- Promotion of the application of a risk analysis approach,
- Development of horizontal provisions which would provide methodological consistency.

## 6. Information on the relation between the proposal and other existing Codex documents.

The proposal would build on all the information nationally, regionally and internationally available on the risk management tools to contain and minimise antimicrobial resistance globally and in particular to protect consumer health such as the Codex Code of practice to minimise and contain antimicrobial resistance (CAC/RCP 61/2005).

## 7. Identification of any need for technical inputs for scientific advice.

Not identified at this stage

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### <sup>2</sup> *European Food Safety Authority (EFSA)*

- Opinion of the Scientific Panel on Biological Hazards (BIOHAZ) and of the Scientific Panel on Animal Health and Welfare (AHAW) on “Review of the Community Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents and Antimicrobial Resistance in the European Union in 2004”  
[http://www.efsa.europa.eu/en/science/biohaz/biohaz\\_opinions/biohazahaw\\_ej403\\_zoonoses.html](http://www.efsa.europa.eu/en/science/biohaz/biohaz_opinions/biohazahaw_ej403_zoonoses.html)
- Joint AFC/BIOHAZ guidance document on the submission of data for the evaluation of the safety and the efficacy of substances for the removal of microbial surface contamination of foods of animal origin  
[http://www.efsa.europa.eu/etc/medialib/efsa/science/biohaz/biohaz\\_guidance/guidance\\_ej388.Par.0001.File.dat/bio\\_haz\\_op\\_ej388\\_decontam\\_guidance\\_en.pdf](http://www.efsa.europa.eu/etc/medialib/efsa/science/biohaz/biohaz_guidance/guidance_ej388.Par.0001.File.dat/bio_haz_op_ej388_decontam_guidance_en.pdf)

### **European Medicines Agency (EMA)**

- CVMP Strategy on Antimicrobials 2006-2010 and Status Report on Activities on Antimicrobials  
<http://www.emea.europa.eu/pdfs/vet/swp/35329705.pdf>
- Reflection Paper on the use of fluoroquinolones in food-producing animals in the European Union (revised document to be published shortly at the EMA web page):  
<http://www.emea.europa.eu/pdfs/vet/srwp/18465105en.pdf>
- VICH GL27 - Guidance on pre-approval information for registration on new veterinary medicinal products for food producing animals with respect to Antimicrobial Resistance  
<http://www.emea.europa.eu/pdfs/vet/vich/064401en.pdf>
- A Risk Management Strategic Plan for controlling Antimicrobial Resistance through the Authorisation of Veterinary Medicines: Recommendations consequent to the Report and Qualitative Risk Assessment of the CVMP of July 1999 <http://www.emea.europa.eu/pdfs/vet/regaffair/081899en.pdf>
- Antibiotic Report: Antibiotic Resistance in the European Union associated with Therapeutic Use of Veterinary Medicines - Report and Qualitative Risk Assessment by the Committee for Veterinary Medicinal Products  
<http://www.emea.europa.eu/pdfs/vet/regaffair/034299ENC.pdf>
- EMA Risk Assessment on Antimicrobial Resistance in Veterinary Medicines  
<http://www.emea.europa.eu/pdfs/vet/press/pos/237999en.pdf>

### **European Commission**

- Report from the commission to the council on the basis of member states ‘report on the implementation of the Council recommendation ( 2002/77/EC) on prudent use of antimicrobial agents in human medicine  
[http://ec.europa.eu/health/ph\\_threats/com/mic\\_res/com684\\_en.pdf](http://ec.europa.eu/health/ph_threats/com/mic_res/com684_en.pdf)
- Communication from the Commission on a Community Strategy Against Antimicrobial Resistance, Brussels, 20.06.2001, COM(2001) 333 final [http://europa.eu/eur-lex/en/com/cnc/2001/act333en01/com2001\\_0333en01-01.pdf](http://europa.eu/eur-lex/en/com/cnc/2001/act333en01/com2001_0333en01-01.pdf) and [http://europa.eu/eur-lex/en/com/cnc/2001/act333en01/com2001\\_0333en01-02.pdf](http://europa.eu/eur-lex/en/com/cnc/2001/act333en01/com2001_0333en01-02.pdf)
- European Commission - Opinion of the Scientific Steering Committee on Antimicrobial Resistance, 28 May 1999  
[http://ec.europa.eu/food/fs/sc/ssc/out50\\_en.pdf](http://ec.europa.eu/food/fs/sc/ssc/out50_en.pdf)
- European Commission - Scientific Steering Committee 2nd Opinion on Anti-Microbial Resistance Adopted on 10-11 May 2001 [http://ec.europa.eu/food/fs/sc/ssc/out203\\_en.pdf](http://ec.europa.eu/food/fs/sc/ssc/out203_en.pdf)

**8. Identification of any need for technical input to the standard from external bodies that this can be planned for.**

It would be necessary to gather expertise from different areas (food science, animal health, the pharmaceutical industry, specialised practitioners, the food industry; microbiology and food hygiene; risk assessors and risk managers ...)

**9. The proposed timeline for completion of the new work, including the start date, the proposed date for adoption at Step 5 and the proposed date for adoption by the Commission; the timeframe for developing a standard should not normally exceed 5 years.**

## **JAPAN**

The Government of Japan would like to thank the Republic of Korea for its hosting and organizing the new Task Force on Antimicrobial Resistance.

In reply to CL 2006/38-AMR, we would like to submit the following comments regarding new work for the Task Force.

Since much work has already been done on the issue of antimicrobial resistance nationally and internationally including the work of Codex, WHO, FAO and OIE, duplication of work should be avoided. Also, it is important to note that antibiotic resistance has emerged not only through food production but mainly through treatments of infections in humans. This perspective should not be forgotten in the new work, although the work may have to be focused on antimicrobial usage in food production.

The guidance on methodology and processes for risk assessment, which is included in the terms of reference, should cover the entire steps of the risk assessment. In the case of antimicrobial resistance, hazard is antimicrobial resistant microorganism or resistant determinant that emerges as a result of the use of antimicrobials, not antimicrobial itself which is the subject of risk management. Therefore, it is necessary to include the process of evaluating the relation between antimicrobial resistant microorganism or resistant determinant and the usage of antimicrobials in terms of the probability and extent of the occurrence of antimicrobial resistance. The guidance should be corresponding to the existing OIE guidelines, "Risk Assessment for Antimicrobial Resistance Arising from the Use of Antimicrobials in Animals", but its purpose should focus exclusively on protecting the health of the consumers.

Regarding risk management options, if the use of a specific antimicrobial agent is prohibited or restricted, the occurrence of disease may increase or the use of other antimicrobial agents may increase. Therefore, the guidance for risk assessment should take into account such secondary risk.

We consider that the Task Force should also develop general guidance for risk management of antimicrobial resistance, which can be applied to various conditions of member countries, e.g. different usages of antimicrobials, different occurrences of antimicrobial resistance and different occurrences of food-borne diseases. The guidance should be developed on the basis of risk management practices in member countries.

Japan established the "Guidelines for Risk Assessment on Human Health Consequences Resulting from Non-Human Usage of Antimicrobial Agents" in 2004, in line with the OIE guidelines. We are currently assessing the risk of antimicrobial resistance of specific agents according to the Guidelines. We are pleased to provide our experience of its application for the discussion of the Task Force.

## **MEXICO**

Mexico appreciates the opportunity to make comments on document CL 2006/38-AMR "Request for proposals for new work for the Codex *ad hoc* Intergovernmental Task Force on Antimicrobial Resistance" being considered at the 1<sup>st</sup> Session of the Codex *ad hoc* Intergovernmental Task Force on Antimicrobial Resistance).

In this regard, Mexico has defined the following position on the above mentioned document:

“In order to obtain information on the substances which are currently used in different countries, it is advisable to refer to the list of substances which are used as antimicrobials in animal and plant health, including the use levels in each country.

It is appropriate to obtain information on antimicrobials to which resistance has been shown or developed.

The promotion of good practice in the use of antimicrobials is an important activity and, for this reason, it is suggested to develop a document which specifies the good use of these substances.”

## **REPUBLIC OF KOREA**

Republic of Korea appreciates the opportunity to address the Codex Alimentarius Commission’s request for comments and proposals for new work to be undertaken by Codex *Ad Hoc* Intergovernmental Task Force on Antimicrobial Resistance.

Korea supports the document CAC29/LIM18, the result of in-session working group meeting in 29<sup>th</sup> CAC. These proposed projects are described to encompass the CAC29/LIM18 scope and activities in Annex 2, as well as to build upon the recommendations of the prior FAO/WHO/OIE Joint Consultations.

The proposals contain two main purposes,

- 1) Develop guidance on a risk assessment methodology to reduce risks by use of antimicrobials
- 2) Develop risk management options for the prudent use of antimicrobials and the containment of antimicrobial resistance

### 1. The purposes and the scope of the Task Force

- Codex *Ad Hoc* Intergovernmental Task Force on Antimicrobial Resistance (Codex Task Force) is organized to be consolidated for establishing guidance and policy on the use of antimicrobial agents and its resistance, which previously have been managed under other Codex Committee and other international organizations such as FAO, WHO, and OIE.
- Task Force’s objectives include analysis of the non-human antimicrobial usages in animal farming including aquaculture and its impact on microbial resistance, as well as assessment of risk factors to human health in relation to such outcome. In doing so, the Task Force intends to ultimately provide guidelines and policies for proper usage and control of antimicrobial agents by preemptively reducing bacterial resistance to antimicrobial agents.
- In order to achieve such outcome, Task Force needs to review and examine the ongoing and previous risk analysis and risk management documents by other previously responsible parties including FAO, WHO, OIE, Codex, and establish Task Force’s guidelines according to its mission.
- These guidelines should be based on solid scientific data and its analysis. Establishing guidelines should take into consideration at the level of regional, national, and international levels. Furthermore, these guidelines should be practical enough that all the Codex member countries including developing countries should be able to easily adopt and adapt to these guidelines.

### 2. Its relevance and timeline

- In controlling resistance to antimicrobials, particular action and management by specific country or region may be helpful. However more importantly, proper management and control should be taken place at the multi-factorial and multi-disciplinary level by an international controlling committee such as Task Force. Multiple and broadly encompassing countries should gather to a common ground to cooperatively search for solution as a unity against antimicrobial resistance problem at the level of food safety as well.

- As the risk factors associated with antimicrobial resistance become more significant, FAO/WHO/OIE played central role in establishing risk analysis and risk management on antimicrobial resistance since 2003. This work would be in line with recommendation of the 1<sup>st</sup> (Geneva, 2003) and 2<sup>nd</sup> (Oslo, 2004) meetings. In recognition, joint FAO/WHO/OIE workshop recommended that Task Force in Codex should be organized and this Task Force should develop science based guidance for the risk assessment and risk management options on antimicrobial resistance.
- In majority of countries, the rate of resistance to antimicrobial agents has already reached to a staggering level. At this critical juncture, Codex guidelines are much needed to prevent further over usage and misuse of antimicrobial agents, to reduce resistance to antimicrobials by prudent use of antimicrobials, to produce and provide much safer foods, and to provide safe human health by prevention of infection by such resistance acquired pathogens.
- Antimicrobial resistance related to non-human use of antimicrobials is a food safety issue, and Codex should be involved in relevant risk analysis activities in relation to non-human use of antimicrobials.

### 3. The main aspects to be covered

- In Geneva workshop (2003), it was concluded that a Codex Task Force should be established to develop risk management options for antimicrobial resistance related to non-human use of antimicrobials. Risk communication and transparency are critical to the achievement of effective risk management. Furthermore, International Code of Practice and General Principles of Food Hygiene of Codex and OIE should be reviewed to consider antimicrobial resistance in Codex Task Force.
- In Seoul workshop (2006), it was recommended that the Task Force on Antimicrobial Resistance with respect to the Food Safety should work in close collaboration with OIE to develop risk analysis principles and risk assessment guidelines. Within this process a full risk assessments should be developed in the priority areas.
- According to CAC 29/LIM 18 and other related documents and guidance, the main work of Task Force can be summarized into two major projects ; develop risk assessment methodology and process, develop specific risk management advice.

#### **Project 1:**

##### **Develop Guidance on a Risk Assessment Methodology to Reduce Risks by Use of Antimicrobials**

- For the risk assessment, priority list has to be determined on the type of antimicrobials and antimicrobial resistant bacteria. Priority is given to antimicrobials important to human and animal health and therefore, it should follow the Critically Important Antimicrobials list determined by FAO, WHO, and OIE.
- In relation to the antimicrobial resistance in food borne pathogens, risk profile has to be established on the antimicrobials used in food and livestock feeds.

The following areas should be considered for establishing risk profile: each country's animal and aquatic livestock production amount, the type of antibiotics and its volume, rate of antimicrobial resistance, distribution and incidence of antimicrobial resistant food borne pathogens in foods, rate of food poisoning outbreaks and infectivity, and possibility of resistance gene transfer.

- Information and data on antimicrobial resistant food borne pathogens and usage of antimicrobials need to be identified in junction to food production.

In order to achieve this, surveillance program on antimicrobial resistance need to be reviewed on an on-going basis and materials related to risk assessment need to be collected and analyzed. A system needs to be installed so that such data can be shared by all Codex member countries. Task Force shall establish a system utilizing such database so that all Codex member countries can have access to it.



- Standardize risk assessment methodology by consideration of related documents, such as Codex's Principles and Guidelines for the Conduct of Microbial Risk Assessment (CAC/GL-30, 1999) and OIE's Risk Assessment for Antimicrobial Resistance Arising from the Use of Antimicrobials in Animals (OIE Terrestrial Animal Health Code, 2006)

### **Project 2:**

#### **Develop Risk Management Options for the Prudent Use of Antimicrobials and the Containment of Antimicrobial Resistance**

- Develop specific risk management advice based on the identified priorities, the risk profiles, the results of risk assessment as well as existing and ongoing document/guidelines from FAO, WHO and OIE related to the containment of antimicrobial resistance in animals for food, Codex Code of Practice and Code of Hygienic Practice (especially those from CCRVDF and CCFH) and ongoing work from FAO, WHO and OIE on critically important antimicrobials.
- Use of antibiotics and antimicrobial resistance analysis and management on aquatic farming has been already established in 2006 at Seoul Workshop, and thus Codex Task Force shall review these.
- Harmonization and implementation of methods for monitoring the prevalence of resistant bacteria in foods.
- Risk management shall be considered at the international, intra-national, and each regional level, and shall be constructed so that each member country can utilize it.

#### 4. An assessment against the Criteria for the establishment of work priorities.

##### **General Criteria**

*Consumer protection from the point of health, food safety, ensuring fair trade practices in the food trade and taking into account the identified needs of developing countries:*

- Through establishing Codex guidelines, prudent use of antimicrobials can be developed, which ultimately leads to reduction of the antimicrobial resistance, decreased infection of human and animals by multi-antimicrobial resistant pathogens, and improvement of safety in industrial animal farming and aquaculture.
- Codex guidelines should be utilized by trade of food-producing animals and fisheries and should promote installment and practice of proper management of antimicrobials by each and every country.
- For this to occur, Codex Task Force and other related international organizations should cooperate not only to actively promote management systems in developed countries, but also assist those underdeveloped and developing countries to adopt management system that are appropriate to that country's condition and status.
- Through these international and systematic collaborations, developed countries should serve as benchmarking countries and provide exemplary cases to those nations that do not yet have active antimicrobial management system. In addition, every nation should be able to utilize documents, data, and other materials available at Codex, FAO, WHO and OIE for the establishment of their own proper strategies.

##### **Criteria applicable to general subjects**

*a. Diversification of national legislations and apparent resultant or potential impediments to international trade:*

- Management of antimicrobial resistance should be carried out at the level of national, regional and international policy and management. Each nation, according to their status and condition, should develop and adopt antimicrobial resistance management system. These systems may include investigation of antimicrobial agent usage, monitoring program for antimicrobial resistant microbial organisms, and establishment of management system according to Good Animal Practice and HACCP regulations.

- At the international level, Task Force, FAO, WHO, OIE, and other organizations should serve as a central embodiment in establishing guidelines that will reduce the spread and induction of antimicrobial resistant organisms by proper and prudent use of antimicrobials. By doing so, it should also provide such guidelines and related information to member countries. In order to prevent potential dispute in international trade that may arise from the antimicrobial resistance, Codex guidelines have to be established and all member countries should be willing to adhere to the guidelines.

*b. Scope of work and establishment of priorities among various sections of work:*

- Scope of work related to this has been considered high priority by Codex among its given tasks.

*c. Work already undertaken by other organizations in this field and/or suggested by the relevant international intergovernmental body:*

- Task Force's new work is related to the work carried out by other organizations such as FAO, WHO, OIE, and CCFH, CCRVDF, JEMRA.

5. Relevance to the Codex strategic objectives

- The mission of Codex is to keep human health by providing safe foods to the world and establishing guidelines and promoting such guidelines for the food safety. In addition, the newly developed guidelines will be useful for amicable resolution of any possible international food trade dispute and to promote the application of scientific principles and risk analysis.

6. Information on the relation between the proposal and other existing Codex documents

- Good practice manuals and guidelines were discussed by other Codex Committees such as CCRVDF and CCFH. Guidelines developed at Codex committees need to be thoroughly discussed at Task Force.

