codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD HYGIENE

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PROGRESS REPORTS ON THE JOINT FAO/WHO EXPERT MEETINGS ON MICROBIOLOGICAL RISK ASSESSMENT (JEMRA) AND RELATED MATTERS

Prepared by FAO and WHO

INTRODUCTION

As Codex endeavours to provide risk management guidance on a wide range of issues pertinent to the safety and quality of food in international trade in order to protect consumer health, FAO and WHO aim to provide the relevant scientific advice in a timely manner. This paper describes the scientific advice FAO and WHO have developed relevant to the specific agenda items of the 38th Session of the Codex Committee on Food Hygiene (CCFH) and provides an update on follow-up activities to previous work of the Committee.

A) RECENT FAO/WHO ACTIVITIES RELEVANT TO THE ONGOING WORK OF CCFH

1. The use of microbiological risk assessment outputs to develop practical risk management strategies: metrics to improve food safety. Report of an FAO/WHO expert meeting, Kiel Germany, 3 – 7 April 2006. *(Relevant to Agenda items 4, 5 and 6)*

This meeting was implemented, taking into account the needs of CCFH for scientific advice on the application of risk assessment outputs to support risk management. The objective was defined as: *The elaboration of guidelines for the use of the outputs of qualitative and quantitative microbiological risk assessments (MRA) in developing practical strategies and risk management standards for microbiological hazards in foods.* Considering the wide range of issues to be addressed a stepwise approach was warranted. The first step was to develop a number of background papers, including six pathogen-product case studies, to evaluate the risk management application of MRA outputs with a particular focus on the establishment of targets. These fed into the expert meeting, the report of which is now available on the FAO[1] and WHO[2] web sites.

[1] FAO website: http://www.fao.org/ag/agn/jemra/riskmanagement_en.stm
[2] WHO website: http://www.who.int/foodsafety/micro/jemra/meetings/2005/en/index.html

The report describes the outcomes of discussions on the use of MRA in microbiological risk management. In particular, it addresses the progress made and the challenges being faced in elaborating practical guidance on the use of MRA outputs to develop risk management strategies. The meeting was only able to begin the process of developing practical guidance in this area. It (a) summarized the current state of play, (b) used the aforementioned case studies to identify the technical areas where guidance is needed, and (c) identified priority issues for further discussion to enable the elaboration of practical guidance. Thus, the report should be considered a step in the continuing international effort to establish a sound technical basis for adopting a risk analysis approach to microbiological food safety concerns.

The meeting sought to outline the range of potential applications of MRA in risk management including its role in the development of quantitative risk-based microbiological targets, the selection and evaluation of control measures, the articulation of levels of control expected of food safety systems in a manner consistent with the goals of the Codex Alimentarius, FAO, WHO and the International Health Regulations (IHR), and the verification of compliance.

Recently there has been particular focus on the use of MRA to establish and/or implement quantitative risk-based microbiological targets such as Food Safety Objectives (FSOs), Performance Objectives (POs) and Performance Criteria (PCs), that are intended to relate public health goals with the degree of stringency required of food safety systems and control measures to achieve these goals. While these targets have been defined by Codex there is little experience to date regarding their establishment or implementation. The meeting considered that MRA has a critical role in the establishment and implementation of such targets, however the means by which MRA can be used to achieve this was an important area of discussion. It was noted that while an FSO may be used as a metric for translating control measures into public health outcomes, PO and PC are more likely to be the metrics used for establishing the stringency of a food safety system, given that PO and PC can be utilised at points in the food supply chain where control measures can be implemented and verified, through the implementation of appropriate microbiological criteria, processing criteria and product criteria.

An important consideration was the type of MRA that could be used to establish quantitative targets. Quantitative MRA can be deterministic or probabilistic. While deterministic risk assessment provides a relatively straightforward means of using MRA to develop such targets, it has disadvantages, for example it provides limited insights into uncertainty. Probabilistic risk assessment provides the means to overcome such disadvantages and, while in principle it offers the best opportunity for operationalizing such targets, it poses a challenge in terms of using outputs in the form of a distribution of values as a basis for the establishment of such targets and for taking decisions that are consistent with the legal systems of various countries. The meeting provided general guidance on how some of the identified difficulties could be avoided, and highlighted several other technical issues that need to be considered to successfully develop guidance in this area. For instance, substantial discussion was devoted to whether the current definitions of FSO, PO and PC, and particularly the use of the term “maximum” therein, are fully compatible with what is currently accepted as the outputs of probabilistic risk assessment. As different opinions were expressed on this issue, further work is needed to resolve this.

The meeting also noted that a well designed risk assessment provides the means to evaluate and compare the effects of different control measures on public health risk to consumers (i.e. risk per servings) or risk to a country (i.e. risk per annum) on an industry wide basis. Although it does have limitations, this *direct* application of MRA has been demonstrated by a number of risk assessments at both national and international level and is widely recognized as one of the strengths of MRA.

