codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

JOINT OFFICE: Viale delle Terme di Caracalla 00100 ROME Tel: 39 06 57051 www.codexalimentarius.net Email: codex@fao.org Facsimile: 39 06 5705 4593

Agenda Item 9 **CX/FH 05/37/9**
February 2005

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD HYGIENE

Thirty-Seventh Session

Buenos Aires, Argentina 14 - 19 March 2005

REPORTS OF THE *AD HOC* FAO/WHO EXPERT CONSULTATIONS ON RISK ASSESSMENT OF MICROBIOLOGICAL HAZARDS IN FOOD 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 strive to provide the relevant scientific advice in a timely manner. The scientific advice that FAO and WHO provide to the Codex Committee on Food Hygiene (CCFH) is not limited to risk assessment of microbiological hazards in foods but covers a range of issues pertinent to the work of the committee, both ongoing and completed work. An example of the latter is the FAO/WHO guidance to governments on the application of HACCP in small and/or less developed businesses that is currently under development. This paper describes the FAO/WHO activities relevant to the specific agenda items of the 37th Session of the Committee and follow-up activities to previous work of the Committee.

A) FAO/WHO ACTIVITIES RELEVANT TO THE AGENDA ITEMS OF THE 37TH SESSION OF THE COMMITTEE

Agenda Item 3: Discussion Paper on the Management of the Work of the Committee.

In relation to this issue FAO/WHO have informed the Codex Alimentarius Commission (CAC), and by this note the CCFH, about the criteria used by both organizations in the prioritisation of requests for scientific advice from Codex. These criteria are as follows:

- clear scope of the advice requested;
- urgency of the advice requested,
- availability of required data or commitment of countries to provide such data; and
- availability of financial resources.

Agenda Item 4: Proposed Draft Revision of the Recommended International Code of Practice for Foods for Infants and Children.

At the 36th session FAO/WHO presented the preliminary report of the expert meeting on *Enterobacter sakazakii* and other microorganisms in powdered infant formula. The final report, which provides recommendations with regard to minimizing the risk and includes a preliminary risk assessment, has been published as number 6 in the FAO/WHO Microbiological Risk Assessment Series. It is available on the FAO (http://www.fao.org/es/ESN/index_en.stm) and WHO (http://www.who.int/foodsafety/en/) webpage's and a copy of the report has been sent to all Codex Contact Points.

In response to the need identified by the 36th session of the CCFH to continue with the risk assessment work FAO and WHO established a small advisory group and issued a call for data. The "call" resulted in the collection of additional industry data which was used together with data from an extensive literature review as a basis for further development of the risk assessment. This new risk assessment model and supporting documentation will be reviewed by a FAO/WHO technical meeting Later this year (2005).

Two FAO/WHO risk assessment consultants attended the working group meeting on the revision of the Recommended International Code of Practice for Foods for Infants and Children, that took place in Ottawa, Canada in November 2004, in order to present an overview of the new draft risk assessment model and its capabilities and receive feedback from the group on the types of issues that it needed to have addressed using risk assessment. The Working Group meeting identified "Handling and Storage of Powdered Infant Formula and the Associated Risks of *E. sakazakii* Infection in Infants" as a particular area of concern, given the incidental presence of pathogens in infant formula. The model was applied to address this issue and the preliminary findings were subsequently made available for consideration (see Annex 1).

Other issues that the risk assessment model could examine include, for example, the impact of the method of manufacture on risk, the reduction in risk achieved through the implementation of different microbiological criteria, sampling and testing regimes, etc. FAO/WHO will only undertake this work if it is identified as a specific need of the committee.