7. Identification of any requirement for and availability of expert scientific advice

- Expert scientific advice should provide materials based on sound scientific basis in order to establish strategies for reduction of antimicrobial resistance risks. These strategies include guidance on prudent use of antimicrobials, consolidation of data analysis method and data collection, method for antimicrobial sensitivity test, use of antimicrobials on animal farming, risk analysis and others.
- The 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> FAO/OIE/WHO Expert Workshop on non-human antimicrobial usage and antimicrobial resistance (Geneva, 1-5 December 2003 / Oslo, 15-18 March 2004 / Seoul, 13-16 June 2006 ) took place and the outcome should be reviewed in the preparation of this new document.

8. Identification of any need for technical input to the Task Force from external bodies for proper planning

- Knowledge and experience of medical doctors and veterinarians are needed to establish Critically Important Antimicrobials and prioritization of antimicrobials used in medical and livestock/aquaculture field.
- To undertake risk analysis of antimicrobial resistance, information from each country is needed on the area of antimicrobial resistant bacterial incidence, antimicrobial agent usage and amount, scientific documents on relationship of antimicrobial gene transfer between agricultural usage and medical human usage. For these data collection and analysis, multi-disciplinary participation is necessary from various expertise from microbiologists, statisticians, veterinarians, medical doctors, food scientists, and others.

9. The proposed time-line for completion of the new work, including the start date, the proposed date for Step 5 and the proposed date for adoption by the Commission; the time frame for developing guideline should not normally exceed five years

- It is expected that the Task Force work can be completed within the four years timeframe.

## THE UNITED STATES OF AMERICA

The United States appreciates the opportunity to respond to the Codex Alimentarius Commission's request for proposals for new work to be undertaken by the Codex ad Hoc Intergovernmental Task Force on Antimicrobial Resistance.

### < Executive Summary >

The attached Project Documents (Appendix) outline the projects necessary to advance the work of the Codex Ad-Hoc Intergovernmental Task Force on Antimicrobial Resistance ("the Task Force") as specified in the August 2006 Circular Letter (CL2006/38-AMR)

([ftp://ftp.fao.org/codex/Circular\\_Letters/CXCL2006/cl06\\_38e.pdf](ftp://ftp.fao.org/codex/Circular_Letters/CXCL2006/cl06_38e.pdf)) issued by the Codex Alimentarius commission (CAC).

Three proposed projects were developed to encompass the scope and activities as described in the Report of the In-Session Working Group to Analyze Comments Received and to Prepare Proposals for the Title, Objectives, Terms of Reference and Time Frame for the Proposed Task Force (CAC29/LIM18), as well as to build upon the recommendations of the prior two Joint Food and Agriculture Organization (FAO)/Office of International Epizootics (OIE)/ World Health Organization (WHO) Expert Workshops on Non-Human Antimicrobial Usage and Antimicrobial Resistance in 2003 and 2004 ([http://whqlibdoc.who.int/hq/2004/WHO\\_CDS\\_CPE\\_ZFK\\_2004.7.pdf](http://whqlibdoc.who.int/hq/2004/WHO_CDS_CPE_ZFK_2004.7.pdf) and

[http://www.who.int/foodsafety/publications/micro/en/oslo\\_report.pdf](http://www.who.int/foodsafety/publications/micro/en/oslo_report.pdf)).

The purpose of this work is to provide Codex guidance on risk analysis<sup>3</sup> for addressing human health concerns<sup>4</sup> regarding antimicrobial resistant microorganisms and antimicrobial resistance genes (determinants) in foods and animal feeds for use by the Joint FAO/WHO Meetings on Microbiological Risk Assessment (JEMRA) or by national/regional authorities to direct their activities related to food safety, including food and feed safety regulators as well as veterinary drug licensing authorities.

With this purpose in mind, we propose that the Task Force undertake the following projects as described in detail in the attached Appendix:

- 1) **Develop appropriate criteria, procedures, and other standards for identifying microbiological food safety issues and establishing risk profiles in order for the Task Force to set food safety priorities for possible commissioning of antimicrobial resistance risk assessments.**
- 2) **Develop science-based risk assessment guidance regarding food-borne antimicrobial resistant microorganisms, using established Codex risk assessment principles and the relevant work and standards of other national, regional, and international organizations, such as FAO, WHO, and OIE.**
- 3) **Provide specific risk management and, as appropriate, risk communication advice for national/ regional level action to minimize and contain antimicrobial resistant microorganisms such as those associated with the use of antimicrobials in food and feed production and processing (including aquaculture) based on the outcome of risk assessments undertaken according to the defined methodology developed in Project #2 above.**

<sup>3</sup> Risk analysis is a process consisting of three components: risk assessment, risk management, and risk communication. [Procedural Manual, Fifteen Edition, Joint FAO/WHO Food Standards Programme, Codex Alimentarius Commission]. Risk communication by the risk assessor and/or the risk manager to the public often is dependent on the regulatory infrastructure, the available resources, and the specific procedures of national/regional authorities; therefore, while the Codex definition of "risk communication" is quite broad, the Task Force should restrict its work on risk communication to formulating recommendations for appropriate communications between the risk assessor and the risk manager.

<sup>4</sup> In this document the term "human health concerns" specifically refers to the risks to human health associated with the presence in food and feed, and the transmission through food and feed, of antimicrobial resistant microorganisms and antimicrobial resistance genes [from CL2006/38-AMR]. [We note that a further more detailed description of this term, and thus of the specific scope of the Task Force work, may be desirable and should be considered.]

Development of these projects will result in guidance and work on setting priorities for work and data needs, a risk assessment process for implementation by JEMRA and/or by national/regional authorities, a range of risk management options that can be adopted at national/regional levels to minimize risk based on national/regional human health priorities<sup>5</sup>, and risk communication guidance, especially to enhance essential communication between risk assessors and risk managers. Together, the net result of the three projects will be a Codex antimicrobial resistance risk analysis approach that allows countries or regions to implement actions based upon identified and prioritized needs and resources.

The Task Force will first develop criteria for identifying food safety issues and establishing preliminary risk profiles for antimicrobial resistant microbiological food safety risks and for setting priorities for subsequent elaboration of complete antimicrobial risk profiles. When considering the risk related to a specific antimicrobial resistance concern, the Task Force will take into consideration both positive and negative aspects to human food safety of that risk. Criteria will also be based upon existing WHO and OIE information about critically important antimicrobials used in human and veterinary medicine as relevant to human health concerns together with other relevant data relating to antimicrobial resistant microorganisms in feed, food animals (including aquaculture species), food production/processing, and retail foods. The development of these criteria should also rely on national resistance monitoring program data, published sources and other data recognized as valid. Also, the Task Force should identify important data that may need to be collected and analyzed as well as other documents/guidelines from FAO, WHO, OIE, and Codex related to antimicrobial resistance. Other relevant activities undertaken in this area at international, regional and national levels should also be considered. For example, the CCFH Proposed Principles and Guidelines for the Conduct of Microbiological Risk Management (CX/FH 03/7) and the 2006 Consultation Report from Kiel, Germany provide a model for the development of an appropriate decision tree/flow chart.

## **PROJECT DOCUMENT # 1**

### **DEVELOP APPROPRIATE CRITERIA, PROCEDURES, AND OTHER STANDARDS FOR IDENTIFYING MICROBIOLOGICAL FOOD SAFETY ISSUES AND ESTABLISHING RISK PROFILES IN ORDER FOR THE TASK FORCE TO SET FOOD SAFETY PRIORITIES FOR POSSIBLE COMMISSIONING OF ANTIMICROBIAL RESISTANCE RISK ASSESSMENTS.**

#### **1. Purpose and scope of the proposed work**

The purpose of this project is to specify criteria to identify food safety issues, acquire data to develop risk profiles<sup>6</sup>, and then set food safety priorities concerning antimicrobial resistance risks so that JEMRA and/or national/regional authorities can undertake possible full risk assessments in the future.

The development of these priority-setting criteria will take full account of the prior work on risk analysis principles and standards of Codex and other relevant international organizations, such as FAO, WHO and OIE, as well as of national/regional authorities. The intent of this guidance is to set priorities that will enable JEMRA and/or national/regional authorities to assess the potential risks to human health associated with the presence in food and feed (including aquaculture), and the transmission through food and feed, of antimicrobial resistant microorganisms. Other relevant completed or on-going work undertaken in similar areas directed at assessing preliminary data and setting priorities at national, regional and international levels should also be taken into account, keeping in mind that the focus of the proposed work should be the food safety assessment, built on Codex and OIE foundational documents.

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<sup>5</sup> National and/or regional human health priorities should reflect the Appropriate Level of Protection (ALOP) as described in the World Trade Organization's Agreement on the Application of Sanitary and Phytosanitary Measures: "The level of protection deemed appropriate by the Member [State] establishing a sanitary or phytosanitary measure to protect human, animal, or plant life or health within its territory."

<sup>6</sup> Risk profiles (the description of the food safety problem and its context) may be developed to identify a possible causal pathway from feed (where applicable) to food animal to food to potential failure of treatment and other human health consequences. It is anticipated that the Risk Profiles would be "customized" by regional or national food safety authorities, taking into consideration data relevant to particular use experience. Risk profiles are usually followed by risk assessments to prioritize the Risk Management options for implementation appropriate for their area. As examples, several Risk Profiles on food borne bacteria have been completed [http://www.foodrisk.org/risk\\_profiles.cfm](http://www.foodrisk.org/risk_profiles.cfm).

## **2. Relevance and timeliness**

The 2001 WHO Global Strategy for Containment of Antimicrobial Resistance ([http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_2\\_EN/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_2_EN/en/)) recognizes that antimicrobial resistance is a serious human health problem and that “improving antimicrobial use must be a key action in efforts to contain resistance.” In order to address that portion of resistance in human pathogens attributable to antimicrobial resistant food-borne bacteria, additional consultations were convened. Antimicrobial resistance has been discussed at two prior joint consultations of WHO/OIE/FAO (cited above) and the 29<sup>th</sup> CAC Session (July, 2006) recommended that the formation of the Task Force and the development of Project Documents are relevant next steps to be taken in a timely manner. Initial discussion of antimicrobial resistance within Codex is contained in CX/RVDF 01/10 July 2001. One key point from the consultations is that certain antimicrobial resistant food-borne bacteria were identified as being possible microbiological food safety hazards.

Development of this project should result in setting priorities for possible future risk assessments.

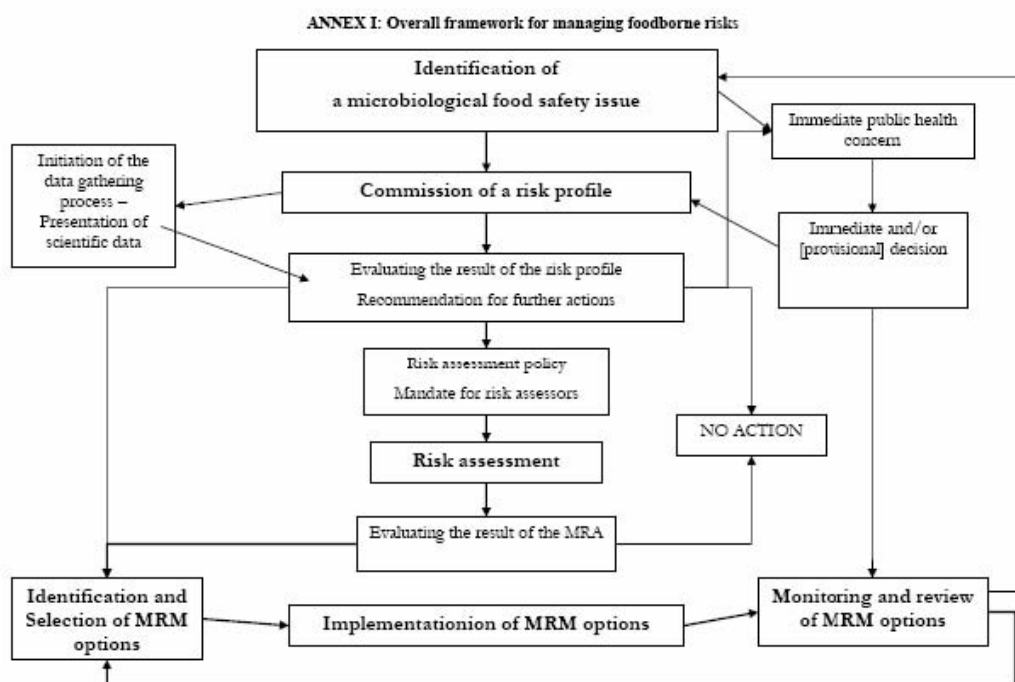
## **3. Main aspects to be covered**

This Project Document Proposal, while it can be implemented independently, is meant to be developed with an understanding of the risk assessment criteria and standards that will be elaborated as part of Project Document #2. Setting food safety priorities will be based on information that may be the same or similar information as would be needed for a complete risk assessment. Therefore, criteria to be used in setting priorities will build upon the risk assessment processes that have already been identified, particularly those that are in place within Codex and within OIE for risk assessment (see OIE Risk Analysis Terrestrial Animal Code guideline) ([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm)) which was begun by the work of the OIE Ad hoc Group of Experts on Antimicrobial Resistance in 2001 (<http://www.oie.int/eng/publicat/rt/2003/VOSE.PDF>). To facilitate the work of the Task Force, the OIE Risk Analysis document already contains an Appendix C that compares the Codex and OIE risk assessment processes.

This Project Document proposes that the Task Force will specify criteria necessary to identify food safety issues, develop risk profiles, and then set priorities which will be used by JEMRA and/or national/regional authorities for undertaking future full risk assessments. This prioritization is necessary because of the complex matrix of antimicrobials used in food animals, food-borne bacteria, foods derived from these food-producing animals, and human uses of antimicrobials as they may relate to the food-borne route of transmission of antimicrobial resistant microorganisms. Priorities will be set based on an evaluation of risk profiles as to which antimicrobials, food-borne bacteria and food animal species should be evaluated first, second, etc. and whether resources should be allocated to a more detailed scientific risk assessment. These food safety issue identifications and risk profiles will be based on appropriate data and information that is currently available. The Task Force will collect and describe relevant data that is available concerning antimicrobial resistant microorganisms in feed, food animals (including aquaculture species), food production/processing, and retail foods as well as identification of important data that may need to be collected and analyzed; relying on national resistance monitoring program data, published sources and other data recognized as valid. The Task Force will determine applicability of ongoing international and national bacterial resistance monitoring programs of food-borne bacterial pathogens to provide data for risk assessment at the food animal and carcass or retail food level. The WHO document on Antimicrobial Resistance Surveillance Standards and the OIE Terrestrial Code on Surveillance could be useful to this exercise. The WHO SalmSurv program may also provide some useful information. Antibiotic categorization or class lists can assist in the prioritization of which risk profiles to undertake first, second, etc., but this information alone should not be used as a substitute for the risk profile itself because antimicrobial resistant microorganisms should appropriately be associated with or attributed to a food product (which originated from a treated food animal).

This being said, it should be understood that food safety issue identifications and risk profiles and their use in the prioritization of food-borne antimicrobial resistance risks may require change or amendment based on new relevant information that may be forthcoming. It is anticipated that the procedures and criteria to develop these food safety issue identifications and risk profiles will take into consideration WHO information (see [http://www.who.int/foodborne\\_disease/resistance/FBD\\_CanberraAntibacterial\\_FEB2005.pdf](http://www.who.int/foodborne_disease/resistance/FBD_CanberraAntibacterial_FEB2005.pdf)) and OIE information that may be relevant to human health concerns (Report of the Meeting of the OIE Ad Hoc Group on Antimicrobial Resistance, Paris, 6-8 February 2006, work in progress) about critically important antimicrobials and current information available concerning the incidence of antimicrobial resistance in food-borne bacteria recovered from animals, food, and humans. It is also anticipated that scientific advice may be required to help set these priorities through requests by the Task Force to JEMRA or other relevant organizations such as appropriate WHO Collaborating Centers and national or regional antimicrobial resistance monitoring programs. As a result of this process, a specific risk profile may result in the decision to undertake a risk assessment.

The setting of appropriate priorities for the potential undertaking of future complete risk assessments is an element of risk management under both the U.S. National Academy of Sciences<sup>7</sup> and the Covello-Merkhofer<sup>8</sup> schemes for risk analysis. Therefore, for this Project Document Proposal the Task Force should consider the risk management recommendations made in the 2001 WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food ([http://whqlibdoc.who.int/hq/2001/WHO\\_CDS\\_CSR\\_DRS\\_2001.2a.pdf](http://whqlibdoc.who.int/hq/2001/WHO_CDS_CSR_DRS_2001.2a.pdf)). In addition, the Joint FAO/WHO expert meeting report on “The Use of Microbiological Risk Assessment Outputs to Develop Practical Risk Management Strategies: Metrics to Improve Food Safety” (Kiel, Germany, 3-7 April 2006) provides further clarification and guidance which the Task Force can employ as outlined below.



Source: Consultation Report from Kiel, Germany, 2006

<sup>7</sup> Hazard identification, dose response assessment, exposure assessment, and risk characterization are the components of risk assessment that have been endorsed and incorporated into the principles of risk assessment adopted by the U.S. Advisory Committee on Microbiological Criteria for Foods (1995).