As the selection of appropriate control measures must be followed up with monitoring activities to determine the level of compliance, the effectiveness of a particular control measure can be highly influenced by the level of compliance with that measure. The application of MRA also extends to this part of risk management activities allowing consideration and comparison of, for example different levels of compliance, to facilitate the selection of the most appropriate risk management option(s).

2. Enterobacter sakazakii and *Salmonella* in powdered infant formula *(Relevant to Agenda Item 7)*

i) FAO/WHO expert meeting, 16 – 20 January 2006.

In response to the request of the 37th session of the CCFH for additional scientific advice on issues related to *E. sakazakii* and *Salmonella* in powdered infant formula (PIF) and the request of the 58th session of the World Health Assembly (WHA), the governing body of WHO (resolution WHA58.32), FAO and WHO commissioned the further development of a probabilistic risk assessment on *E. sakazakii* in PIF. FAO and WHO subsequently organized an expert meeting in FAO headquarters in Rome from 16 to 20 January 2006 to review the risk assessment model and to address the questions raised by the 37th session of the CCFH. To facilitate the work of the Committee the provisional report of that expert meeting was made available in advance of the Codex working group meeting on the proposed draft code of hygienic practice for powdered formula for infants and young children which met in Ottawa, Canada from 15 to 17 May 2006. The risk assessment model was presented to the Codex working group and the model together with the FAO/WHO consultants who developed it were made available to the working group to facilitate their deliberations. The expert meeting also considered the issue of *Salmonella* in powdered infant formula. While no risk assessment was carried out for *Salmonella*, the expert meeting provided some information relevant to potential control measures. The report of this meeting has been published in the FAO/WHO microbiological risk assessment series (No. 10) and is available to download from the FAO[3] and WHO[4] web sites. The specific replies to the issues raised at the 37th session of the CCFH and the recommendations of the expert meeting are attached as Annex 1**.**

ii) Web based model

One of the objectives of FAO and WHO in developing a risk assessment model for *E. sakazakii* in PIF was to develop a model that was user-friendly and could be made available for direct use by a wide audience of risk managers. In order to achieve this FAO and WHO commissioned the development of a web-based interface for the risk assessment model thereby enabling users to interact with the model via standard Internet browsers. Such an approach would mean that the user would not need to have any specialist software other than an Internet platform nor require specialist training to use the tool. Rather its use would be facilitated by a User Manual, and thereby would facilitate a widespread use of the model. FAO and WHO plan to have a prototype available for presentation during the 38th Session of the Committee.

iii) Guidelines for the Safe Preparation, Storage and Handling of Powdered Infant Formula

One of the recommendations from the FAO/WHO meeting on *E.sakazakii* and other pathogens in (PIF) in 2004 was that guidelines should be developed for the preparation, use and handling of PIF in order to minimize the risk to infants. In May 2005, the 58th Session of the WHA adopted a resolution (WHA58.32) on infant and young child nutrition requesting inter alia WHO to develop in collaboration with FAO guidelines for the safe preparation, use and storage of PIF.

WHO and FAO have developed guidelines to this effect. The document which aims to deliver the guidelines requested by the WHA and recommended by the expert meeting will be available on the FAO and WHO web sites in late November 2006 and presented at the 38th Session of the Committee.

The recommendations made in the guidelines are largely based on the findings of the quantitative risk assessment on *E. sakazakii* in PIF and the outputs of the expert meeting described in 2(i) above. The guidelines address situations found in the home and in health care environments. The draft guidelines were also presented and made available at the of the Codex working group meeting which met in Ottawa, Canada on May 15 – 17 2006 and comments on the draft version were also sought via the INFOSAN network. All feedback received has been taken into consideration in finalising these guidelines.

iv) World Health Assembly

The WHA, in its resolution 58.32 on infant and young child nutrition, urged the Codex Alimentarius Commission to urgently complete work currently under way on addressing the risk of microbiological contamination of PIF and establish appropriate microbiological criteria or standards related to *E. sakazakii*

[3] FAO website: http://www.fao.org/ag/agn/jemra/enterobacter_en.stm
[4] WHO website: http://www.who.int/foodsafety/publications/micro/en/index.html

and other relevant microorganisms in PIF; and to provide guidance on safe handling and on warning messages on product packaging. WHO is requested to report on the progress of Codex on this work every second year. Such report will go back to the WHA every even year.