At the recent Executive Board meeting of the WHO (Geneva, 17-25 January 2005), a draft resolution on infant and young child nutrition was discussed and finalized to be presented for endorsement at the forthcoming World Health Assembly session in May 2005. Several paragraphs of this resolution are relevant to the present issue of *E. sakazakii* in powdered infant formula. In particular the draft resolution calls on the Codex Alimentarius to "*establish standards, guidelines and recommendations on foods for infants and young children formulated in a manner that ensures the development of safe and appropriately labelled products that meet their known nutritional and safety needs, thus reflecting WHO policy, in particular the global strategy for infant and young child feeding and the International Code of Marketing of Breast-milk Substitutes*". It also requests Codex "*to urgently complete work currently under way on addressing the risk of microbiological contamination of powdered infant formula and establish appropriate microbiological criteria or standards related to E. sakazakii and other relevant microorganisms in powdered infant formula; and to provide guidance on safe handling and explore the necessity of adding warning messages on product packaging"*.

Agenda Item 5: Proposed Draft Guidelines on the Application of General Principles of Food Hygiene to the [Management] of Listeria monocytogenes in foods.

The FAO/WHO risk assessment on *Listeria monocytogenes* in ready-to-eat foods was published in the Microbiological Risk Assessment Series in 2004 and a copy of the technical report (No. 5 in the series) and the interpretative summary (No 4 in the series) has been sent to all Codex Contact Points. Both documents are also available on the FAO (http://www.fao.org/es/ESN/index_en.stm) and WHO (http://www.who.int/foodsafety/en/) WebPages.

The document was made available to the Codex working group on this issue, which met in Berlin, Germany in September 2004, for consideration and inclusion in their work. Both FAO and WHO representatives

participated in this working group meeting. FAO and WHO noted the difficulties that the group were having in terms of incorporating the outcome of the risk assessment and converting it to risk management guidance. As a result FAO/WHO, with support from the Institute for Hygiene and Food Safety, Kiel, Germany, plan to implement a technical meeting in July 2005 to address this issue in more detail.

FAO and WHO view this as a very important meeting to help ensure that optimal use is being made of the international risk assessment work both at the Codex and the country level and also envisage that the outcome could contribute to the finalisation of the Draft Principles and Guidelines for the Conduct of Microbiological Risk Management. More details on this meeting are provided in Annex 2. FAO and WHO are currently in the process of identifying potential experts to participate in this meeting. For more information and details of application for the roster of experts please see the FAO (http://www.fao.org/es/ESN/index_en.stm) and WHO (http://www.who.int/foodsafety/en/) WebPages.

Agenda Item 6: Proposed Draft Principles and Guidelines for the Conduct of Microbiological Risk Management

FAO/WHO have noted that the report of the consultation "Principles and guidelines for incorporating microbiological risk assessment in the development of food safety standards, guidelines and related texts" (FAO/WHO, 2002; available from the FAO (http://www.fao.org/es/ESN/index_en.stm) and WHO (http://www.who.int/foodsafety/en/) WebPages) has been used in the elaboration of the Draft Principles and Guidelines for the Conduct of Microbiological Risk Management. FAO and WHO will provide further guidance on this issue through the implementation of a meeting in July 2005 to address the Development of Practical Risk Management Strategies based on Microbiological Risk Assessment Outputs. More details are presented above under agenda item 5.

Agenda item 8: Proposed draft revision of the code of hygienic practice for egg products and *Agenda Item 10: Discussion paper on the guidelines for the application of the general principles of food hygiene to the risk based control of Salmonella spp. in poultry.*

As previously reported the interpretative summary and technical report of the FAO/WHO risk assessments on *Salmonella* in eggs and broiler chickens have been published as numbers 1 and 2 respectively of the FAO/WHO Microbiological Risk Assessment Series. FAO/WHO are very much interested in receiving feedback from the drafting groups on their experience of using the risk assessments in the development of these risk management documents (codes of hygienic practice) and on difficulties encountered in doing so.

Agenda Item 11: Discussion Paper on the Guidelines for the Application of the General Principles of Food Hygiene to the risk based control of enterohaemorrhagic E. coli in ground beef and fermented sausages.