<sup>8</sup> An alternative mode of risk assessment presented by Covello and Merkhofer (1994) regards hazard identification as an altogether separate process that is necessarily conducted prior to risk assessment.

With regard to priority-setting for future risk assessments, the Joint FAO/WHO Consultation in Kiel, Germany in 2002 <http://www.who.int/foodsafety/publications/micro/en/march2002.pdf> articulated the following:

“Preliminary risk management activities comprise the initial process. It includes the establishment of a risk profile to facilitate consideration of the issue within a particular context, and provides as much information as possible to guide further action. As a result of this process, the risk manager may commission a risk assessment as an independent scientific process to inform decision-making.”

Again, this Project Document Proposal seeks to build upon this FAO/WHO document and others for adaptation to the specific situation of antimicrobial resistance within the CAC29/LIM18 and CL2006/38-AMR scope, objectives, and terms of reference to maximize the productivity of the Task Force to deliver useful guidance.

The Task Force will determine applicability of ongoing international and national bacterial resistance monitoring programs to provide data for risk assessment at the food animal (zoonotic pathogens and commensal organisms) and retail food level. The WHO document on Antimicrobial Resistance Surveillance Standards and the OIE Terrestrial Code on Surveillance could be useful to this exercise. The WHO SalmSurv program may also provide some useful information.

Prior to the first meeting of the Task Force, a complete library of existing Codex and related organization documents/guidelines on antimicrobial resistance interventions, usage guidelines, and reports; and a review of guidelines for food processing that minimizes contamination should be established. This is consistent with No. 6 below. The following is a tentative list of these documents:

- **Resistance monitoring for food animals, food and feed**

[http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.1.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.1.htm)

[http://www.oie.int/eng/normes/mmanual/A\\_00021.htm](http://www.oie.int/eng/normes/mmanual/A_00021.htm)

[http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.2.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.2.htm)

- National regulatory authority risk assessment reviews

U.S. Food and Drug Administration

(<http://www.fda.gov/cvm/Documents/fguide152.pdf>)

Australian Pesticides and Veterinary Medicines Authority's Part 10, Special Data: Antibiotic Resistance ([http://www.apvma.gov.au/MORAG\\_vet/vol\\_3/part\\_10\\_antibiotic\\_resistance.html](http://www.apvma.gov.au/MORAG_vet/vol_3/part_10_antibiotic_resistance.html))

1) Canadian Veterinary Drugs Directorate Current Thinking on Risk Management Measures to Address Antimicrobial Resistance Associated with the Use of Antimicrobial Agents in Food-Producing Animals ([http://www.hc-sc.gc.ca/dhp-mpps/vet/antimicrob/amr-ram\\_rep-rap\\_06\\_05\\_e.html](http://www.hc-sc.gc.ca/dhp-mpps/vet/antimicrob/amr-ram_rep-rap_06_05_e.html))

International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Guidance on Pre-Approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals with Respect to Antimicrobial Resistance ([http://www.vichsec.org/pdf/01\\_2004/g127\\_st7f.pdf](http://www.vichsec.org/pdf/01_2004/g127_st7f.pdf))

Guidance on Pre-Approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals With Respect to Antimicrobial Resistance  
<http://www.emea.europa.eu/pdfs/vet/vich/064401en.pdf>

- **Responsible Use guidelines**

[http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.3.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.3.htm)

CCRVDF code for containing AMR

- **Feed control processes and guidelines**

Regulation (EC) No. 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed safety

([http://europa.eu.int/eurex/lex/LexUriServ/site/en/oj/2005/l\\_035/l\\_03520050208en00010022.pdf](http://europa.eu.int/eurex/lex/LexUriServ/site/en/oj/2005/l_035/l_03520050208en00010022.pdf))

U.S. FDA Animal Feed Safety System (<http://www.fda.gov/cvm/AFSS.htm>)

Codex Code of Practice for Good Animal Feeding ALINORM 04/27/38

([http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool\\_data/codex\\_0/en\\_cxc\\_054\\_2004e.pdf](http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool_data/codex_0/en_cxc_054_2004e.pdf))

- **Food processing controls, food safety objectives**

Recommended International Code of Practice General Principles of Food Hygiene, including Annex on HACCP and Guidelines for its application. CAC/RCP 1-1969, Rev. 4-2003  
([www.codexalimentarius.net/download/standards/23/cxp\\_001e.pdf](http://www.codexalimentarius.net/download/standards/23/cxp_001e.pdf))

#### **4. Assessment against the criteria for the establishment of work priorities**

*Consumer protection from the point of view of health, food safety, ensuring fair practices in the food trade and taking into account the identified needs of developing countries:* This Project Document Proposal would provide priorities for JEMRA and/or national/regional authorities for undertaking risk assessments concerning the safety of food containing antimicrobial resistant bacteria, thus assisting in establishing the overall safety of the food and appropriate level of protection for consumers. The project could particularly assist countries that have limited experience with food safety priority setting activities and risk assessments, particularly for evaluating antimicrobial resistant microorganisms.

*Diversification of national legislations and apparent resultant or potential impediments to international trade:* This Project Document Proposal would provide internationally-recognized scientific guidance that JEMRA, and/or national/regional authorities may use to carry out set priorities for undertaking risk assessments of food safety concerns related to the presence of antimicrobial resistant microorganisms. Such internationally-agreed guidance can help ensure consistent approaches for the food safety assessment for such foods.

*Scope of work and establishment of priorities between the various sections of the work:* The scope of the work relates to work previously undertaken by Codex on a high priority basis.

*Work already undertaken by other organizations in this field:* This Project Document Proposal is consistent with, complements, and builds upon work already undertaken by other international organizations such as WHO, OIE and FAO; and is an extension or adaptation of work developed in the CCFH, CCRVDF, and JEMRA that focuses on food-borne bacteria that are resistant to antimicrobials.

#### **5. Relevance to the Codex strategic objectives**

This proposal is consistent with the following strategic goals presented in the Codex Draft Strategic Plan 2008-2013:

- Promoting Sound Regulatory Frameworks; and,
- Promoting Widest and Consistent Application of Scientific Principles and Risk Analysis
- Promoting Cooperation between Codex and other Relevant International Organizations

#### **6. Information on the relation between the proposal and other existing Codex documents**

There are several existing Codex documents which are related and that must be considered in the development of the proposed guidance:

- Review of existing standards on Risk Analysis (OIE, WHO) including Microbial Risk Assessment
- Review of Good Practices manuals, including Codes of practice and codes of hygiene (especially those from the work of CCRVDF and CCFH)  
<http://www.fao.org/docrep/005/Y1579E/y1579e02.htm>  
<ftp://ftp.fao.org/docrep/fao/005/Y1579e/Y1579e.pdf>  
[www.codexalimentarius.net/download/standards/10213/CXP\\_061e.pdf](http://www.codexalimentarius.net/download/standards/10213/CXP_061e.pdf)
- Review of existing documents/guidelines on containment of antimicrobial resistance in animals for food. Those of the WHO website are listed, but there are many other national, regional, and international guidelines that are pertinent.  
[http://www.who.int/foodborne\\_disease/resistance/en/index.html](http://www.who.int/foodborne_disease/resistance/en/index.html)
- Additional Codex documents that may be of relevance are listed separately below.



## **7. Identification of any requirement for and availability of expert scientific advice**

It is anticipated that expert scientific advice will be needed to help identify and acquire data that will be useful to the completion of risk profiles. The Task Force and any other body (e.g., JEMRA) providing advice to the development of this Codex guidance must include a diversity of scientific disciplines including:

- Veterinarians representing expertise in major food animal species
- Risk Assessors/Modelers
- Experts experienced in pre-market scientific reviews of veterinary antimicrobial products with regard to human food safety
- Risk managers
- Food Industry processors, packers, quality assurance experts
- Production company personnel (e.g. quality assurance, live production veterinarian)
- Epidemiologists
- Microbiologists (with expertise in genetics of antimicrobial resistance, food technology and processing, antimicrobial susceptibility testing/clinical microbiology, and veterinary microbiology)

## **8. Identification of any need for technical input to the standard from external bodies so that this can be planned for**

The inclusion of technical input from the veterinary profession, representing the major food animal species, including aquaculture, will likely be necessary to ensure accuracy and implementation of proposed actions at the on-farm level. Additionally, input from food technologists, HACCP experts, and others in the microbial food safety arena will be needed to address current practices to minimize and contain antimicrobial resistant bacterial contamination of food products.

## **9. The proposed time-line for completion of the new work, including the start date, the proposed date for adoption at Step 5, and the proposed date for adoption by the Commission; the time frame for developing a standard should not normally exceed five years**

It is expected that the Task Force work can and should be completed within the proposed four meeting schedule.

### **Relevant Codex Alimentarius Documents List<sup>9</sup>:**

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2001 (CX/FH 01/12).  
[www.codexalimentarius.net/download/report/116/al03\\_13e.pdf](http://www.codexalimentarius.net/download/report/116/al03_13e.pdf)

Codex Committee on Food Hygiene. *Discussion paper on antimicrobial -resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 1999 ( CX/FH 99/12; [ftp://ftp.fao.org/codex/ccfh32/FH99\\_12e.pdf](ftp://ftp.fao.org/codex/ccfh32/FH99_12e.pdf) )

Codex Committee on Food Hygiene. Report of the Thirty-second Session, Washington, DC, 29 November–4 December 1999. Rome, Food and Agriculture Organization of the United Nations, 2001 (ALINORM 01/13; [ftp://ftp.fao.org/codex/alinorm01/AI01\\_13e.pdf](ftp://ftp.fao.org/codex/alinorm01/AI01_13e.pdf)).

Codex Committee on Residues of Veterinary Drugs in Foods. *Antimicrobial resistance and the use of antimicrobials in animal production*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/RVDF 00/4; [ftp://ftp.fao.org/codex/ccrvdf12/rv00\\_04e.pdf](ftp://ftp.fao.org/codex/ccrvdf12/rv00_04e.pdf) [ftp://ftp.fao.org/codex/alinorm01/AI01\\_31e.pdf](ftp://ftp.fao.org/codex/alinorm01/AI01_31e.pdf)

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/FH 00/11; [ftp://ftp.fao.org/codex/ccfh33/fh00\\_11e.pdf](ftp://ftp.fao.org/codex/ccfh33/fh00_11e.pdf)

<sup>9</sup> Not all documents listed were cited above.

Codex Committee on Residues of Veterinary Drugs in Foods. *Proposed Draft Code of Practice to Minimize and Contain Antimicrobial Resistance*. Rome, Food and Agriculture Organization of the United Nations, 2002 (CX/RVDF 03/6;

[ftp://ftp.fao.org/codex/ccrvdf14/rv03\\_06e.pdf](ftp://ftp.fao.org/codex/ccrvdf14/rv03_06e.pdf)

<ftp://ftp.fao.org/codex/alinorm03/A10331ae.pdf>

Codex Committee on Residues of Veterinary Drugs in Foods. *Discussion paper on antimicrobial resistance and the use of antimicrobials in animal production*. Rome, Food and Agriculture Organization of the United Nations, 2001 (CX/RVDF 01/10;

[ftp://ftp.fao.org/codex/ccrvdf13/rv01\\_10e.pdf](ftp://ftp.fao.org/codex/ccrvdf13/rv01_10e.pdf)

[ftp://ftp.fao.org/codex/alinorm03/al03\\_31e.pdf](ftp://ftp.fao.org/codex/alinorm03/al03_31e.pdf)

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/FH 00/11;

[ftp://ftp.fao.org/codex/ccfh33/fh00\\_11e.pdf](ftp://ftp.fao.org/codex/ccfh33/fh00_11e.pdf)

[ftp://ftp.fao.org/codex/alinorm03/al03\\_13e.pdf](ftp://ftp.fao.org/codex/alinorm03/al03_13e.pdf)

Recommended International Code of Practice General Principles of Food Hygiene, including Annex on HACCP and Guidelines for its application. CAC/RCP 1-1969, Rev. 4-2003

([www.codexalimentarius.net/download/standards/23/cxp\\_001e.pdf](http://www.codexalimentarius.net/download/standards/23/cxp_001e.pdf))

## OTHER DOCUMENTS

*Food Safety Risk Analysis: A Guide for National Governments*, FAO Food and Nutrition Paper 87, 2006

(<ftp://ftp.fao.org/docrep/fao/009/a0822e/a0822e00.pdf>)

*Risk Assessment for Antimicrobial Resistance Arising from the Use of Antimicrobials in Animals*, OIE Terrestrial Animal Health Code 2006, Part 3, Section 3.)

([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm))

*Guidelines for the Responsible and Prudent Use of Antimicrobial Agents in Veterinary Medicine*, OIE Terrestrial Animal Health Code 2006, Part 3, Section 3.9, Chapter

(3.9.3([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.3.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.3.htm)))

Joint FAO/WHO Consultation in Kiel, Germany in 2002

(<http://www.who.int/foodsafety/publications/micro/en/march2002.pdf>)

Joint FAO/WHO expert meeting report on “*The Use of Microbiological Risk Assessment Outputs to Develop Practical Risk Management Strategies: Metrics to Improve Food Safety*” (Kiel, Germany, 3-7 April 2006)

(<ftp://ftp.fao.org/ag/agn/food/kiel.pdf>)

Joint FAO/OIE/WHO Expert Workshops on Non-Human Antimicrobial Usage and Antimicrobial Resistance in 2003 and 2004 ([http://whqlibdoc.who.int/hq/2004/WHO\\_CDS\\_CPE\\_ZFK\\_2004.7.pdf](http://whqlibdoc.who.int/hq/2004/WHO_CDS_CPE_ZFK_2004.7.pdf) and [http://www.who.int/foodsafety/publications/micro/en/oslo\\_report.pdf](http://www.who.int/foodsafety/publications/micro/en/oslo_report.pdf)).

2001 WHO Global Strategy for Containment of Antimicrobial Resistance ([http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_2\\_EN/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_2_EN/en/)).

Vose, D., J. Acar, F. Anthony, A. Franklin, R. Gupta, T. Nicholls, Y. Tamura, S. Thompson, E. J. Threlfall, M. Van Vuunen, D. G. White, H. C. Wegener & M. L. Costarrica. Antimicrobial resistance: risk analysis methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin. *Rev. sci. tech. Off. Int. Epiz.* 20(3):811-827. (<http://www.oie.int/eng/publicat/rt/2003/VOSE.PDF>).

U.S. Food and Drug Administration, 2003, Guidance to Industry. Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern (<http://www.fda.gov/cvm/Documents/fguide152.pdf>)

## PROJECT DOCUMENT # 2

### **DEVELOP SCIENCE-BASED RISK ASSESSMENT GUIDANCE REGARDING FOOD-BORNE ANTIMICROBIAL RESISTANT MICROORGANISMS, USING ESTABLISHED CODEX RISK ASSESSMENT PRINCIPLES AND THE RELEVANT WORK AND STANDARDS OF OTHER NATIONAL, REGIONAL, AND INTERNATIONAL ORGANIZATIONS, SUCH AS FAO, WHO, AND OIE.**

#### **1. Purpose and scope of the proposed work**

The purpose of the proposed work is to develop rational, science-based guidance, taking full account of the prior work on risk assessment principles and standards of Codex and other relevant international organizations, such as FAO, WHO and OIE, as well as of national/regional authorities. The intent of this guidance is to enable JEMRA and/or national/regional authorities to assess the potential overall risk to human health concerns<sup>2</sup> associated with the presence in food and feed (including aquaculture), and the transmission through food and feed, of antimicrobial resistant microorganisms.

To provide this guidance, the proposed work would identify the risk assessment components that are deemed essential to food/feed safety assessments that have been developed by Codex, WHO, FAO, OIE, and/or national/regional authorities and would adapt them to the specific circumstance of antimicrobial use and antimicrobial resistant food-borne microorganisms. For example, the Principles and Guidelines for the Conduct of Microbiological Risk Assessment (CAC-GL 30-1999) (<http://www.who.int/foodsafety/publications/micro/cac1999/en/>) provides a Microbiological Risk Assessment (MRA) process representing a structured method that has been developed to be applied to microbiological or other biological hazards. Although the MRA process and its implementation continue to be refined and modified, MRA guidelines and methods still can serve as useful templates for the work of the Task Force. The proposed work should also take into account existing work of OIE on the risk assessment for antimicrobial resistance (Risk Assessment for Antimicrobial Resistance Arising from the Use of Antimicrobials in Animals, OIE Terrestrial Animal Health Code 2006, Part 3, and Section 3.) ([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm)) and the work of the OIE Ad hoc Group of Experts on Antimicrobial Resistance in 2001 (<http://www.oie.int/eng/publicat/rt/2003/VOSE.PDF>).

Other relevant completed or on-going work undertaken in similar areas at national, regional and international levels should also be taken into account, keeping in mind that the focus of the proposed work should be the food safety risk assessment, built on Codex and OIE foundational documents.

National authorities will need to have certain necessary information available to be able to use the proposed Codex risk assessment guidance or to enable JEMRA to do so on their behalf. In specifying the needed information within a risk profile outline, the proposed guidance should indicate the data and resources needed. Consideration might be given to assisting developing nations in the establishment of infrastructure and/or appropriate national capacities needed to implement the Codex risk assessment guidelines. The Codex guidance developed by the Task Force may provide a framework for developing countries to respond to antimicrobial resistance risk when they lack the capacity to carry out risk assessments.