3. Benefits and potential risks of the lactoperoxidase system of raw milk preservation *(Relevant to Agenda Item 10)*

Since 2002 issues relating to the lactoperoxidase system of raw milk preservation have been discussed in various Codex meetings. The 27th session of the Codex Alimentarius Commission in 2004, while adopting the Draft Code of Practice for Milk and Milk Products, added the following text to the code; "The use of the lactoperoxidase system (LP-s) for milk and milk products in international trade will be re-examined by the Committee on Food Hygiene (CCFH) after completion of an expert review by FAO and WHO of available data and considering the FAO Lactoperoxidase Expert Group report about potential risks and benefits of lactoperoxidase system. CCFH will then review the issue in 2006". FAO and WHO therefore implemented a technical meeting to provide scientific advice to the 38th session of the CCFH on the benefits and possible risks associated with the LP-s for raw milk preservation and any dairy products derived from treated milk. It also sought to address member country concerns arising from the decision of the Codex Alimentarius Commission, when adopting the Codex guidelines for the application of the lactoperoxidase system in 1991, to emphasise that the LP-s should not be used for products intended for international trade.

The meeting examined all the available relevant information on this issue from the published literature as well as data submitted to FAO and WHO in response to the call for data. Based on this, the meeting noted that the LP-s elicits antimicrobial activity against a wide variety of milk spoilage and pathogenic microorganisms, and observed that after completion of the bacteriostatic effect there is no evidence to indicate subsequent proliferation of pathogenic microorganisms. The activated LP-s is effective in raw milk of different species, the overall activity being primarily bacteriostatic depending on the initial total bacterial load, species and strains of contaminating bacteria and the temperature of milk. Observations from laboratory and field studies indicate that the LP-s does not induce any significant adverse effects on the chemical, physical or sensory characteristics of raw milk and processed dairy products. Under practical conditions of use the activated LP-s cannot be used to disguise milk of poor microbiological quality. None of the components of the LP-s were considered by the meeting to present a significant toxicological risk to public health at the levels proposed. Where iodine deficiency is common, public health measures to rectify the iodine deficiency are needed whether or not the LP-s is used. The technical meeting thus considered the LP-s to be a safe method of raw milk preservation when implemented according to established Codex guidelines and concluded that the meetings report should provide Codex with a scientific basis to reconsider the provision related to the limitation on the international trade of LP-s treated milk and dairy products. The report of the meeting has been distributed to all Codex contact points and is available in English, French and Spanish from http://www.fao.org/ag/agn/food/risk_lacto_en.stm.

4. Enterohaemorrhagic *Escherichia coli* in meat and meat products: approaches for the provision of scientific advise *(Relevant to Agenda Item 10)*

Considering the ongoing public health problem of enterohaemorrhagic *E. coli* (EHEC) in foods, the impact of this pathogen on meat trade and the suggestion from the 36th session of the CCFH to undertake a risk assessment, FAO and WHO together with the Food Safety Authority of Ireland convened a meeting on EHEC in raw meat and meat products from 4 to 7 September, 2006 in Dublin, Ireland. With the aim of providing guidance to FAO and WHO on future work in this area, the meeting reviewed existing risk assessments on EHEC in meat and meat products in terms their ongoing and potential application to both risk assessment and risk management. It also sought to identify the key issues faced by risk managers in addressing the problems associated with EHEC in raw beef and beef products, and provide guidance on how to address them.

The meeting noted that the risk assessments undertaken to date are reflections of the published evidence and scientific opinion at the time and place of their development. Having been developed over a ten year period, they reflect a continuum of development of risk assessment approaches and have played an important role in

building capacity and expertise in the area of risk assessment. In considering the risk of *E coli* O157:H7 in ground beef/ground beef products, they do not address other meats (e.g. sheep/lamb), other food products or other EHECs. The meeting thus noted that additional information is required before a risk assessment that specifically addresses other EHECs could be developed.

To date most risk management issues associated with EHEC have been addressed in the absence of risk assessments. The meeting noted that while they are not needed for common sense risk management activities, risk assessment is likely to assist when more difficult decisions or complex interventions throughout the food chain are needed. While the existing risk assessments were undertaken subsequent to or as a separate exercise to risk management activities, their use to re-evaluate risk management actions is planned in some countries, for example the United States of America and Ireland.

The scope of issues faced by risk managers are extensive, thus requirements for scientific advice will vary accordingly. As there are numerous factors which may constrain the application of a particular risk assessment, such as global food movement, the meeting tried to identify approaches to the provision of scientific advice that could be applied to a wide range of risk management issues. In this regard the meeting noted that full production-to-consumption risk assessments are huge endeavours and prioritization of the particular areas which require attention may be necessary. This can be achieved by means of an iterative approach, for example starting with a risk profile, then moving on to a qualitative or simple quantitative risk assessment before finally focussing on key areas and increasing the resolution of quantitative risk assessment at such points. Thus, risk assessment is one part of an information package to facilitate decision-making. Critical to ensuring such an information package meets the risk managers' requirements is the need to pose more specific and accurate risk management questions. The meeting developed a table to provide examples of points in the production-to-consumption chain at which a risk assessment may commence and the types of questions that such a risk assessment could address as a guide for risk managers in their deliberations to request scientific advice.