FAO and WHO work on this issue has been postponed pending the decision of the committee on the specific nature of the scientific advice it requires. CX/FH 05/37/11 outlines a number of risk management questions and notes that any risk assessment should seek to answer these questions. However, these questions as they are currently written do not provide a clear scope for any risk assessment work, for example the types of mitigations to be considered at slaughter/processing are not identified. Furthermore, the data gaps that have been identified in the Risk Profile (included in CX/FH 05/37/11) indicates that it is currently not possible to address some of the risk management questions such as those related to the effect of probiotics and cross-contamination among carcasses and strategies/processes to reduce the number of EHEC on ground beef. To make optimal use of the outcome of any risk assessment work it is critical that the committee identifies exactly what it wants from the risk assessment and how it intends to use the output before any work begins. This will ultimately speed up the elaboration of risk management guidance.

Agenda Item 13: Other business and Future work:

a) Risk profile of Vibrio spp. in seafood

Work on the FAO/WHO risk assessments on *Vibrio* species in seafood have continued and the risk assessments on *Vibrio cholerae* in warm water shrimp for export and *Vibrio vulnificus* in oysters have been peer-reviewed and will be published within the coming months. Work is ongoing to finalise the risk assessments on *Vibrio parahaemolyticus.*

FAO/WHO have noted the consideration given to the CCFH discussion paper on Risk management strategies for *Vibrio* spp. in seafood in the Codex Committee for Fish and Fishery Products (CCFFP) (ALINORM 04/27/18) and the questions that have been posed by that committee. Some of the issues raised by CCFFP such as the effect of using disinfected water and the impact of setting limits or criteria are being looked at in at least one of the *Vibrio* risk assessments. A more detailed response to some of these questions can be provided if needed to facilitate the work of the committee.

b) Discussion paper on viruses in food

FAO/WHO recognize that food- and waterborne transmission plays an important role in spread of enteric viruses and this has been well documented in the case of noroviruses. Control of such viruses is often not considered in the establishment of food control systems although there are estimates that suggest that up to 50% of cases of foodborne illnesses are caused by viruses. The lack of scientific data has hindered progress in the control of food borne viruses to date; however, much progress has been made in terms of research and data collection in the past few years. In order to begin collection of data, which would facilitate any future risk assessment work, a network of food virologists is being established. Those interested in participating in this network should contact WHO (jansenj@who.int or benembarekp@who.int).

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

Guidance to Governments on the Application of HACCP in Small and/or Less Developed Businesses

In response to the need identified by member countries and the offer made by FAO/WHO in the 35th session of the committee, the preparation of the guidance to governments on the application of HACCP in small and/or less developed businesses is at an advanced stage. The current draft has been developed based on discussions in earlier sessions of this committee, inputs received from an electronic working group and a technical meeting that was held in Rome in December 2004. Complete details and the draft document are available in CRD XXX

C) OTHER FAO/WHO ACTIVITIES RELEVANT TO THE WORK OF THE COMMITTEE.

Lactoperoxidase

In response to the request identified in the 28th session of the Commission (Alinorm 04/27/41, Joint FAO/WHO Food Standards Programme Codex Alimentarius Commission, Twenty-seventh Session, Centre International de Genève, Geneva, Switzerland, 28 June – 3 July 2004, Draft Code of Practice for Milk and Milk Products. 45), FAO/WHO are in the process of organising an expert review / technical meeting to consider available data on potential risks and benefits of the use of the lactoperoxidase system. The secretariat of the Global Lactoperoxidase Programme (GLP) based in the Animal Production Service (AGAP) in FAO's Animal Production and Health Division (AGA) is working in close collaboration with the Codex secretariat in finalising this event.

D) OTHER RELATED ISSUES:

Training tools

FAO and WHO are in the process of finalising a CD-ROM training package on ***Food Safety Risk Analysis***, which includes a framework and overview manual, a training module, case studies in risk analysis, and access to FAO/WHO resources related to food safety risk analysis. An FAO/WHO workshop was held in Bali, Indonesia on 4 March 2004 to introduce the package to some potential users and to provide participants

with practical tools for risk analysis. The workshop report is available from the following FAO Webpage: ftp://ftp.fao.org/es/esn/food/meetings/bali_report_mar04.pdf

FAO and WHO are currently developing 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 has been field-tested in Africa and the Pacific and it is expected to be available in final form in the first half of 2005. The manual provides information on the Codex process and the development of national Codex programmes. It should serve both as a reference document for those involved in national Codex activities and as a training tool for national/regional training courses on Codex.