## **2. Relevance and timeliness**

The 2001 WHO Global Strategy for Containment of Antimicrobial Resistance ([http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_2\\_EN/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_2_EN/en/)) recognizes that antimicrobial resistance is a serious human health problem and that “improving antimicrobial use must be a key action in efforts to contain resistance.” In order to address that portion of antimicrobial resistance in human pathogens attributable to antimicrobial resistant food-borne bacteria, additional consultations were convened. Antimicrobial resistance has been discussed at two prior joint consultations of WHO/OIE/FAO (cited above) and the 29<sup>th</sup> CAC Session (July, 2006) recommended that the formation of the Task Force and the development of a Project Document are relevant next steps to be taken in a timely manner. Initial discussion of antimicrobial resistance within Codex is contained in CX/RVDF 01/10 July 2001. One key point from the consultations is that certain antimicrobial resistant food-borne bacteria were identified as being a possible microbiological food safety hazard. As such, Codex work on microbiological risk assessment and risk management for food-borne microorganisms are relevant because the presence of resistance gene reservoirs, gene acquisition, amplification, transmission and spread to susceptible hosts require propagation of resistance determinants within microbial hosts (i.e. resistance determinants themselves are not self-replicating). In addition, Codex and other work on risk analysis principles as applied to veterinary drugs used in food-producing animals are relevant because these drugs can select for resistant microbes in animals, which can be the source of antimicrobial resistant bacteria on food and/or in human patients with relevant illness. Therefore, the application of the relevant existing and developing Codex and other documents and guidelines on risk assessment and risk management should be used and modified or extended where necessary to encompass risk analysis of the human health concerns associated with antimicrobial resistant food-borne bacteria.

## **3. Main aspects to be covered**

The Codex Principles of Risk Analysis are well established for application to food-borne microbiological risks. The existing Codex risk analysis process may apply to the overall evaluation framework of microbiological risk assessment and risk management and may be adapted for application to risks from food-borne microorganisms containing antimicrobial resistance determinants and may be found in food animals, including aquaculture species, or their feed (see CAC/GL30 –Principles and Guidelines for the Conduct of Microbiological Risk Assessment) ([http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool\\_data/codex\\_0/en\\_cxg\\_030e.pdf](http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool_data/codex_0/en_cxg_030e.pdf)).

This Project Document Proposal will build upon the risk analysis processes already in place within Codex and within OIE for risk assessment and risk management with regard to human health concerns by adapting them to include antimicrobial resistance aspects similar to the OIE Risk Analysis Terrestrial Animal Code guideline ([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm)) which was begun by the work of the OIE Ad hoc Group of Experts on Antimicrobial Resistance in 2001 (<http://www.oie.int/eng/publicat/rt/2003/VOSE.PDF>). To facilitate the work of the Task Force, the OIE Risk Analysis document already contains an Appendix C that compares the Codex and OIE Risk Assessment processes. The development of risk assessment methodology and process must be appropriate for the range of individual animal/drug/bacterial species combinations identified by the priority-setting process described in Project Document #1 above.

The Task Force will develop an appropriate risk assessment set of criteria and a process for JEMRA and/or national authorities to use to determine the overall risk to human health concerns<sup>2</sup> of antimicrobial use in food animals. When considering the risk related to a specific antimicrobial resistance concern, the Task Force will take into consideration both positive and negative aspects to human food safety of that risk. Criteria will also be based upon existing WHO and OIE information about critically important antimicrobials used in human and veterinary medicine as relevant to human health concerns together with other relevant data relating to antimicrobial resistant microorganisms in feed, food animals (including aquaculture species), food production/processing, and retail foods. The development of these criteria should also rely on national resistance monitoring program data, published sources and other data recognized as valid.

This will be done by considering relevant information developed by other Codex groups, by other international organizations, such as FAO, WHO, and OIE and by other national or regional authorities such as the pre-market approval risk assessment process used by the U.S. Food and Drug Administration (<http://www.fda.gov/cvm/Documents/fguide152.pdf>), the Australian Pesticides and Veterinary Medicines Authority's Part 10, Special Data: Antibiotic Resistance ([http://www.apvma.gov.au/MORAG\\_vet/vol\\_3/part\\_10\\_antibiotic\\_resistance.html](http://www.apvma.gov.au/MORAG_vet/vol_3/part_10_antibiotic_resistance.html)), the Canadian Veterinary Drugs Directorate Current Thinking on Risk Management Measures to Address Antimicrobial Resistance Associated with the Use of Antimicrobial Agents in Food-Producing Animals ([http://www.hc-sc.gc.ca/dhp-mpps/vet/antimicrob/amr-ram\\_rep-rap\\_06\\_05\\_e.html](http://www.hc-sc.gc.ca/dhp-mpps/vet/antimicrob/amr-ram_rep-rap_06_05_e.html)), the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Guidance on Pre-Approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals with Respect to Antimicrobial Resistance ([http://www.vichsec.org/pdf/01\\_2004/gl27\\_st7f.pdf](http://www.vichsec.org/pdf/01_2004/gl27_st7f.pdf)), and the European Medicines Agency guidance (<http://www.emea.europa.eu/pdfs/vet/vich/064401en.pdf>).

The Task Force should outline a work plan to enable capacity-building in those countries or regions which may require assistance. Prior to the first meeting of the Task Force, a complete library of existing Codex and related organization documents/guidelines on antimicrobial resistance interventions, usage guidelines, and reports; and a review of guidelines for food processing that minimizes contamination should be established. This is consistent with No. 6 below. The following is a tentative list of these documents:

- **Resistance monitoring for food animals, food and feed**

[http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.1.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.1.htm)

[http://www.oie.int/eng/normes/mmanual/A\\_00021.htm](http://www.oie.int/eng/normes/mmanual/A_00021.htm)

[http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.2.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.2.htm)

- **National regulatory authority risk assessment reviews**

U.S. Food and Drug Administration (<http://www.fda.gov/cvm/Documents/fguide152.pdf>)

Australian Pesticides and Veterinary Medicines Authority's Part 10, Special Data: Antibiotic Resistance ([http://www.apvma.gov.au/MORAG\\_vet/vol\\_3/part\\_10\\_antibiotic\\_resistance.html](http://www.apvma.gov.au/MORAG_vet/vol_3/part_10_antibiotic_resistance.html))

i) Canadian Veterinary Drugs Directorate Current Thinking on Risk Management Measures to Address Antimicrobial Resistance Associated with the Use of Antimicrobial Agents in Food-Producing Animals ([http://www.hc-sc.gc.ca/dhp-mpps/vet/antimicrob/amr-ram\\_rep-rap\\_06\\_05\\_e.html](http://www.hc-sc.gc.ca/dhp-mpps/vet/antimicrob/amr-ram_rep-rap_06_05_e.html))

International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Guidance on Pre-Approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals with Respect to Antimicrobial Resistance ([http://www.vichsec.org/pdf/01\\_2004/gl27\\_st7f.pdf](http://www.vichsec.org/pdf/01_2004/gl27_st7f.pdf))

Guidance on Pre-Approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals With Respect to Antimicrobial Resistance <http://www.emea.europa.eu/pdfs/vet/vich/064401en.pdf>

- **Responsible Use guidelines**

[http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.3.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.3.htm)

CCRVDF code for containing AMR

- **Feed control processes and guidelines**

Regulation (EC) No. 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed safety ([http://europa.eu.int/eurex/lex/LexUriServ/site/en/oj/2005/l\\_035/l\\_03520050208en00010022.pdf](http://europa.eu.int/eurex/lex/LexUriServ/site/en/oj/2005/l_035/l_03520050208en00010022.pdf))

U.S. FDA Animal Feed Safety System (<http://www.fda.gov/cvm/AFSS.htm>)

Codex Code of Practice for Good Animal Feeding ALINORM 04/27/38 ([http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool\\_data/codex\\_0/en\\_cxc\\_0\\_54\\_2004e.pdf](http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool_data/codex_0/en_cxc_0_54_2004e.pdf))

- **Food processing controls, food safety objectives**

Recommended International Code of Practice General Principles of Food Hygiene, including Annex on HACCP and Guidelines for its application. CAC/RCP 1-1969, Rev. 4-2003 ([www.codexalimentarius.net/download/standards/23/cxp\\_001e.pdf](http://www.codexalimentarius.net/download/standards/23/cxp_001e.pdf))

#### **4. Assessment against the criteria for the establishment of work priorities**

*Consumer protection from the point of view of health, food safety, ensuring fair practices in the food trade and taking into account the identified needs of developing countries:* This Project Document Proposal would provide additional guidance for JEMRA and national/regional authorities to use in assessing the overall risk of food containing antimicrobial resistant bacteria, thus assisting in establishing the overall safety of the food and the subsequent risk management options and appropriate level of protection for consumers. The project could particularly assist countries that have limited experience with food safety risk assessments, particularly for evaluating antimicrobial resistant microorganisms.

*Diversification of national legislations and apparent resultant or potential impediments to international trade:* This Project Document Proposal would provide internationally-recognized scientific guidance that JEMRA and national/regional authorities may use to carry out risk assessment activities. Such internationally-agreed guidance can help ensure consistent approaches for the food safety assessment for such foods.

*Scope of work and establishment of priorities between the various sections of the work:* The scope of the work relates to work previously undertaken by Codex on a high priority basis.

*Work already undertaken by other organizations in this field:* This Project Document Proposal is consistent with, complements, and builds upon work already undertaken by other international organizations such as WHO, OIE and FAO; and is an extension or adaptation of work developed in the CCFH, CCRVDF, and JEMRA that focuses on food-borne bacteria that are resistant to antimicrobials.

#### **5. Relevance to the Codex strategic objectives**

This proposal is consistent with the following strategic goals presented in the Codex Draft Strategic Plan 2008-2013:

- Promoting Sound Regulatory Frameworks; and,
- Promoting Widest and Consistent Application of Scientific Principles and Risk Analysis
- Promoting Cooperation between Codex and other Relevant International Organizations

#### **6. Information on the relation between the proposal and other existing Codex documents**

There are several existing Codex documents which are related and that must be considered in the development of the proposed guidance:

- Review of existing standards on Risk Analysis (OIE, WHO) including Microbial Risk Assessment
- Review of Good Practices manuals, including Codes of practice and codes of hygiene (especially those from the work of CCRVDF and CCFH)  
<http://www.fao.org/docrep/005/Y1579E/y1579e02.htm>  
<ftp://ftp.fao.org/docrep/fao/005/Y1579e/Y1579e.pdf>  
[www.codexalimentarius.net/download/standards/10213/CXP\\_061e.pdf](http://www.codexalimentarius.net/download/standards/10213/CXP_061e.pdf)
- Review of existing documents/guidelines on containment of antimicrobial resistance in animals for food. Those of the WHO website are listed, but there are many other national, regional, and international guidelines that are pertinent.  
[http://www.who.int/foodborne\\_disease/resistance/en/index.html](http://www.who.int/foodborne_disease/resistance/en/index.html)
- Additional Codex documents that may be of relevance are listed separately below.

#### **7. Identification of any requirement for and availability of expert scientific advice**

It is anticipated that expert scientific advice will be needed to help identify data that will be useful to the identification of risk assessment considerations. The Task Force and any other body (e.g., JEMRA) providing advice to the development of this Codex guidance must include a diversity of scientific disciplines including:

- Veterinarians representing expertise in major food animal species
- Risk Assessors/Modelers

- Experts experienced in pre-market scientific reviews of veterinary antimicrobial products with regard to human food safety
- Risk managers
- Food Industry processors, packers, quality assurance experts
- Production company personnel (e.g. quality assurance, live production veterinarian)
- Epidemiologists
- Microbiologists (with expertise in genetics of antimicrobial resistance, food technology and processing, antimicrobial susceptibility testing/clinical microbiology, and veterinary microbiology)

**8. Identification of any need for technical input to the standard from external bodies so that this can be planned for**

The inclusion of technical input from the veterinary profession, representing the major food animal species, including aquaculture, will likely be necessary to ensure accuracy in identifying all risks related to on-farm activities. Additionally, input from food technologists, HACCP experts, and others in the microbial food safety arena will be needed to address risks associated with current food processing practices, including those to minimize and contain antimicrobial resistant bacterial contamination of food products.

**9. The proposed time-line for completion of the new work, including the start date, the proposed date for adoption at Step 5, and the proposed date for adoption by the Commission; the time frame for developing a standard should not normally exceed five years.**

It is expected that the Task Force work can and should be completed within the proposed four meeting schedule.

**Relevant Codex Alimentarius Documents List<sup>10</sup>:**

Codex Alimentarius Commission Guideline 30 – Principles and Guidelines for the Conduct of Microbiological Risk Assessment)

( [http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool\\_data/codex\\_0/en\\_cxg\\_030e.pdf](http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool_data/codex_0/en_cxg_030e.pdf)).

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2001 (CX/FH 01/12).  
[www.codexalimentarius.net/download/report/116/al03\\_13e.pdf](http://www.codexalimentarius.net/download/report/116/al03_13e.pdf)

Codex Committee on Food Hygiene. *Discussion paper on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 1999 ( CX/FH 99/12;  
[ftp://ftp.fao.org/codex/ccfh32/FH99\\_12e.pdf](ftp://ftp.fao.org/codex/ccfh32/FH99_12e.pdf) )

Codex Committee on Food Hygiene. *Report of the Thirty-second Session, Washington, DC, 29 November–4 December 1999*. Rome, Food and Agriculture Organization of the United Nations, 2001 (ALINORM 01/13;  
[ftp://ftp.fao.org/codex/alinorm01/Al01\\_13e.pdf](ftp://ftp.fao.org/codex/alinorm01/Al01_13e.pdf)).

Codex Committee on Residues of Veterinary Drugs in Foods. *Antimicrobial resistance and the use of antimicrobials in animal production*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/RVDF 00/4;  
[ftp://ftp.fao.org/codex/ccrvdf12/rv00\\_04e.pdf](ftp://ftp.fao.org/codex/ccrvdf12/rv00_04e.pdf)  
[ftp://ftp.fao.org/codex/alinorm01/Al01\\_31e.pdf](ftp://ftp.fao.org/codex/alinorm01/Al01_31e.pdf) )

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/FH 00/11;  
[ftp://ftp.fao.org/codex/ccfh33/fh00\\_11e.pdf](ftp://ftp.fao.org/codex/ccfh33/fh00_11e.pdf) )

Codex Committee on Residues of Veterinary Drugs in Foods. *Proposed Draft Code of Practice to Minimize and Contain Antimicrobial Resistance*. Rome, Food and Agriculture Organization of the United Nations, 2002 (CX/RVDF 03/6;  
[ftp://ftp.fao.org/codex/ccrvdf14/rv03\\_06e.pdf](ftp://ftp.fao.org/codex/ccrvdf14/rv03_06e.pdf)  
<ftp://ftp.fao.org/codex/alinorm03/Al0331ae.pdf> )

<sup>10</sup> Not all documents listed were cited above.

Codex Committee on Residues of Veterinary Drugs in Foods. *Discussion paper on antimicrobial resistance and the use of antimicrobials in animal production*. Rome, Food and Agriculture Organization of the United Nations, 2001 (CX/RVDF 01/10)

[ftp://ftp.fao.org/codex/ccrvdf13/rv01\\_10e.pdf](ftp://ftp.fao.org/codex/ccrvdf13/rv01_10e.pdf) ;

[ftp://ftp.fao.org/codex/alnorm03/al03\\_31e.pdf](ftp://ftp.fao.org/codex/alnorm03/al03_31e.pdf)

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/FH 00/11;

[ftp://ftp.fao.org/codex/ccfh33/fh00\\_11e.pdf](ftp://ftp.fao.org/codex/ccfh33/fh00_11e.pdf)

[ftp://ftp.fao.org/codex/alnorm03/al03\\_13e.pdf](ftp://ftp.fao.org/codex/alnorm03/al03_13e.pdf)

Recommended International Code of Practice General Principles of Food Hygiene, including Annex on HACCP and Guidelines for its application. CAC/RCP 1-1969, Rev. 4-2003

([www.codexalimentarius.net/download/standards/23/cxp\\_001e.pdf](http://www.codexalimentarius.net/download/standards/23/cxp_001e.pdf))

## **OTHER DOCUMENTS**

Food Safety Risk Analysis: A Guide for National Governments, FAO Food and Nutrition Paper 87, 2006

(<ftp://ftp.fao.org/docrep/fao/009/a0822e/a0822e00.pdf>)

Risk Assessment for Antimicrobial Resistance Arising from the Use of Antimicrobials in Animals, OIE Terrestrial Animal Health Code 2006, Part 3, Section 3.)