Although this meeting specifically addressed the risk associated with *E. coli* O157 in beef, it noted the broader need to address risks associated with this and other EHECs in the environment and on other meats and foods. It was observed that elements of the existing risk assessments could potentially be applied to other products and routes of EHEC transmission associated with or impacted by beef production. The meeting made the assumption that EHECs other than *E. coli* O157:H7 will respond to food safety measures in the same manner and further concluded that that controls for EHEC will also impact on other pathogens. The report of this meeting is been finalized and a pre-publication version will be released in advance of CCFH.

B) FOLLOW-UP ACTIVITIES TO PREVIOUS WORK OF THE COMMITTEE

Terms of reference for the FAO/WHO expert consultation on the uses of active chlorine

Following the approval of the Terms of Reference for the expert consultation on the uses of active chlorine, developed by the 37th session of the Committee, and adopted by the 28th session of the Commission, FAO and WHO are in the process of planning the work necessary to address this issue. Consequent to an extensive preparatory period it is anticipated that an expert meeting will be convened in November 2007.

C) OTHER RELATED ISSUES

1. New and forthcoming publications in the FAO/WHO Microbiological Risk assessment series:
The following publications are in press and will be available within 2006.

- Exposure assessment of microbiological hazards in foods: Guidelines. Microbiological Risk Assessment Series, No. 7
- Risk assessment of *Vibrio vulnificus* in oysters: Interpretative summary and technical report. Microbiological Risk Assessment Series, No. 8
- Risk assessment of choleragenic *Vibrio cholera* O1 and O139 in warm water shrimp in international trade:. Interpretative summary and technical report. Microbiological Risk Assessment Series, No. 9.

- *Enterobacter sakazakii* and *Salmonella* in powdered infant formula: Meeting Report. Microbiological Risk Assessment Series, No. 10.
- Risk assessment of *Campylobacter* spp. in broiler chickens: Interpretative summary Microbiological Risk Assessment Series, No. 11.
- Risk assessment of *Campylobacter* spp. in broiler chickens: Microbiological Risk Assessment Series, No. 12.

2. Non-human Antimicrobial Usage and Antimicrobial Resistance

As part of an FAO/WHO/OIE consultative process on Non-human Antimicrobial Usage and Antimicrobial Resistance, workshops were held in Geneva in December 2003 and in Oslo in March 2004. One of the main recommendations of this consultative process was that WHO should convene an international expert panel to propose a list of "critically important antimicrobials for humans" with a view to implementing specific management strategies related to non-human use for such antimicrobials. critical

In response to this recommendation WHO organized a meeting in Canberra, Australia (12-19 February 2005) to establish a list of *critically important antimicrobials* to human medicine, i.e. those antimicrobials for which loss of efficacy resulting from bacterial resistance would be calamitous for human health. The list will subsequently be considered by the Codex Alimentarius Commission, along with a list of critically important antimicrobials for veterinary medicine to be proposed by the OIE, in defining risk management strategies for non-human use of antibacterial agents.

3. FAO/WHO consultative process on provision of scientific advice to Codex and member countries

a) The FAO/WHO **Framework for the Provision of Scientific Advice**, compiling all written procedures currently followed by FAO and WHO in relation to the provision of scientific advice, is now available for public comment at: http://www.fao.org/ag/agn/proscad/index_en.stm. The documentation of these procedures aims to enhance the transparency of this work. The procedures will be revised periodically.

b) FAO/WHO, together with the Institute of Bromatology, Belgrade University, implemented an expert meeting on **Enhancing developing country participation in FAO/WHO scientific advice activities** in December 2005 in Belgrade, to consider means of achieving full participation of developing countries in the FAO/WHO activities on the provision of scientific advice The meeting proposed recommendations in three main areas: i) greater inclusion of data from developing countries; ii) enhancement of the potential for experts from developing countries to be selected as members and participate effectively in these meetings; and iii) enhancing the enabling environment at national, regional and international levels. The meeting also suggested mechanisms and processes to enable FAO, WHO and member countries to better communicate with experts and institutions. The report of the meeting is now available at: http://www.fao.org/ag/agn/proscad/index_en.stm. The CCFH is invited to note the above recommendations.

4 Training and capacity building

FAO and WHO have developed a training manual on ***Improving Participation in the Work of Codex***, designed to strengthen national food safety and quality systems through enhanced participation in the Codex process. It is available at http://www.fao.org/ag/agn/food/capacity_codex_en.stm.

FAO/WHO together with the Industry Council for Development (ICD) have developed a short introductory course on microbiological risk assessment and its use in risk management. This course is aimed at both risk managers and scientists/future risk assessors from both government and scientific institutions or academia. The final trilingual (English, French and Spanish) version of the CD-Rom is currently under preparation.

FAO and WHO have just completed work on “Food Safety Risk Analysis – A Guide for National Food Safety Authorities” which aims to provide countries with the basics with regard to applying risk analysis in food control systems. It aims to complement the work of the Codex Committee on General Principles which is currently developing risk analysis principles for application by national governments.

FAO and WHO supported the implementation of the Second International Conference on Microbial Risk Assessment (MRA): Foodborne Hazards (20 to 23 February, 2006) in Sydney, Australia. which considered

in particular the value of MRA in supporting risk management decisions. The conference noted that progress was being made in this direction but that the potential of risk assessment is not yet being fully realized. Many decision making environments are not yet conducive to using risk assessment and risk managers are still learning how to ask the right questions. It was also observed that risk assessment appears to have greater uptake in other sectors such as animal health compared to food safety. Reducing the time taken to do risk assessment e.g. by building on existing risk assessments, was considered critical to enhancing their utility. FAO and WHO also implemented a pre-conference workshop on Food Safety Risk Assessment.

5. Guidelines for Good Agricultural Practices

FAO is developing an approach to support the implementation of Good Agricultural Practices (GAP) along the food-chain. This focuses on information, technical assistance and capacity building to help developing countries cope with changing and globalizing food systems and the proliferation of requirements on GAP from the food industry and others, while not compromising their sustainable development objectives. FAO's approach on GAPs is one that is non-prescriptive and should not affect the definition or scope of good agricultural practices as they appear in existing texts, for example the Codex Alimentarius. Instead, in the GAP work that FAO is implementing, local-level GAPs defined by concerned stakeholders would support farmers and governments to adopt agricultural practices that help them comply with international regulatory frameworks such as the IPPC, Codex Alimentarius and OIE, as well as implement GAP that generate environmental, economic and social sustainability in different local settings. Upon request by members, FAO is undertaking technical assistance and capacity building activities on GAP for crops, fruit and vegetables, meat, milk or feed in different countries in Africa, Latin America and Asia.

ANNEX 1: RESPONSE TO QUESTIONS RAISED BY THE 37TH SESSION OF THE CCFH ON *E SAKAZAKII* AND *SALMONELLA* IN POWDERED INFANT FORMULATION AND RECOMMENDATIONS OF THE FAO/WHO EXPERT MEETING ON *ENTEROBACTER SAKAZAKII* AND *SALMONELLA* IN POWDERED INFANT FORMULA

RESPONSE TO CODEX

Codex requested that the expert meeting address a number of specific questions. While the details of how these questions were addressed are provided in the meeting report, the response to each of the questions is summarized below.

i) Taking into consideration any existing and new information on E. sakazakii *and existing and new data on* Salmonella,[1] *identify if possible the distribution of cases linked to the different types of powdered formula*[2] *as a function of age, and define specifically the age groups and other groups of infant and young children at greatest risk.*

The meeting reviewed the information available on the most recent outbreaks of *E. sakazakii* illness in infants and also considered information on, and further analysis of, previous cases and outbreaks of *E. sakazakii*-related illnesses. In noting that *E. sakazakii* has caused invasive infection in all age groups, the meeting reiterated the findings of the 2004 FAO/WHO meeting that infants appear to be the group at particular risk. Neonates and infants under 2 months of age are at greatest risk. The meeting noted that there do appear to be two distinct infant groups in terms of the syndrome they develop – premature infants who develop bacteraemia outside of the neonatal period with most cases occurring in infants under 2 months and term infants who develop meningitis during the neonatal period. This difference in timing of infection may however be related to differences in timing of exposure to *E. sakazakii* rather than differences in susceptibility; it was also noted that any infant can develop either syndrome at any age. The meeting pointed out that infections have occurred in both hospital and outpatient settings and it was noted that as older infants generally live at home in the community, infections in such infants may be more likely to be under-reported. Considering that cases of *E. sakazakii* illnesses have occurred in a variety of settings and infant populations, prevention efforts must be multifaceted. This issue is addressed in section 2.1 of the meeting report.

With regard to *Salmonella*, data from the United States of America in 2002 indicated that the incidence of salmonellosis was more than eight times greater in infants than in the general population. It was unclear whether the increased rate among infants results from greater susceptibility, or whether infants are more likely than persons in other age groups to seek medical care or have stool cultures performed for symptoms of salmonellosis. However, the meeting concluded that infants are more likely to experience severe illness or death from salmonellosis, and infants with immunocompromising conditions are particularly vulnerable. This issue is addressed in section 5.1 of the meeting report.

ii) Review the dose-response and growth models of E. sakazakii*, using new data that is becoming available.*

Although studies are underway in relation to pathogenicity and virulence of *E. sakazakii* and despite two outbreaks of *E. sakazakii* illness in infants since the first FAO/WHO expert meeting, there was no new information available to better define the dose-response relationship. Therefore, the meeting considered the approach to describe the dose-response relationship developed in 2004 (FAO/WHO, 2004) to still be relevant. The meeting also noted that it was unlikely that an accurate picture of the dose response for neonates will ever really be possible and, while any animal model data generated will provide better estimates than are currently available, it will only be at best an extrapolated estimate. This is addressed in sections 2.3 and 2.4 of the meeting report.