([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm))

Guidelines for the Responsible and Prudent Use of Antimicrobial Agents in Veterinary Medicine, OIE Terrestrial Animal Health Code 2006, Part 3, Section 3.9, Chapter 3.9.3

([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.3.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.3.htm))

Joint FAO/WHO Consultation in Kiel, Germany in 2002

(<http://www.who.int/foodsafety/publications/micro/en/march2002.pdf>)

Joint FAO/WHO expert meeting report on “The Use of Microbiological Risk Assessment Outputs to Develop Practical Risk Management Strategies: Metrics to Improve Food Safety” (Kiel, Germany, 3-7 April 2006)

(<ftp://ftp.fao.org/ag/agn/food/kiel.pdf>)

Joint FAO/OIE/WHO Expert Workshops on Non-Human Antimicrobial Usage and Antimicrobial Resistance in 2003 and 2004

([http://whqlibdoc.who.int/hq/2004/WHO\\_CDS\\_CPE\\_ZFK\\_2004.7.pdf](http://whqlibdoc.who.int/hq/2004/WHO_CDS_CPE_ZFK_2004.7.pdf) and

[http://www.who.int/foodsafety/publications/micro/en/oslo\\_report.pdf](http://www.who.int/foodsafety/publications/micro/en/oslo_report.pdf) ).

2001 WHO Global Strategy for Containment of Antimicrobial Resistance

([http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_2\\_EN/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_2_EN/en/)).

## **PROJECT DOCUMENT #3**

**PROVIDE SPECIFIC RISK MANAGEMENT AND, AS APPROPRIATE, RISK COMMUNICATION ADVICE FOR NATIONAL/REGIONAL LEVEL ACTION TO MINIMIZE AND CONTAIN ANTIMICROBIAL RESISTANT MICROORGANISMS SUCH AS THOSE ASSOCIATED WITH THE USE OF ANTIMICROBIALS IN FOOD AND FEED PRODUCTION AND PROCESSING (INCLUDING AQUACULTURE) BASED ON THE OUTCOME OF RISK ASSESSMENTS UNDERTAKEN ACCORDING TO THE DEFINED METHODOLOGY DEVELOPED IN PROJECT #2 ABOVE.**

### **1. Purpose and scope of the proposed work**

The purpose of the proposed work is to develop appropriate risk management advice that may be necessary following risk assessments undertaken as described in Project Document #2 by JEMRA and/or national/regional authorities. The Task Force will also provide advice on elements and standards for communication that is necessary between the risk managers and the risk assessors. Measurement (i.e. monitoring) of the effectiveness of the selected risk management options should also be provided for to establish a baseline for monitoring for subsequent change.



The Task Force will develop appropriate risk management guidance and advice proportionate to the risk identified in the above risk assessment process, including the use of good agricultural practices, good veterinary practices, good manufacturing practices, and/or appropriate criteria and standards for pre-approval of substances used in food production that may affect the safety of food. The CCFH Proposed Principles and Guidelines for the Conduct of Microbiological Risk Management (CX/FH 03/7) could serve as a good resource. The Task Force should consider the risk management recommendations made in the 2001 WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food ([http://whqlibdoc.who.int/hq/2001/WHO\\_CDS\\_CSR\\_DRS\\_2001.2a.pdf](http://whqlibdoc.who.int/hq/2001/WHO_CDS_CSR_DRS_2001.2a.pdf)). In addition, the Joint FAO/WHO expert meeting report on “The Use of Microbiological Risk Assessment Outputs to Develop Practical Risk Management Strategies: Metrics to Improve Food Safety” (Kiel, Germany, 3-7 April 2006) provides further clarification and guidance which the Task Force can employ. The Joint FAO/WHO Consultation in Kiel, Germany in 2002 <http://www.who.int/foodsafety/publications/micro/en/march2002.pdf> articulated some components of a generic framework for managing food-borne risks:

“Evaluation of risk management options is the weighing of available options for managing a food safety issue in light of scientific information on risks and other factors, and may include reaching a decision on an appropriate level of consumer protection. Optimization of food control measures in terms of their efficiency, effectiveness, technological feasibility and practicality at selected points throughout the food chain is an important goal. A cost-benefit analysis could be performed at this stage.”

“Implementation of the risk management decision will usually involve regulatory food safety measures, which may include the use of HACCP. Flexibility in the choice of individual measures applied by industry is a desirable element, as long as the overall program can be objectively shown to achieve the stated goals. On-going verification of the application of food safety measures is essential.”

“Monitoring and review is the gathering and analyzing of data so as to give an overview of food safety and consumer health. Monitoring of contaminants in food and food-borne disease surveillance should identify new food safety problems as they emerge. Where there is evidence that required public health goals are not being achieved, redesign of food safety measures will be needed.”

The Task Force should consider a continuum of possible interventions along the entire food chain, each step of which can reduce risk by minimizing and containing antimicrobial resistant microorganisms, appropriate to the food animal species, bacteria, and other practical considerations. As noted above in the Kiel 2006 consultation, weighing of appropriate risk management options is required.

## **2. Relevance and timeliness**

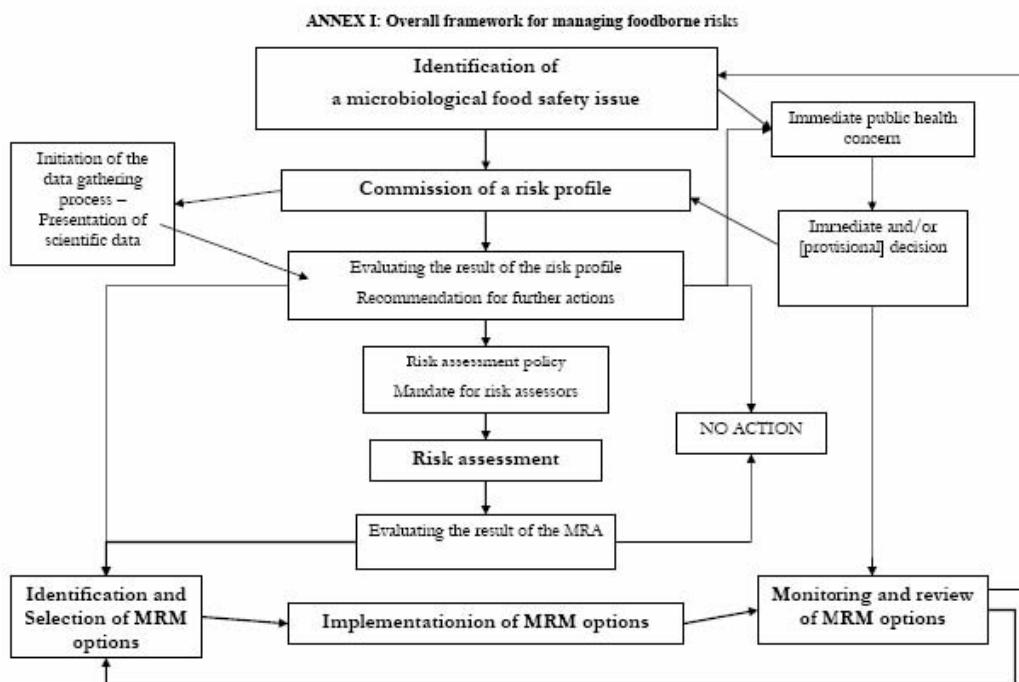
The 2001 WHO Global Strategy for Containment of Antimicrobial Resistance ([http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_2\\_EN/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_2_EN/en/)) recognizes that antimicrobial resistance is a serious human health problem and that “improving antimicrobial use must be a key action in efforts to contain resistance.” In order to address that portion of resistance in human pathogens attributable to antimicrobial resistant food-borne bacteria, additional consultations were convened. Antimicrobial resistance has been discussed at two prior joint consultations of WHO/OIE/FAO (cited above) and the 29<sup>th</sup> CAC Session (July, 2006) recommended that the formation of the Task Force and the development of a Project Document are relevant next steps to be taken in a timely manner. Initial discussion of antimicrobial resistance within Codex is contained in CX/RVDF 01/10 July 2001. One key point from the consultations is that certain antimicrobial resistant food-borne bacteria were identified as being possible microbiological food safety hazard agents. As such, Codex work on microbiological risk assessment and risk management for food-borne microbes are very relevant because the presence of resistance gene reservoirs, gene acquisition, amplification, transmission and spread to susceptible hosts requires propagation of resistance determinants within microbial hosts (i.e. resistance determinants themselves are not self-replicating). In addition, Codex and other work on risk analysis principles as applied to veterinary drugs used in food-producing animals are very relevant because these drugs can select for resistant microbes in animals which can be the source of resistant microbes on food and/or in human patients with relevant illness. Therefore, the application of the relevant existing and developing Codex and other documents and guidelines on risk assessment, risk management, and risk communication should be used and modified or extended where necessary to encompass risk analysis of the human health concerns associated with antimicrobial resistant food-borne bacteria.

**3. Main aspects to be covered**

This Project Document Proposal is linked to the risk assessment guidance developed in Project Document #2. Furthermore, clear guidance should be developed for risk communication standards and processes for communications between the risk assessor and the risk manager. Appropriate communication is essential to the proper integration of the components of risk analysis processes that will be followed and are already in place within Codex and within OIE with regard to human health concerns. These processes will be adapted by the Task Force to include antimicrobial resistance aspects similar to the OIE Risk Analysis Terrestrial Animal Code guideline ([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm)) which was begun by the work of the OIE Ad hoc Group of Experts on Antimicrobial Resistance in 2001 (<http://www.oie.int/eng/publicat/rt/2003/VOSE.PDF>). To facilitate the work of the Task Force, the OIE Risk Analysis document already contains an Appendix C that compares the Codex and OIE Risk Analysis processes.

The Task Force should consider a continuum of possible interventions along the entire food chain, each step of which can reduce risk by minimizing and containing antimicrobial resistant microorganisms, appropriate to the food animal species, bacteria, and other practical considerations as described above. As noted above in the Kiel 2006 consultation, weighing of appropriate risk management options is required.

Building on codes and guidelines already established for antimicrobial use and food hygiene, Project Document #3 will develop guidance that could enable national/regional authorities to set appropriate levels of protection (ALOP) as identified in the Joint FAO/WHO Consultation Report from Kiel (<ftp://ftp.fao.org/ag/agn/food/kiel.pdf>). See page 61 for flow process (diagram below). The establishment of specific levels of concern (or risk), as mentioned in the Second Joint Consultation at Oslo and LIM18, could be considered as corresponding to an ALOP on a national/regional basis. In the U.S., for example, the 2010 Public Health Goals include target rates for food-borne disease and there are plans for targets for specific antimicrobial resistant Salmonella.



Source: Consultation Report from Kiel, Germany, 2006

The Task Force will incorporate risk management recommendations made in many of the documents listed below.

Appropriate codes of practice for veterinary antimicrobial products should be implemented as much as practicable in each country or region as a primary step. Although codes of practice generally contain many recommendations, progress on practices to mitigate antimicrobial resistance could be expedited if necessary. The Codex Code of Practice for Good Animal Feeding would be appropriate to address issues related to concerns relative to feed. The Task Force should consider all relevant codes of practice. (Please refer to the list of Codes of Practice for WHO, OIE, and others below).

Embedded within these codes of practice are the responsibilities of regulatory licensing authorities to conduct microbiological food safety evaluations of veterinary antimicrobial products under both pre-market review procedures and standards and under post-market surveillance programs. The application of the OIE risk analysis of antimicrobial resistant bacteria can be used for specific regulatory risk assessments as part of the registration reviews performed by national licensing authorities as part of their risk management activities. Generally, recent risk assessments for licensing of antimicrobials for use in food-producing animals have utilized the OIE risk analysis framework ([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm)), and, therefore, the Task Force can first focus on these guidelines and could recommend their implementation on a broader scale at the national/regional level.

A system to monitor the effectiveness of risk management programs; e.g., antimicrobial resistance monitoring, food hygiene practices (i.e. HACCP), or other means should be identified by the Task Force. The practicality of sampling, analysis and timeliness also need to be taken into consideration ([http://whqlibdoc.who.int/hq/2002/WHO\\_CDS\\_CSR\\_DRS\\_2001.5.pdf](http://whqlibdoc.who.int/hq/2002/WHO_CDS_CSR_DRS_2001.5.pdf)).

An additional tool to measure risk management options and effectiveness could be a part of the risk assessment process to alter key inputs according to the anticipated effectiveness and determine what the outcome might be.

The Task Force may choose to provide a list of risk management options to national/regional authorities, as outlined in the Kiel consultation, matched to the prioritized list of risk profiles and risk assessments to be developed.

The Task Force may wish to outline a work plan to enable capacity-building in those countries or regions which may require assistance. Some suggestions to accommodate resource-constrained countries are described in the Kiel document referenced above.

Prior to the first meeting of the Task Force, a complete library of existing Codex and related organization documents/guidelines on antimicrobial resistance interventions, usage guidelines, and reports; and a review of guidelines for food processing that minimizes contamination should be established. This is consistent with No. 6 below. The following is a tentative list of these documents:

- **Resistance monitoring for food animals, food and feed**

- [http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.1.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.1.htm)

- [http://www.oie.int/eng/normes/mmanual/A\\_00021.htm](http://www.oie.int/eng/normes/mmanual/A_00021.htm)

- [http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.2.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.2.htm)

- **National regulatory authority risk assessment reviews**

- U.S. Food and Drug Administration

- (<http://www.fda.gov/cvm/Documents/fguide152.pdf>)

- Australian Pesticides and Veterinary Medicines Authority's Part 10, Special Data: Antibiotic Resistance

- ([http://www.apvma.gov.au/MORAG\\_vet/vol\\_3/part\\_10\\_antibiotic\\_resistance.html](http://www.apvma.gov.au/MORAG_vet/vol_3/part_10_antibiotic_resistance.html))

- 1) Canadian Veterinary Drugs Directorate Current Thinking on Risk Management Measures to Address Antimicrobial Resistance Associated with the Use of Antimicrobial Agents in Food-Producing Animals

- ([http://www.hc-sc.gc.ca/dhp-mps/vet/antimicrob/amr-ram\\_rep-rap\\_06\\_05\\_e.html](http://www.hc-sc.gc.ca/dhp-mps/vet/antimicrob/amr-ram_rep-rap_06_05_e.html))

- International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Guidance on Pre-Approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals with Respect to Antimicrobial Resistance

([http://www.vichsec.org/pdf/01\\_2004/g127\\_st7f.pdf](http://www.vichsec.org/pdf/01_2004/g127_st7f.pdf))

Guidance on Pre-Approval Information for Registration of New Veterinary Medicinal Products for Food Producing Animals With Respect to Antimicrobial Resistance  
<http://www.emea.europa.eu/pdfs/vet/vich/064401en.pdf>

- **Responsible Use guidelines**

[http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.3.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.3.htm)

CCRVDF code for containing AMR

- **Feed control processes and guidelines**

Regulation (EC) No. 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed safety

([http://europa.eu.int/eurex/lex/LexUriServ/site/en/oj/2005/l\\_035/l\\_03520050208en00010022.pdf](http://europa.eu.int/eurex/lex/LexUriServ/site/en/oj/2005/l_035/l_03520050208en00010022.pdf))

U.S. FDA Animal Feed Safety System (<http://www.fda.gov/cvm/AFSS.htm>)

Codex Code of Practice for Good Animal Feeding ALINORM 04/27/38

([http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool\\_data/codex\\_0/en\\_cxc\\_054\\_2004e.pdf](http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool_data/codex_0/en_cxc_054_2004e.pdf))

- **Food processing controls, food safety objectives**

Recommended International Code of Practice General Principles of Food Hygiene, including Annex on HACCP and Guidelines for its application. CAC/RCP 1-1969, Rev. 4-2003

([www.codexalimentarius.net/download/standards/23/cxp\\_001e.pdf](http://www.codexalimentarius.net/download/standards/23/cxp_001e.pdf))

#### **4. Assessment against the criteria for the establishment of work priorities**

*Consumer protection from the point of view of health, food safety, ensuring fair practices in the food trade and taking into account the identified needs of developing countries:* This Project Document Proposal would provide additional guidance for national/regional authorities to employ appropriate risk management actions to minimize and contain any antimicrobial resistant microorganisms in or on food of animal origin, thus assisting in establishing the overall safety of the food and appropriate protection of consumers. The project could particularly assist countries that have limited experience with food safety risk assessment and risk management decision-making, particularly with regard to antimicrobial resistant microorganisms.

*Diversification of national legislations and apparent resultant or potential impediments to international trade:* This Project Document Proposal would provide internationally-recognized scientific guidance that national/regional authorities may use to carry out risk management actions and risk communication activities. Such internationally-agreed guidance can help ensure consistent approaches for the food safety assessment for such foods.

*Scope of work and establishment of priorities between the various sections of the work:* The scope of the work relates to work previously undertaken by Codex on a high priority basis.

*Work already undertaken by other organizations in this field:* This Project Document Proposal is consistent with, complements, and builds upon work already undertaken by other international organizations such as WHO, OIE and FAO; and is an extension or adaptation of work developed in the CCFH, CCRVDF, and JEMRA that focuses on food-borne bacteria that are resistant to antimicrobials.

#### **5. Relevance to the Codex strategic objectives**

This proposal is consistent with the following strategic goals presented in the Codex Draft Strategic Plan 2008-2013:

- Promoting Sound Regulatory Frameworks; and,
- Promoting Widest and Consistent Application of Scientific Principles and Risk Analysis
- Promoting Cooperation between Codex and other Relevant International Organizations

#### **6. Information on the relation between the proposal and other existing Codex documents**

There are several existing Codex documents which are related and that must be considered in the development of the proposed guidance:

- Review of existing standards on Risk Analysis (OIE, WHO) including Microbial Risk Assessment
- Review of Good Practices manuals, including Codes of practice and codes of hygiene (especially those from the work of CCRVDF and CCFH)  
<http://www.fao.org/docrep/005/Y1579E/y1579e02.htm>  
<ftp://ftp.fao.org/docrep/fao/005/Y1579e/Y1579e.pdf>  
[www.codexalimentarius.net/download/standards/10213/CXP\\_061e.pdf](http://www.codexalimentarius.net/download/standards/10213/CXP_061e.pdf)
- Review of existing documents/guidelines on containment of antimicrobial resistance in animals for food. Those of the WHO website are listed, but there are many other national, regional, and international guidelines that are pertinent.  
[http://www.who.int/foodborne\\_disease/resistance/en/index.html](http://www.who.int/foodborne_disease/resistance/en/index.html)
- Additional Codex documents that may be of relevance are listed separately below.

### **7. Identification of any requirement for and availability of expert scientific advice**

It is anticipated that expert scientific advice may be needed to help identify data that will be useful to the development of risk management and risk communication standards and principles. The Task Force and any other body (e.g., JEMRA) providing advice to the development of this Codex guidance must include a diversity of scientific disciplines including:

- Veterinarians representing expertise in major food animal species
- Risk Assessors/Modelers
- Experts experienced in pre-market scientific reviews of veterinary antimicrobial products with regard to human food safety
- Risk managers
- Food Industry processors, packers, quality assurance experts
- Production company personnel (e.g. quality assurance, live production veterinarian)
- Epidemiologists
- Microbiologists (with expertise in genetics of antimicrobial resistance, food technology and processing, antimicrobial susceptibility testing/clinical microbiology, and veterinary microbiology)

### **8. Identification of any need for technical input to the standard from external bodies so that this can be planned for**

The inclusion of technical input from the veterinary profession, representing the major food animal species, including aquaculture, will likely be necessary to ensure accuracy and implementation of proposed actions at the on-farm level. Additionally, input from food technologists, HACCP experts, and others in the microbial food safety arena will be needed to address current practices to minimize and contain antimicrobial resistant bacterial contamination of food products.

### **9. The proposed time-line for completion of the new work, including the start date, the proposed date for adoption at Step 5, and the proposed date for adoption by the Commission; the time frame for developing a standard should not normally exceed five years.**

It is expected that the Task Force work can and should be completed within the proposed four meeting schedule.

#### **Relevant Codex Alimentarius Documents List<sup>11</sup>:**

Codex Committee on Food Hygiene. Risk profile on antimicrobial-resistant bacteria in food. Rome, Food and Agriculture Organization of the United Nations, 2001 (CX/FH 01/12).  
[www.codexalimentarius.net/download/report/116/al03\\_13e.pdf](http://www.codexalimentarius.net/download/report/116/al03_13e.pdf)

<sup>11</sup> Not all documents listed were cited above.

Codex Committee on Food Hygiene. Discussion paper on antimicrobial -resistant bacteria in food. Rome, Food and Agriculture Organization of the United Nations, 1999 ( CX/FH 99/12;  
[ftp://ftp.fao.org/codex/ccfh32/FH99\\_12e.pdf](ftp://ftp.fao.org/codex/ccfh32/FH99_12e.pdf) )

Codex Committee on Food Hygiene. Report of the Thirty-second Session, Washington, DC, 29 November–4 December 1999. Rome, Food and Agriculture Organization of the United Nations, 2001 (ALINORM 01/13;  
[ftp://ftp.fao.org/codex/alinorm01/A101\\_13e.pdf](ftp://ftp.fao.org/codex/alinorm01/A101_13e.pdf)).

Codex Committee on Residues of Veterinary Drugs in Foods. Antimicrobial resistance and the use of antimicrobials in animal production. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/RVDF 00/4;  
[ftp://ftp.fao.org/codex/ccrvdf12/rv00\\_04e.pdf](ftp://ftp.fao.org/codex/ccrvdf12/rv00_04e.pdf)  
[ftp://ftp.fao.org/codex/alinorm01/A101\\_31e.pdf](ftp://ftp.fao.org/codex/alinorm01/A101_31e.pdf)

Codex Committee on Food Hygiene. Risk profile on antimicrobial-resistant bacteria in food. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/FH 00/11;  
[ftp://ftp.fao.org/codex/ccfh33/fh00\\_11e.pdf](ftp://ftp.fao.org/codex/ccfh33/fh00_11e.pdf)

Codex Committee on Residues of Veterinary Drugs in Foods. Proposed Draft Code of Practice to Minimize and Contain Antimicrobial Resistance. Rome, Food and Agriculture Organization of the United Nations, 2002 (CX/RVDF 03/6;  
[ftp://ftp.fao.org/codex/ccrvdf14/rv03\\_06e.pdf](ftp://ftp.fao.org/codex/ccrvdf14/rv03_06e.pdf)  
<ftp://ftp.fao.org/codex/alinorm03/A10331ae.pdf>

Codex Committee on Residues of Veterinary Drugs in Foods. Discussion paper on antimicrobial resistance and the use of antimicrobials in animal production. Rome, Food and Agriculture Organization of the United Nations, 2001 (CX/RVDF 01/10;  
[ftp://ftp.fao.org/codex/ccrvdf13/rv01\\_10e.pdf](ftp://ftp.fao.org/codex/ccrvdf13/rv01_10e.pdf)  
[ftp://ftp.fao.org/codex/alinorm03/al03\\_31e.pdf](ftp://ftp.fao.org/codex/alinorm03/al03_31e.pdf)

Codex Committee on Food Hygiene. Risk profile on antimicrobial-resistant bacteria in food. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/FH 00/11;  
[ftp://ftp.fao.org/codex/ccfh33/fh00\\_11e.pdf](ftp://ftp.fao.org/codex/ccfh33/fh00_11e.pdf)  
[ftp://ftp.fao.org/codex/alinorm03/al03\\_13e.pdf](ftp://ftp.fao.org/codex/alinorm03/al03_13e.pdf)

Recommended International Code of Practice General Principles of Food Hygiene, including Annex on HACCP and Guidelines for its application. CAC/RCP 1-1969, Rev. 4-2003  
([www.codexalimentarius.net/download/standards/23/cxp\\_001e.pdf](http://www.codexalimentarius.net/download/standards/23/cxp_001e.pdf))

## **OTHER DOCUMENTS**

Food Safety Risk Analysis: A Guide for National Governments, FAO Food and Nutrition Paper 87, 2006  
<ftp://ftp.fao.org/docrep/fao/009/a0822e/a0822e00.pdf>

Risk Assessment for Antimicrobial Resistance Arising from the Use of Antimicrobials in Animals, OIE Terrestrial Animal Health Code 2006, Part 3, Section 3.)  
([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm))

Guidelines for the Responsible and Prudent Use of Antimicrobial Agents in Veterinary Medicine, OIE Terrestrial Animal Health Code 2006, Part 3, Section 3.9, Chapter 3.9.3  
[http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.3.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.3.htm))

Joint FAO/WHO Consultation in Kiel, Germany in 2002  
(<http://www.who.int/foodsafety/publications/micro/en/march2002.pdf>)

Joint FAO/WHO expert meeting report on “The Use of Microbiological Risk Assessment Outputs to Develop Practical Risk Management Strategies: Metrics to Improve Food Safety” (Kiel, Germany, 3-7 April 2006)  
(<ftp://ftp.fao.org/ag/agn/food/kiel.pdf>)

Joint FAO/OIE/WHO Expert Workshops on Non-Human Antimicrobial Usage and Antimicrobial Resistance in 2003 and 2004  
([http://whqlibdoc.who.int/hq/2004/WHO\\_CDS\\_CPE\\_ZFK\\_2004.7.pdf](http://whqlibdoc.who.int/hq/2004/WHO_CDS_CPE_ZFK_2004.7.pdf)  
and [http://www.who.int/foodsafety/publications/micro/en/oslo\\_report.pdf](http://www.who.int/foodsafety/publications/micro/en/oslo_report.pdf) ).

2001 WHO Global Strategy for Containment of Antimicrobial Resistance

([http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_2\\_EN/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_2_EN/en/)).

Additional references to specific HACCP plans, specific antimicrobial resistance monitoring plans, and specific Good Veterinary Practice and Good Agricultural Practice guidance would be useful.

### **CI (Consumers International)**

Consumers International would like to submit to two interrelated proposals for new work for consideration by the Codex ad hoc Intergovernmental Task Force on Antimicrobial Resistance, hereafter referred to as the AR Task Force: 1) Antimicrobial Resistance Risk Management Methodologies, including Risk Assessment Policies Guidance Document; and 2) Criteria and Setting of Priorities for Antimicrobial Resistance Risk Management Work.

The first project is the development of a document setting out the risk management policy to be used by the Task Force and as a guide to member states antimicrobial resistance risk analysis efforts. Risk management methodologies would include risk assessment policy and the development of appropriate risk management options.

The second project would be to determine the criteria for risk management priorities followed by the actual setting of risk management priorities.

## **DRAFT PROJECT DOCUMENT 1**

### **Antimicrobial Resistance Risk Management Methodologies, Including Risk Assessment Policies Guidance Document.**

#### **1. Purpose and scope of the proposed work**

The purpose of this document is to specify risk management methodologies, including risk assessment policies in the Codex Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance

The scope of the proposed work is antimicrobial resistance risk analysis including establishment of risk management, risk assessment, and risk communication roles and providing a frame work for Codex risk assessment and risk management activities related to reducing the risk from antimicrobial resistant microorganisms in feed and food.

#### **2. Relevance and timeliness**

The 2001, WHO Global Strategy for Containment of Antimicrobial Resistance recognizes that resistance is a serious human health problem and that improving antimicrobial use must be a “key action in efforts to contain resistance.” CAC created the Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance to address the issue at the 29th meeting in July 2006.

#### **3. The main aspects to be covered**

3.1 Review existing risk analysis work by WHO, FAO, Codex, member countries and other intergovernmental organisations

3.2 Determine preliminary risk management activities to be carried out by Task Force including establishment of priority list.

3.2.1 Identification of microbiological food safety issue. This step has been completed by a series of Joint FAO/OIE/WHO Expert Workshop which have identified antimicrobial resistance as the result of antimicrobial use in animals as a public health concern. The 2003 Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment Geneva, December 1 – 5, 2003 describes the human health consequences resulting from antimicrobial resistant bacteria following non-human usage of antimicrobials.

3.2.2 Creation of Task Force policy on antimicrobial resistance risk profiles. A risk profile is “the description of the food safety problem and its context”. This risk profile should include all of the human health consequences related to antimicrobial resistance in foods and feed. The level of specificity of the risk profiles created by the Task Force needs to be decided. Because resistance determinants are often on mobile genetic elements containing genes that confer resistance to a wide variety of antimicrobials, it may not be possible to evaluate risks as a simple pathogen drug combination. The Task Force will need to clarify what types of profiles are needed within the overarching food safety issue of antimicrobial resistance. These could refer to the presence of a specific class of drug resistance in a specific pathogen, i.e. fluoroquinolone resistant *Salmonella enterica* or it could refer to the presence of multiple drug resistant plasmids in food independent of bacterial host.

The WHO (2005) ranking of critically important antibacterial agents for human medicine for risk management strategies of non-human use should be included when profiles are created for individual classes of drugs.

3.2.3 Creation of criteria for ranking of the antimicrobial resistance hazard for setting risk management priorities. Consumers International recommends that the creation of criteria for ranking hazards be the subject of another project document.

3.2.4 Determination of potential initial risk management options. Upon the completion of risk profiles and the risk ranking, an initial risk management decision should be made. This could include a request for more information, a decision to commission a risk assessment, or the decision to make a risk management recommendation in the form of a guidance document. The Task Force should create a framework for making initial risk management decisions.

Given the high level of resources needed for antimicrobial resistance risk assessments every effort should be made to find alternatives to commissioning risk assessment when there is already sufficient information to make risk management recommendations. For example, the WHO has already made the recommendation that antiviral drugs be banned for use in animals. It is difficult to see how a complete risk assessment would provide any more clarity on this antimicrobial resistance problem. Given the large number of antimicrobial drugs currently used it is unlikely that resources will be available to complete assessments in a timely manner.

Similarly, the Task Force must acknowledge the lack of resources in member states to carry out risk assessments and risk management activities. These resource restraints are particularly clear for developing countries, but even some of the wealthiest nations have not allocated sufficient resources to do public health evaluations of the use of growth promoters as recommended by the WHO. Because of this reality, it is important that this Task Force give specific risk management guidance that all member states can implement to reduce the significant public health consequences of antimicrobial resistance.

3.3 Define risk assessment methodology and policy for use by FAO and WHO (JEMRA) in this area taking into account previous work undertaken in this area.

3.3.1 Criteria should be set to determine whether a qualitative or quantitative risk assessment is most appropriate given available data.

3.3.2 Any risk assessments should consider the full range of public health consequences of antimicrobial resistance in food. Most existing antimicrobial resistance risk assessments (WHO, 2003) have failed to consider “the broad range of potential human health impacts, or the spectrum of antimicrobials and organisms relevant to a comprehensive assessment of risk”.

3.3.3 The types of risk assessment outputs should be specified. For qualitative risk assessment this may be in terms of “high”, “medium”, or “low” risks of adverse human health consequences. For quantitative risk assessments where data are available to quantify only part of likely risk, outputs must make clear that significant aspects of risk have not been considered.

3.4 Determine risk management options to be considered for recommendation by the Task Force.

3.4.1 Risk management recommendations can be based on a relative risk ranking and risk profile, or based upon the outcomes of antimicrobial resistance risk assessments.



3.4.2 Risk management options should be scaled to be commensurate with risks.

3.4.3 Risk management recommendation should include (WHO, 2003):

For critically important antimicrobials:

- do not use these drugs at all.
- use only in individual animals based on culture results and lack of alternative agents.
- use only in individual animals.
- use in groups of animals after risk assessment demonstrates acceptable level of safety.

For zoonotic pathogenic bacteria in food or food production animals containing multi-drug resistance:

- recall associated foods.
- restrict movement of infected or colonized animals.
- processing that guarantees removal of all resistant bacteria
- destroy food items
- destroy groups of animals infected or colonized

3.4.4 While existing codes of practice for veterinary antimicrobial drug use are important tools there is no evidence currently available showing that they are effective at reducing the public health consequences of antimicrobial resistance in food. Without evidence of their effectiveness they should not form the basis of antimicrobial resistance risk management.

3.4.5 Where appropriate risk management options may be linked to specific food safety objectives (FSOs). This approach is currently being developed for microbial risks not related to antimicrobial resistance (WHO, 2006). Different metrics may be needed for antimicrobial resistance such as measurements of the amounts of antimicrobial drug used in animals.

3.5 Recommend systems to monitor the effectiveness of risk management program.

3.5.1 Monitoring should where possible be based on existing surveillance systems.

3.5.2 National systems to monitor both antimicrobial resistance and antimicrobial drug use should be implemented.

3.5.3 Monitoring systems need to be robust enough to determine whether risk management steps are effective.

3.6 Determine risk communication policy. Risk communication in Codex is “the interactive exchange of information and opinions throughout the risk analysis process concerning risk, risk-related factors and risk perceptions, among risk assessors, risk managers, consumers, industry, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of risk management decisions”.

#### **4. Assessment against the *Criteria for the establishment of work priorities***

*Consumer protection from the point of view of health, food safety, ensuring fair practices in the food trade and taking into account the identified needs of developing countries.*

The project will be the basis for Codex work to contain the public health risk from antimicrobial resistance in foods. The project will provide a framework for developing countries to manage antimicrobial resistance risk when they lack the capacity to carry out risk assessments.

*Diversification of national legislations and apparent resultant or potential impediments to international trade:* The project aims to create an internationally accepted framework for managing antimicrobial resistance in food.

*Work already undertaken by other organisations in this field:* The project builds upon work undertaken by other international organisations. This document should incorporate the OIE risk analysis methodology adapting it to CODEX. The document should also incorporate risk management recommendations made in the WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food (Global Principles) and in successive Joint WHO/FAO expert consultations..

## **5. Relevance to Codex Strategic Objectives**

This proposal is consistent with the following strategic goals presented in the Codex Draft Strategic Plan 2008-2013:

*Promoting Sound Regulatory Framework*

*Promoting Widest and Consistent Application of Scientific Principles and Risk Analysis*

*Promoting Cooperation between Codex and other relevant international organisations*

## **6. Information on the relation between the proposal and other existing Codex documents**

This document should be based upon the Working Principles for Risk Analysis for Application in the Framework of the Codex Alimentarius. Several other Codex committees (CCRVDF, CCFH, and CCGP) have risk analysis and risk management documents in progress.

## **7. Identification of any requirements for and availability of expert scientific advice**

None identified.

## **8. Identification of any need for technical input to the standard from external bodies so that this can be planned for**

Consultation with WHO (JEMRA) would be required to establish roles and interactions with Task Force to complete risk assessments.

## **9. The proposed timeline for completion of the new work, including start date, the proposed date for adoption at Step 5 and the proposed date for adoption by the Commission; the timeframe for developing a standard should not normally exceed 5 years**

The project should be completed during the 4 year term of the Task Force.