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[1] The need for any risk assessment work on *Salmonella* will be reviewed following an initial literature review and consideration of available data.

[2] "Powdered formula" is used here to describe powdered infant formula, follow-up formula, formula for Special Medical Purposes (FSMP) intended for infant, and human milk fortifiers, as described in section 6.1 of the 2004 Meeting Report "*Enterobacter sakazakii* and other microorganisms in powdered infant formula" (FAO/WHO, 2004).

Any information on the growth of *E. sakazakii* that was available either in the published literature or provided in response to the FAO/WHO call for data was considered in the development of the risk assessment model. Details on the elaboration of the model are provided in section 3 of the meeting report.

iii) Evaluate specific control measures for different manufacturing operations (depending on data provided by manufacturers of powdered formula), which could minimize product contamination by E. sakazakii *and evaluate how microbiological criteria for Enterobacteriaceae can be used as an indication of process hygiene.*

While data were provided by industry sources in response to the call for data and used to inform the development of the risk assessment model, there were not suitable data on the impact of specific control measures within the manufacturing environment to facilitate the development of a component in the risk assessment model to assess such measures. However, an analysis of the available industry data led to a number of conclusions by the expert meeting. It was noted that the control of recontamination of PIF with *E. sakazakii* from the processing environment following heat treatment was the critical activity required to minimize the risk associated with PIF. Achieving this required the implementation of a number of measures modified according to the needs of individual manufacturing facilities. Such measures include:

- The effective implementation of preventive measures (GMP/GHP and HACCP).
- The strengthening of these measures to further minimize entry of the microorganisms and to avoid their multiplication by excluding water from the processing environment, the most effective means of which was considered to be the implementation of systematic dry-cleaning.
- The selection of suppliers of dry-mix ingredients according to specified needs.
- The implementation of monitoring and environmental management programmes.

Further descriptions of industry practices are provided in section 4.1 of the meeting report.

Monitoring for Enterobacteriaceae is considered by industry to be a good means of monitoring process hygiene. However, in the case of *Salmonella* it was pointed out that low levels of Enterobacteriaceae are not a guarantee of the absence of *Salmonella* and for this reason the programmes targeting Enterobacteriaceae and *Salmonella* are only useful if run in parallel. It is likely that the situation with *E. sakazakii* is similar. The expert meeting considered the application of criteria for Enterobacteriaceae as an indicator microorganism for *E. sakazakii*. Such an application would require the establishment of a correlation between Enterobacteriaceae and *E. sakazakii* levels. The meeting considered the data available on this and used a correlation function to try and establish whether or not such a correlation existed. However, the meeting concluded that the available data did not indicate any correlation between Enterobacteriaceae and *E. sakazakii*. Yet neither was it possible with the available data to rule out a possible correlation. Without such a correlation, the meeting was unable to develop a meaningful set of scenario evaluations. However, the meeting did note that industry scientists feel that controlling Enterobacteriaceae is an effective tool to help control *E. sakazakii*. Therefore, the availability of additional information either through expert elicitation or data collection efforts may allow further consideration of this in the future. This issue is addressed in section 4.3.2 of the meeting report.

iv) a) In light of new data submitted by ISDI/industry request that the risk assessment be updated to take into consideration this new information and make the output available to the Working Group (in charge of redrafting the proposed draft Code) for the development of microbiological criteria; b) Use the risk assessment to evaluate the risk reduction associated with various control measures, microbiological criteria and sampling plans.

a) The data available from industry were considered in the development of the risk assessment. While this included some information on the levels of contamination, the true contamination level is an area of uncertainty. Therefore, the available data were not used directly as an input on contamination level, but guided the selection of a range of options on the level of contamination. The user of the risk assessment is thus provided with the three options: -5 log cfu/g (0.00001 cfu/g), -4 log cfu/g (0.0001 cfu/g), -3 log cfu/g (0.001 cfu/g), and can select that which is considered most appropriate, or can replace them with a figure

based on actual data where available. More information on the elaboration of the model and the data used therein are provided in section 3 of the meeting report.

b) The risk assessment model has the capacity to evaluate the risk reduction associated with sampling plans for *E. sakazakii* as well as a range of measures relevant to the preparation and use of PIF. As there were no specific criteria and sampling plans proposed for evaluation, the meeting selected a range of 162 different sampling scenarios with the aim of illustrating how this module of the risk assessment works and to provide insights into the effectiveness of different sampling plans in terms of risk reduction. The model can also estimate the proportion of lots rejected in association with the implementation of a specific sampling plan. This means that the risk assessment also provides a picture in terms of the impact of not meeting the established criteria. By allowing a comparison of different scenarios, the risk assessment illustrated that the better the process in terms of producing a product with a low mean concentration of pathogen, the lower the level of losses due to lot rejection.

The expert meeting did not recommend any specific criteria and sampling plans for *E. sakazakii* in powdered infant formula. However, by looking at a total of 162 sampling plan scenarios, it was considered that some of these could be useful for the purposes of Codex. This tool can be made available to the relevant Codex Committees and working groups to evaluate any additional sampling plans not considered in the course of the meeting. This issue is addressed in detail in section 4.2 of the meeting report.

v) Request that the aspects of the risk assessment model addressing preparation, storage and handling of powdered formula be revisited to ensure that all currently used preparation procedures are evaluated.

An important component of the risk assessment model is its ability to assess the relative risk associated with various consumer practices in terms of the preparation, storage and use of powdered infant formula. As there was not much published information on such practices, a questionnaire was developed to collect some information through hospitals, consumer groups and others. This information was used as a basis for the 574 different preparation and use scenarios considered and evaluated by the risk assessment in the course of the meeting. Details of all the scenarios evaluated are provided in section 4.2. In general, scenarios that involve periods of holding at room temperature are associated with greatest risk. This effect is exaggerated for warmer room temperatures. The same holding times at refrigeration temperatures indicated less than 1.3-fold risk increase. Reconstitution of PIF with liquid of 70°C was evaluated to be an effective risk mitigation strategy for all scenarios investigated. The highest risk scenarios were associated with reconstitution at temperatures of 40° and 50°C, when the formula is not consumed immediately. As a result, quick cooling to lower temperatures to minimize growth is essential. When PIF reconstituted at temperatures of 10° or 20°C was evaluated, minimal growth and inactivation was observed, but subsequent holding for long periods at room temperatures, including extended feeding periods, can result in growth and therefore increase risk. In the case of reconstitution at 60°C, some initial inactivation occurs but, depending on the particular preparation scenario, this inactivation can be overwhelmed by the magnitude of growth that may occur if temperatures permit, for example with extended feeding times. It was observed that extended feeding periods of more than 1 hour, particularly at warm ambient temperatures, were associated with increasing relative risk. Also the use of larger containers for cooling of the formula was associated with increased risk as a result of the slower cooling rate of the formula, indicating that formula should be cooled in small containers if possible. It was noted that some of the scenarios evaluated which exhibited increasing relative risk, such as extended feeding periods at a warm or very warm ambient room temperature, may be similar to those in hospitals and intensive care units. Also the higher relative risk associated with holding of reconstituted formula at room temperature for long periods highlights the importance of providing good guidance and educational messages on the safe preparation and use of powdered infant formula.

Several international reference documents specify that labelling should include adequate information to enable safe use of the product. For example, in the International Code of Marketing of Breast milk Substitutes, article 9 on Labelling states (in section 9.2 of the meeting report) that manufacturers and distributors of infant formula should include “instructions for appropriate preparation, and a warning against the health hazards of inappropriate preparation”. The General Principles of Food Hygiene (CAC/RCP 1-

1969, REV. 4-2003) states in section 9.3 on Labelling: "Pre-packaged foods should be labelled with clear instructions to enable the next person in the food chain to handle, display, store, and use the product safely."

Considering the results of the model, and also the Codex requirement for clear labelling with regard to safe use of pre-packaged foods, the meeting considered that measures to provide appropriate messages to users, including consumer education activities and product labels, will need to be reviewed and revised as appropriate. For example, many labels call for mixing PIF at temperatures around 50°C, which, according to this risk assessment, generally results in the greatest risks for the range of scenarios considered, unless, as is sometimes recommended, the reconstituted formula is consumed immediately. The model indicated that reconstituting PIF at 70°C provides the greatest risk reduction. However, it also recognized that not all PIF products are formulated to be mixed at 70°C. Some of the other considerations associated with reconstitution at this temperature are outlined in Appendix D of the meeting report. In addition, the meeting considered that the development of international guidelines for users of PIF, as requested by the WHA, could be informed by the outcome of this series of scenario analysis.

The CCFH also noted that "the need for any risk assessment work on Salmonella *will be reviewed following an initial literature review and consideration of available data". The meeting therefore also considered the issue of* Salmonella *in powdered infant formula.*

The meeting considered the industry practices currently in place – or at least available for implementation – for the control of *Salmonella*, and concurred with the conclusion of the previous FAO/WHO meeting that the current Codex-recommended criteria for *Salmonella* are appropriate given the current methodology with regard to testing and the limit of detection.