References:

WHO, 2001. WHO Global Strategy for Containment of Antimicrobial Resistance: Executive Summary. WHO/CDS/CSR/DRS/2001.2a.  
[http://www.who.int/csr/resources/publications/drugresist/WHO\\_CDS\\_CSR\\_DRS\\_2001\\_2\\_EN/en/](http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_DRS_2001_2_EN/en/).  
Accessed February 23, 2007.

WHO, 2003. Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment, Geneva, December 1 – 5, 2003

WHO, 2005. Critically important antibacterial agents for human medicine for risk management strategies of non-human use: report of a WHO working group consultation, 15-18 February 2005, Canberra, Australia.  
[http://www.who.int/entity/foodborne\\_disease/resistance/FBD\\_CanberraAntibacterial\\_FEB2005.pdf](http://www.who.int/entity/foodborne_disease/resistance/FBD_CanberraAntibacterial_FEB2005.pdf).  
Accessed February 23, 2007.

WHO, 2006. Joint FAO/WHO expert meeting report on “*The Use of Microbiological Risk Assessment Outputs to Develop Practical Risk Management Strategies: Metrics to Improve Food Safety*” (Kiel, Germany, 3-7 April 2006) <ftp://ftp.fao.org/ag/agn/food/kiel.pdf>

## **DRAFT PROJECT DOCUMENT 2**

### **Criteria and Setting of Priorities for Antimicrobial Resistance Risk Management Work Document.**

#### **1. Purpose and scope of the proposed work**

The purpose of this document is to specify the criteria by which antimicrobials will be prioritized for consideration by the Task Force and to create an initial priority list of drugs to be considered for further risk analysis.

The criteria should give emphasis to the public health and animal health significance of the antimicrobials under consideration and take into account existing documents/guidelines from FAO, WHO, OIE, Codex related to the containment of antimicrobial resistance, the ongoing work on critically important antimicrobials, as well as activities undertaken in this area at international, regional and national level.

## **2. Relevance and timeliness**

The 2001, WHO Global Strategy for Containment of Antimicrobial Resistance recognizes that resistance is a serious human health problem and that improving antimicrobial use must be a “key action in efforts to contain resistance.” CAC created the Ad Hoc Intergovernmental Task Force on Antimicrobial Resistance to address the issue at the 29th meeting in July 2006.

## **3. The main aspects to be covered**

- Determine criteria for inclusion in priority list based on health significance of the drugs and take into account existing documents/guidelines from FAO, WHO, OIE, Codex related to the containment of antimicrobial resistance, the ongoing work on critically important antimicrobials, as well as activities undertaken in this area at international, regional and national level. Criteria should include a consideration of the needs of developing countries for risk analysis support in this area.
- Create an initial priority list of drugs to be considered for further risk analysis based on established criteria and risk profiles created by the Task Force.

## **4. Assessment against the *Criteria for the establishment of work priorities***

*Consumer protection from the point of view of health, food safety, ensuring fair practices in the food trade and taking into account the identified needs of developing countries.*

The project is an essential aspect of the Codex work to contain the public health risk from antimicrobial resistance in foods. Criteria should take into consideration of the needs of developing nations.

*Work already undertaken by other organisations in this field:* The project builds upon work undertaken by other international organisations. This document should incorporate the WHO and OIE work on critically important antimicrobials. The criteria should also incorporate recommendations made in the WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food (Global Principles).

## **5. Relevance to Codex Strategic Objectives**

This proposal is consistent with the following strategic goals presented in the Codex Draft Strategic Plan 2008-2013:

*Promoting Sound Regulatory Framework*

*Promoting Widest and Consistent Application of Scientific Principles and Risk Analysis*

*Promoting Cooperation between Codex and other relevant international organisations*

## **6. Information on the relation between the proposal and other existing Codex documents**

This document would be referred to in Task Force documents describing risk management methodology.

## **7. Identification of any requirements for and availability of expert scientific advice**

None identified.

## **8. Identification of any need for technical input to the standard from external bodies so that this can be planned for**

None Identified.

## **9. The proposed timeline for completion of the new work, including start date, the proposed date for adoption at Step 5 and the proposed date for adoption by the Commission; the timeframe for developing a standard should not normally exceed 5 years**

The project should be completed during the four-year term of the Task Force.

## **IFAH (International Federation for Animal Health)**

The attached Project Document Proposal conforms to the format for new proposals as described in the Codex Manual, 15th edition, Part 2. This project document proposal outlines the projects necessary to advance the work for the Codex Ad-Hoc Intergovernmental Task Force on Antimicrobial Resistance as specified in the CL2006/38-AMR. Three proposed projects are described to encompass the CAC29/LIM18 scope and Activities in Annex 2; as well as build upon the recommendations of the prior two WHO/OIE/FAO Joint Consultations.

- 1) Development of science-based risk analysis Codex guidance regarding food borne antimicrobial resistant microorganisms, using risk analysis principles and the work and standards of other relevant international organizations, such as FAO, WHO, and OIE.
- 2) Prioritization of Food Safety Issue Identification, Risk Profiles and Risk Assessments; review of existing antimicrobial resistance surveillance programs.
- 3) Provision of specific risk management advice for national level action in relation to reducing risk to human health associated with the use of antimicrobials in food and feed production and processing, including aquaculture, based on the outcome of risk assessments according to the defined methodology and other relevant data.

Development of these projects areas will result in a risk analysis process for countries to implement, guidance on prioritization of work and data needs, and a range of risk management options that can be adopted at the national level to minimize risk based on national human health priorities. Together, the net result of the three projects will be a Codex antimicrobial resistance risk analysis approach that allows countries to implement actions based upon identified needs and resources.

Several key points need to be emphasized in order to be sure these tenets are stated explicitly and clearly in the CL response. First, the establishment of the Risk Analysis process needs to include the consideration of the positive aspects of antimicrobial use in food animals, as indicated in the CL. Second, antibiotic categorization lists can assist in the prioritization of which Risk Profiles a national authority is to undertake first, second, etc.; however, the listing of a particular antimicrobial class cannot be used as a surrogate for the Risk Profile itself to declare an immediate public health concern which progresses to an immediate decision on risk management action that limits the availability or requires restrictive label wording for the use of a veterinary medicinal product or feedstuff. This is because antimicrobial resistant microorganisms must be associated with, or attributed to, a food product (which originated from a treated food animal) in order to comport with Codex Codes and Guidelines. For example, it is necessary to establish that an antimicrobial resistant microorganism, or resistance determinant(s) is actually present on or in a particular food product in sufficient quantity and prevalence so as to result in human illness that is likely to require antimicrobial treatment – and then be non-responsive- and that originally came from a medicated animal. Third, the various Codex, OIE, and WHO documents already developed that pertain to food hygiene, veterinary antimicrobial use practices, various “good practices”, and regulatory activities should form the nucleus of risk management actions, thereby alleviating the need to create new, perhaps redundant or conflicting, guidance. Fourth, the ultimate guidance document produced by the Task Force must not be restrictive to international food trade, or invoke burdensome testing or sampling evaluations that could place an undue burden on the U.S. food animal and meat export industries.

In addition to the CL response and Project Document proposal, it is recommended that the Codex Secretariat compile a library of relevant reference materials from WHO, OIE and FAO, using on-line availability as much as possible. Additional documents or websites that provide supportive information should also be included.

## **Executive Summary**

This project document proposal outlines the projects necessary to advance the work for the Codex *Ad-Hoc* Intergovernmental Task Force on Antimicrobial Resistance as specified in the CL2006/38-AMR. Three proposed projects are described to encompass the CAC29/LIM18 scope and Activities in Annex 2; as well as build upon the recommendations of the prior two WHO/OIE/FAO Joint Consultations.

**The proposed projects are:**

- 1) Develop science-based risk analysis Codex guidance regarding food borne antimicrobial resistant microorganisms, using Risk Analysis principles and the work and standards of other relevant international organizations, such as FAO, WHO, and OIE.**
- 2) Prioritization of Food Safety Issue Identification, Risk Profiles and Risk Assessments; review of existing antimicrobial resistance surveillance programs.**
- 3) Provision of specific risk management advice for national level action in relation to reducing risk to human health associated with the use of antimicrobials in food and feed production and processing, including aquaculture, based on the outcome of risk assessments according to the defined methodology and other relevant data.**

Development of these projects areas will result in a risk analysis process for countries to implement, guidance on prioritization of work and data needs, and a range of risk management options that can be adopted at the national level to minimize risk based on national human health priorities. Together, the net result of the three projects will be a Codex antimicrobial resistance risk analysis approach that allows countries to implement actions based upon identified and prioritized needs and resources.

**1. Purpose and scope of the proposed work**

The purpose of the proposed work is to develop science-based guidance, taking full account of the prior work on risk analysis principles and the work and standards of other relevant international Organizations, such as FAO, WHO and OIE. The intent, or application, of this guidance is to enable countries to be able to assess the risks to human health associated with the presence in food and feed, including aquaculture, and the transmission through food of antimicrobial resistant microorganisms and antimicrobial resistance genes (determinants); and to develop and apply appropriate risk management advice based on that assessment to reduce such risk.

To provide such guidance, the proposed work would identify the risk analysis components applicable/essential to microbiological food safety assessments already in existence in Codex, and seek to adapt them to antimicrobial resistant microorganisms associated with the antimicrobials used in human and veterinary medicine. For example, the *Principles and Guidelines for the Conduct of Microbiological Risk Assessment (CAC-GL 30-1999)* and the Joint FAO/WHO expert meeting report on “The use of microbiological risk assessment outputs to develop practical risk management strategies: Metrics to improve food safety” (Kiel, Germany, 3-7 April 2006) will be useful templates. The proposed work should also take into account existing work on the containment of antimicrobial resistance in animals for food (see OIE Terrestrial Code, CCVDRF and related documents). In this process work undertaken in the field at national, regional and international levels should be taken into account.

The scope of the proposed work is the food safety assessment, built on the foundational documents already in place or in development within Codex. Measurement (i.e. monitoring) of the effectiveness of the selected risk management options must be provided for, much in the same way as Hazard Analysis Critical Control Point procedures establish a baseline and methods to monitor for subsequent change.

Countries will need to have the requisite information to be able to use the proposed guidance. In specifying the needed information within a risk profile outline, the proposed guidance would indicate that data for which the international community proposes for countries to have to conduct their work. Consideration is to be given to assisting developing nations in the establishment of infrastructure and/or appropriate national capacities needed to implement the guideline.

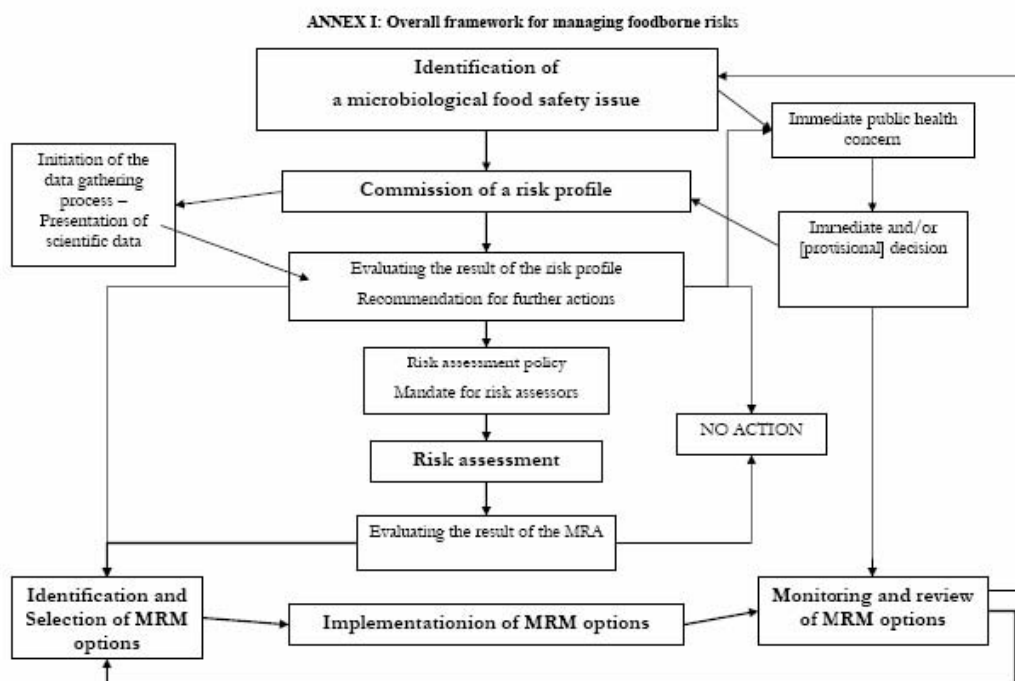
**2. Relevance and timeliness**

Antimicrobial resistance has been discussed at two prior joint consultations of WHO/OIE/FAO and the 29th CAC Session (July, 2006) recommended that the Task Force and the Project Document are relevant next steps to be taken in a timely manner. Initial discussion of antimicrobial resistance within Codex is contained in CX/RVDF 01/10 July 2001. One key point from the consultations is that certain antimicrobial resistant food borne bacteria were identified as being a possible microbiological food safety hazard. As such, Codex

work on microbiological risk assessment and risk management for food borne microbes are most relevant, since the premise of resistance gene reservoirs, gene acquisition, amplification, transmission and spread to susceptible hosts requires replication of resistance determinants within microbial hosts (i.e. resistance determinants themselves are not self-replicating). Therefore, the application of various Codex documents and guidelines on microbiological risk assessment and risk management should be extended to include the subset of antimicrobial resistant food borne bacteria.

### **3. Main aspects to be covered**

The Project Document Proposal is separated into three components, or projects, which can be independently developed, but which must be integrated in the final work product. This section provides a brief overview, building on Codex documents and flow charts already in place.



Source: Kiel Report 2006 (below)

The proposed project concept is to first build upon the excellent framework of Risk Analysis already in place within Codex for microbiological risk assessment and risk management, and risk communication by adapting it to include antimicrobial resistance as the OIE Risk Analysis document has done (Vose *et al.* 2001.). To facilitate this work, the OIE Risk Analysis document already contains an Appendix C that compares the Codex and OIE Risk Analysis processes. Then, it is proposed the Task Force will undertake an Antimicrobial Resistant Microorganism Microbiological Food Safety Issue Identification making use of the Critically Important Antibiotic lists of WHO and OIE with the goal to prioritize subsequent work on Risk Profiles and Risk Assessments of antimicrobial resistant microorganisms that is to be done by national authorities. It is envisioned that provision of scientific advice on the prioritization of Food Safety Issue Identification will be obtained by request to JEMRA or other relevant organizations such as WHO Collaborating Centers. Once Risk Profiles are available, they are to be followed by Risk Assessments at the country level, using Risk Assessment Principles as developed by the Task Force. Finally, the appropriate risk management options are to be described, using existing WHO, OIE and Codex documents already in place; including a description of the measurements to be used to assess effectiveness.

The Joint WHO/FAO Kiel Consultation in 2002 articulated the following four activities regarding risk management:

- Preliminary risk management activities comprise the initial process. It includes the establishment of a risk profile to facilitate consideration of the issue within a particular context, and provides as much information as possible to guide further action. As a result of this process, the risk manager may

- commission a risk assessment as an independent scientific process to inform decision-making.
- Evaluation of risk management options is the weighing of available options for managing a food safety issue in light of scientific information on risks and other factors, and may include reaching a decision on an appropriate level of consumer protection. Optimization of food control measures in terms of their efficiency, effectiveness, technological feasibility and practicality at selected points throughout the food chain is an important goal. A cost-benefit analysis could be performed at this stage.
- Implementation of the risk management decision will usually involve regulatory food safety measures, which may include the use of HACCP. Flexibility in the choice of individual measures applied by industry is a desirable element, as long as the overall program can be objectively shown to achieve the stated goals. On-going verification of the application of food safety measures is essential.
- Monitoring and review is the gathering and analyzing of data so as to give an overview of food safety and consumer health. Monitoring of contaminants in food and food-borne disease surveillance should identify new food safety problems as they emerge. Where there is evidence that required public health goals are not being achieved, redesign of food safety measures will be needed.

The Joint FAO/WHO expert meeting report on “The use of microbiological risk assessment outputs to develop practical risk management strategies: Metrics to improve food safety” (Kiel, Germany, 3-7 April 2006 <ftp://ftp.fao.org/ag/agn/food/kiel.pdf>) provides further clarification and guidance which the Task Force should employ.

The Project Proposal seeks to build upon these documents, for adaptation to the specific situation of antimicrobial resistance, within the LIM18 and Circular Letter scope, objectives and terms of reference to maximize the productivity of the Task Force to deliver useful guidance.

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**PROJECT 1. Develop science-based risk analysis Codex guidance regarding food borne antimicrobial resistant microorganisms, using Risk Analysis principles and the work and standards of other relevant international organizations, such as FAO, WHO, and OIE.**

The intent, or application, of this guidance is to enable countries to be able to establish risk profiles and then risk assessments to human health associated with the presence in food and feed, including aquaculture, and the transmission through food of antimicrobial resistant microorganisms and antimicrobial resistance genes (determinants) balanced with the possible positive aspects to food safety of different antimicrobials used in veterinary medicine; and to develop and apply appropriate risk management advice based on that assessment to reduce such risk.