The meeting considered the need for a quantitative risk assessment on *Salmonella* in PIF and noted that one was under development in Australia and also that, if needed, it would be possible to adapt the *E. sakazakii* risk assessment model for PIF to assess the risk associated with *Salmonella* in PIF. However, the meeting did not consider that a quantitative risk assessment for *Salmonella* in PIF was needed at the present time and concluded that risk management decisions with regard to the management of *Salmonella* in PIF could be made based on existing information. The meeting concluded that there was adequate information about *Salmonella* with regard to dose response and thermal inactivation to provide a basis for risk management decisions related to *Salmonella* in PIF. The meeting noted, for example, that at least some *Salmonella* serotypes have the potential to cause illness at very low doses, which may be a specific concern for infants, particularly those in the higher susceptibility category (premature, low birthweight, immunocompromised). However, given the thermal resistance of *Salmonella*, reconstituting PIF at a temperature of $\geq$70°C, or using commercially sterile formula or fortifiers would provide a high level of protection against *Salmonella* infection from these food sources. Nevertheless, the assessment of more complex risk management options may require a quantitative MRA, but the meeting agreed that the final decision to do a risk assessment should be a risk management (Codex) one.

RECOMMENDATIONS

In considering the recommendations to be made, the meeting firstly re-endorsed those that had been made by the 2004 FAO/WHO meeting on this issue.

The expert meeting made the following additional recommendations:

To member countries, FAO and WHO

- Develop prevention strategies for *E. sakazakii* infections caused by contaminated PIF that address the different stages of production and preparation and use of PIF, taking into consideration the risk to infants – both within and beyond the neonatal period and of any immune status.
- Develop educational messages on the safe handling, storage and use of powdered infant formula, including the health hazards of inappropriate preparation and use; target healthcare workers, parents and other caregivers (in both hospitals and the community), since *E. sakazakii* infections have occurred in hospital and home settings.

- Review and revise product labels, as appropriate, to enable caregivers to handle, store and use the product safely, and to make clear the health hazards of inappropriate preparation.
- Encourage member countries to establish surveillance and rapid response networks, and facilitate coordinated investigation by clinicians, laboratorians and public health and regulatory officials, to enable the timely recognition and cessation of outbreaks of illness associated with *E. sakazakii* and the identification of contaminated PIF.
- Encourage countries to enhance laboratory-based surveillance, including reporting to Salm-Surv, the WHO salmonellosis worldwide surveillance network, since laboratory-based surveillance is the only way in which past outbreaks of salmonellosis associated with intrinsically contaminated PIF have been recognized.
- Encourage laboratories conducting surveillance for *Salmonella*, and manufacturers and regulators testing for *Salmonella* in PIF, to use isolation and diagnostic methods which can identify lactose-fermenting strains of this organism, since these have been the cause of some of the outbreaks of salmonellosis associated with PIF.
- Encourage scientists to determine the optimal isolation and identification methods for *E. sakazakii*, taking into account the new research data demonstrating genetic and phenotypic diversity in the species.
- Encourage research to determine ecological niches and virulence factors for *E. sakazakii* to better target risk mitigation strategies and control measures.
- Develop and review international guidelines – as requested by the 2005 WHA – educational messages and product labels regarding the preparation, storage and handling of PIF, considering the results of the *E. sakazakii* risk assessment model presented in this report.
- At this time, the meeting did **not** recommend that FAO/WHO conduct a quantitative risk assessment for *Salmonella* in PIF.

To Codex

- Make risk management recommendations based on the outputs of the JEMRA (Joint FAO/WHO Expert Meetings on Microbiological Risk Assessment) risk assessment for *E. sakazakii* in PIF and the estimates of potential risk reductions of proposed control measures. In particular, give consideration to the elaboration of sampling plans and microbiological criteria for *E. sakazakii* and Enterobacteriaceae in PIF, and labelling recommendations, specifically in the revision of the Recommended International Code of Practice for Foods for Infants and Children (CAC/RCP 21-1979).

To member countries

- Apply the risk assessment in developing national risk management strategies for the reduction of risks associated with PIF, such as appropriate educational programmes.
- Encourage industry to effectively implement preventive measures and to strengthen those measures that further minimize entry of the microorganisms of concern into the manufacturing environment and avoid their multiplication therein.

To industry

- Effectively implement, to the extent possible and feasible, preventive measures, including the strengthening of those measures that further minimize entry of the microorganisms and avoid their multiplication, such as the exclusion of water from the processing environment to the extent possible and feasible. The most effective means of achieving the latter is considered to be the implementation of systematic dry-cleaning.
- Support research that allows further evaluation of the effectiveness of Enterobacteriaceae as an indicator organism pointing to conditions in the manufacturing environment or final product that have increased potential for harbouring *E. sakazakii* or *Salmonella*.

To FAO and WHO

- In future “calls for data”, provide more specific details with regard to the type and format of data needed in order to enable data providers to target their efforts towards the provision of data which can be effectively used in the risk assessment process.