The development of risk analysis methodology and process must be appropriate for the range of individual animal/drug/bacterial species combinations identified by the antimicrobial prioritization process. As such, the Codex Principles of Risk Analysis are well established for food borne microorganisms. The existing Codex Risk Analysis process will apply to the overall evaluation framework of Microbiological Risk Assessment, Risk Management and Risk Communication and shall be adapted for inclusion of the subset of food borne microorganisms which harbor antimicrobial resistance determinants and may be found in food animals, including aquaculture, or their feed.

CAC/GL30 –Principles and Guidelines for the Conduct of Microbiological Risk Assessment

[http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool\\_data/codex\\_0/en\\_cxg\\_030e.pdf](http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool_data/codex_0/en_cxg_030e.pdf)

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**PROJECT 2. Prioritization of Food Safety Issue Identification, Risk Profiles and Risk Assessments; review of existing antimicrobial resistance surveillance programs**

In general, the Task Force will undertake an Antimicrobial Resistant Microorganism Microbiological Food Safety Issue Identification making use of the Critically Important Antibiotic lists of WHO and OIE with the goal to prioritize subsequent work on Risk Profiles and Risk Assessments of antimicrobial resistant microorganisms that is to be done by national authorities. It is envisioned that scientific advice on the prioritization of Food Safety Issue Identification could be obtained by request to JEMRA (or possibly other relevant organizations such as WHO Collaborating Centers). Additionally, the Task Force will assist these national efforts through the collection or description of relevant data that is available concerning antimicrobial resistant microorganisms in feed, food animals, aquaculture, food production, and retail foods as well as identification of “missing” data that need to be collected and analyzed to enable countries to carry out risk profiles and risk assessment as outlined in Project 1. Once Risk Profiles are done according to the prioritized list for a particular antimicrobial agent, resistant microorganism and food product, they are to be followed by Risk Assessments at the country level, using the Risk Analysis Principles from above.

Specifically, the Task Force will perform Antimicrobial Resistant Microorganism Microbiological Food Safety Issue Identifications, and prioritize subsequent antimicrobial risk profiles<sup>12</sup>, balanced with the possible positive aspects of food safety, based upon the WHO and OIE work on critically important antimicrobial lists<sup>13</sup>, existing documents/guidelines from FAO, WHO, OIE, and Codex related to antimicrobial resistance, as well as activities undertaken in this area at international, regional and national levels. The CCFH Proposed Principles and Guidelines for the Conduct of Microbiological Risk Management (CX/FH 03/7) and the Kiel, 2006 Report (cited above) provides a decision tree/flow chart which the Task Force should itself follow and also recommend to national authorities who will perform the Risk Profiles. (See diagram above).

The Task Force will determine applicability of ongoing international and national bacterial resistance monitoring programs to provide data for risk assessment at the food animal (target pathogens and zoonotic/commensals) and retail food level. The WHO document on Antimicrobial Resistance Surveillance Standards and the OIE Terrestrial Code on Surveillance will be useful to this exercise. The WHO SalmSurv is one example of an ongoing surveillance program which may provide useful information on one genus of bacteria obtained from outbreaks and sporadic cases of salmonellosis, although human isolates are not considered within the scope of this Codex effort.

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**PROJECT 3. Provision of specific risk management advice for national level action in relation to reducing risk to human health associated with the use of antimicrobials in food and feed production and processing, including aquaculture, based on the outcome of the risk assessments according to the defined methodology and other relevant data.**

The Task Force should consider a continuum of possible interventions along the entire food chain, each step of which can reduce risk by minimizing and containing antimicrobial resistant microorganisms, appropriate to the food animal species, bacteria, and other practical considerations. As noted above in the Kiel 2006 consultation, weighing of appropriate risk management options is required.

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<sup>12</sup> \* Risk profiles (the description of the food safety problem and its context) may be developed to identify a possible causal pathway from feed (where applicable) to food animal to food to potential failure of treatment. It is anticipated that the Risk Profiles would be “customized” by regional or national food safety authorities. Risk profiles are usually followed by risk assessments to prioritize the Risk Management options for implementation appropriate for their area. Already, several Risk Profiles on food borne bacteria have been completed [http://www.foodrisk.org/risk\\_profiles.cfm](http://www.foodrisk.org/risk_profiles.cfm).

<sup>13</sup> Antibiotic categorization lists can assist in the prioritization of which Risk Profiles to undertake first, second, etc.; however, the listing of a particular antimicrobial class cannot be used as a surrogate for the Risk Profile itself to declare an immediate public health concern which progresses to an immediate decision on risk management actions. This is because antimicrobial resistant microorganisms must be associated with or attributed to a food product (which originated from a treated food animal) in order to comport with Codex Codes and Guidelines. For example, it is necessary to establish that an antimicrobial resistant microorganism, or resistance determinant(s) is actually present on or in a particular food product in sufficient quantity and prevalence so as to result in human illness that is likely to require antimicrobial treatment – and then be non-responsive- and originated from a medicated food animal.



Building on Codes and guidelines already established for antimicrobial use and food hygiene, this project task will develop guidance that could enable national authorities to set appropriate levels of protection (ALOP). <ftp://ftp.fao.org/ag/agn/food/kiel.pdf> See page 61 for flow process (diagram above). The establishment of specific levels of concern (or risk), as mentioned in the 2nd Joint Consultation at Oslo and LIM18, may be considered as corresponding to an Appropriate Level of Protection (ALOP) on a national basis. In the U.S., for example, the 2010 Public Health goals include targets rates for food borne disease and there are plans for targets for specific antibiotic resistant salmonella.

Codes of Practice for veterinary antimicrobial products should be implemented as much as practicable in each country as a primary step. Although the Code of Practice has many recommendations within it, progress on as many as is feasible is needed. The Good Animal Feeding Code is appropriate to address issues related to concerns relative to feed. Reference to list of Practice Codes (WHO, OIE, etc).

Embedded within the Code of Practice are responsibilities to regulatory authorities to conduct microbiological food safety evaluations of veterinary antimicrobial products. The application of the OIE Risk Analysis of antimicrobial resistant bacteria will be restricted to the specific regulatory risk assessments during the registration review to be performed by national authorities as part of risk management activities; because this is not a Codex responsibility. To date, these registration risk assessments have been developed in general conformance with the OIE Risk Analysis guideline

([http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.4.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.4.htm)), thus, the Task Force would not need to re-draft these guidelines to comply with the Codex risk analysis principles, but could recommend their implementation on a broader scale at the national level.

A system to monitor the effectiveness of risk management programs, e.g. bacterial resistance monitoring, food hygiene practices (i.e. HACCP) or other means are to be identified by the Task Force. The practicality of sampling, analysis and timeliness need to be taken into consideration.

[http://whqlibdoc.who.int/hq/2002/WHO\\_CDS\\_CSR\\_DRS\\_2001.5.pdf](http://whqlibdoc.who.int/hq/2002/WHO_CDS_CSR_DRS_2001.5.pdf)

An additional tool to measure risk management options and effectiveness could be as part of the risk assessment process to alter key inputs according to the anticipated effectiveness and determine what the outcome might be.

The Task Force may choose to provide a list of risk management options to national authorities, as outlined in the Kiel consultation, matched to the prioritized list of risk profiles and risk assessments to be done.

The Task Force should outline a work plan to enable capacity building in those countries or regions which may require assistance. Some suggestions to accommodate resource constrained countries are described in the Kiel document above.

Prior to the Meeting of the Task Force, a complete library of existing Codex and related organization documents/guidelines on antimicrobial resistance interventions, usage guidelines, and reports; and a review of guidelines for food processing that minimizes contamination should be established. This is consistent with No. 6 below.

- Resistance monitoring for food animals, food and feed

- [http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.1.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.1.htm)

- [http://www.oie.int/eng/normes/mmanual/A\\_00021.htm](http://www.oie.int/eng/normes/mmanual/A_00021.htm)

- [http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.2.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.2.htm)

- National regulatory authority risk assessment reviews

- Responsible Use guidelines

- [http://www.oie.int/eng/normes/mcode/en\\_chapitre\\_3.9.3.htm](http://www.oie.int/eng/normes/mcode/en_chapitre_3.9.3.htm)

- Feed control processes and guidelines

- Codex Code of Practice for Good Animal Feeding ALINORM 04/27/38

- Food processing controls, food safety objectives

- [http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool\\_data/codex\\_0/en\\_cxc\\_054\\_2004e.pdf](http://www.ipfsaph.org/servlet/BinaryDownloaderServlet?filename=/kopool_data/codex_0/en_cxc_054_2004e.pdf)

#### **4. Assessment against the Criteria for the establishment of work priorities**

*Consumer protection from the point of view of health, food safety, ensuring fair practices in the food trade and taking into account the identified needs of developing countries:* The project would provide additional guidance for countries to use in assessing the food safety of the low level presence of antibiotic resistance bacteria in/on foods, thus establishing the underlying safety of the food and appropriate protection of consumers. The project could particularly assist countries that have limited experience with food safety risk assessments.

*Diversification of national legislations and apparent resultant or potential impediments to international trade:* The project would provide internationally recognized scientific guidance that countries may use to establish individual standards or guidance. Such internationally agreed guidance can help ensure consistent approaches for the food safety assessment for such foods.

*Scope of work and establishment of priorities between the various sections of the work:* The scope of the work relates to work previously undertaken by Codex on a high priority basis.

*Work already undertaken by other organizations in this field:* The project complements work undertaken by other international organizations such as WHO, OIE and FAO, and is an extension or adaptation of work developed in the CCFH, CCVDRF, and JEMRA that concentrates on the subset of food borne bacteria that are antibiotic resistant.

#### **5. Relevance to the Codex strategic objectives**

This proposal is consistent with the following strategic goals presented in the Codex Draft Strategic Plan 2008-2013:

- Promoting Sound Regulatory Frameworks; and,
- Promoting Widest and Consistent Application of Scientific Principles and Risk Analysis

#### **6. Information on the relation between the proposal and other existing Codex documents**

There are several existing Codex documents which are related and that must be included in the development of the proposed guidance:

- Review of existing standards on Risk Analysis (OIE, WHO) including Microbial Risk Assessment
- Review of Good Practices manuals, including Codes of practice and codes of hygiene (especially from CCRVDF and CCFH)

<http://www.fao.org/docrep/005/Y1579E/y1579e02.htm>

<ftp://ftp.fao.org/docrep/fao/005/Y1579e/Y1579e.pdf>

[www.codexalimentarius.net/download/standards/10213/CXP\\_061e.pdf](http://www.codexalimentarius.net/download/standards/10213/CXP_061e.pdf)

- Review of existing document/guidelines on containment of antimicrobial resistance in animals for food. Those of the WHO website are listed, but there are many others that are pertinent on both an international as well as national scale.

[http://www.who.int/foodborne\\_disease/resistance/en/index.html](http://www.who.int/foodborne_disease/resistance/en/index.html)

Additional Codex documents that may be of relevance are listed separately below.

#### **7. Identification of any requirement for and availability of expert scientific advice**

It is anticipated that expert scientific advice will be needed to help identify data that will be useful to the completion of risk profiles. The Task Force must include a diversity of scientific disciplines which could include:

- Veterinarians representing major food animal species
- Risk Assessor/Modeler
- Risk manager
- Food Industry processor, packer, quality assurance
- Production company personnel (e.g. quality assurance, live production vet)

- Epidemiologist
- Microbiologists (with expertise in genetics of antimicrobial resistance, food technology and processing, antimicrobial susceptibility testing/clinical microbiology, and veterinary microbiologists).
- Economist
- Trade representative

**8. Identification of any need for technical input to the standard from external bodies so that this can be planned for**

The inclusion of technical input from the veterinary profession, representing the major food animal species, including aquaculture, is necessary to ensure accuracy and implementation of proposed actions at the on-farm level. Additionally, the input from food technologists, HACCP experts, and others in the microbial food safety arena will be needed to address current practices to minimize and contain antibiotic resistant bacterial contamination of food products.

**9. The proposed time-line for completion of the new work, including the start date, the proposed date for adoption at Step 5, and the proposed date for adoption by the Commission ; the time frame for developing a standard should not normally exceed five years.**

It is expected that the Task Force work can and should be completed within the proposed four meeting schedule.

**CODEX Document List (needs verification for access)**

Note: not all documents listed were cited above

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2001 (CX/FH 01/12).

Codex Committee on Food Hygiene. *Discussion paper on antimicrobial –resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 1999 ( CX/FH 99/12; [ftp://ftp.fao.org/codex/ccfh32/FH99\\_12e.pdf](ftp://ftp.fao.org/codex/ccfh32/FH99_12e.pdf))

Codex Committee on Food Hygiene. *Report of the Thirty-second Session, Washington, DC, 29 November–4 December 1999*. Rome, Food and Agriculture Organization of the United Nations, 2001 (ALINORM 01/13; [ftp://ftp.fao.org/codex/alinorm01/A101\\_13e.pdf](ftp://ftp.fao.org/codex/alinorm01/A101_13e.pdf)).

Codex Committee on Residues of Veterinary Drugs in Foods. *Antimicrobial resistance and the use of antimicrobials in animal production*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/RVDF 00/4; [ftp://ftp.fao.org/codex/ccrvdf12/rv00\\_04e.pdf](ftp://ftp.fao.org/codex/ccrvdf12/rv00_04e.pdf) [ftp://ftp.fao.org/codex/alinorm01/A101\\_31e.pdf](ftp://ftp.fao.org/codex/alinorm01/A101_31e.pdf))

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/FH 00/11; [ftp://ftp.fao.org/codex/ccfh33/fh00\\_11e.pdf](ftp://ftp.fao.org/codex/ccfh33/fh00_11e.pdf))

Codex Committee on Residues of Veterinary Drugs in Foods. *Proposed Draft Code of Practice to Minimize and Contain Antimicrobial Resistance*. Rome, Food and Agriculture Organization of the United Nations, 2002 (CX/RVDF 03/6; [ftp://ftp.fao.org/codex/ccrvdf14/rv03\\_06e.pdf](ftp://ftp.fao.org/codex/ccrvdf14/rv03_06e.pdf) <ftp://ftp.fao.org/codex/alinorm03/A10331ae.pdf>)

Codex Committee on Residues of Veterinary Drugs in Foods. *Discussion paper on antimicrobial resistance and the use of antimicrobials in animal production*. Rome, Food and Agriculture Organization of the United Nations, 2001 (CX/RVDF 01/10; [ftp://ftp.fao.org/codex/ccrvdf13/rv01\\_10e.pdf](ftp://ftp.fao.org/codex/ccrvdf13/rv01_10e.pdf) [ftp://ftp.fao.org/codex/alinorm03/al03\\_31e.pdf](ftp://ftp.fao.org/codex/alinorm03/al03_31e.pdf))

Codex Committee on Food Hygiene. *Risk profile on antimicrobial-resistant bacteria in food*. Rome, Food and Agriculture Organization of the United Nations, 2000 (CX/FH 00/11; [ftp://ftp.fao.org/codex/ccfh33/fh00\\_11e.pdf](ftp://ftp.fao.org/codex/ccfh33/fh00_11e.pdf) [ftp://ftp.fao.org/codex/alinorm03/al03\\_13e.pdf](ftp://ftp.fao.org/codex/alinorm03/al03_13e.pdf))

Recommended International Code of Practice General Principles of Food Hygiene, including Annex on HACCP and Guidelines for its application. CAC/RCP 1-1969, Rev. 4-2003

#### **OTHER DOCUMENTS**

Vose, D., J. Acar, F. Anthony, A. Franklin, R. Gupta, T. Nicholls, Y. Tamura, S. Thompson, E. J. Threlfall, M. Van Vuunen, D. G. White, H. C. Wegener & M. L. Costarrica. Antimicrobial resistance: risk analysis methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin. Rev. sci. tech. Off.Int. Epiz. 20(3):811-827.

#### **OIE (World Organisation for Animal Health)**

The OIE would like to draw the Task Force's attention to the document CAC/28 INF/3 distributed during the 28<sup>th</sup> CAC in Rome. This document provides an overview, notably on antimicrobial resistance, of OIE activities relevant to the CAC.

As far as the new work on antimicrobial resistance is concerned, OIE would like to stress the importance and usefulness of the initiative. Developing science based guidance, based on risk analysis principles, to help conduct relevant risk management activities, is considered by OIE to be essential.

In fact, this is similar to the OIE's approach to the establishment of specific guidelines on antimicrobial resistance.

The relevant OIE *Terrestrial Animal Health Code* Appendixes are:

- Appendix 3.9.1. : Guidelines for the harmonization of antimicrobial resistance surveillance and monitoring programmes.
- Appendix 3.9.2.: Guidelines for the monitoring of the quantities of antimicrobials used in animal husbandry.
- Appendix 3.9.3.: Guidelines for the responsible and prudent use of antimicrobial agents in veterinary medicine.
- Appendix 3.9.4.: Risk assessment of antimicrobial resistance arising from the use of antimicrobials in animals.

The relevant Chapter in the *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* is:

- Chapter 1.1.10: Laboratory methodologies for bacterial antimicrobial susceptibility testing.

The work of the OIE will continue through its *ad hoc* Group on Antimicrobial Resistance and the OIE Specialist Commissions. A tripartite meeting with WHO and FAO is scheduled for September 2007 to discuss the list of critically important antimicrobials. The OIE would like to reserve the opportunity to make further comments on this circular letter after the OIE General Session and after the tripartite FAO/OIE /WHO meeting have taken place.