FAO/WHO together with the Industry Council for Development (ICD) are developing a short introductory course on microbiological risk assessment and its use in risk management. This course has been developed with both risk managers and scientists/future risk assessors in mind. It is aimed towards participants from both government and scientific institutions or academia. The course will be implemented initially on a regional basis following pilot testing in September 2005 and subsequent finalisation.

Annex 1: Handling and Storage of Rehydrated Powdered Infant Formula and the Associated Risks of *E. sakazakii* Infection in Infants:

Preliminary Findings from a Draft Risk Assessment Model

Prepared For:

Codex Committee on Food Hygiene

Drafting Group for the Code of Hygienic Practice for Foods for

Infants and Children

By:

FAO/WHO Consultants*

PREFACE

This document summarizes a series of preliminary findings regarding post-rehydration handling of powdered infant formula and the relationship of the time and temperature of storage to estimates of relative risk across a number of alternate storage scenarios. The relative risk estimates are based upon outputs from a risk assessment model under development for *E. sakazakii* infection in infants following consumption of rehydrated powdered infant formula. The model is being developed under contract with FAO/WHO, and under the auspices of the FAO/WHO joint activities on microbiological risk assessment. This model was initiated at a FAO/WHO workshop in Geneva in 2004 and is an extension of the model prepared during that meeting. The model is being developed in partnership with an ad-hoc working group organized by FAO and WHO.

COMMON ASSUMPTIONS

This analysis makes the following assumptions:

1) The initial population (before growth) of organisms in the powder to be consumed in a single feeding is 1 CFU. This is based on the expectation of a relatively low concentration of organisms such that the occurrence of more than 1 CFU per serving (before growth in the rehydrated formula) would be very rare.
2) The risk of infection is proportional to the dose for the range of doses considered in this analysis. This is based on the assumption of an exponential dose-response curve that is linear in the region of interest such that risk is proportional to ingested dose. Simply put, when the population of organisms doubles, then the relative risk also doubles.
3) Parameters for microbial growth and lag times are based on scientific literature and responses to a Call for Data conducted by FAO and WHO.

---

* Mr. Gregory Paoli and Dr Emma Hartnett.

These assumptions are unchanged from the FAO/WHO workshop on *E. sakazakii* in powdered infant formula. Note that these assumptions are independent of the source of the pathogen (e.g., manufacturing versus preparation environment).

REFRIGERATED STORAGE

Using the risk assessment model, the relative risk is estimated for storage times of 1, 2, 4, 8, 12, 24 and 48 hours at refrigerator temperatures ranging from 4°C to 10 °C. All results are based upon the following preparation conditions, which are constant for all refrigerated storage scenarios considered:

- Preparation occurs at room temperature (20°C) and lasts ¼ hour
- Warming occurs at 27°C for 30 minutes
- Feeding is carried out at a warmer room temperature of 27°C and lasts 4 hours

Table 1 shows the change in the relative risk. The baseline value (i.e., assigned a relative risk of 1) is the risk at 1 hour of refrigerated storage at 4°C. These results assume a re-hydration liquid temperature of 40°C. The shaded cells of the table highlight the combinations of temperature and time that present a risk at least two-fold greater than the baseline conditions (e.g., storage for 1 hour of refrigeration at 4°C).

Table 1: The relative risk of infection with *E. sakazakii* resulting from alternative refrigeration scenarios specified by duration of storage and refrigeration temperature. Risk estimates are relative to the estimate of risk at 1 hour of refrigerated storage at 4°C.

Time (hours)	***Refrigeration temperature (℃)***						
	4℃	***5℃***	***6℃***	***7℃***	***8℃***	***9℃***	***10℃***
1	**1**	1.0	1.1	1.1	1.2	1.2	1.3
2	1.2	1.3	1.4	1.6	1.8	1.9	2.1
4	1.3	1.5	1.8	2.1	2.5	3.1	3.7
8	1.3	1.6	2.0	2.6	3.5	4.8	7.0
12	1.2	1.6	2.1	3.0	4.6	7.2	12.2
24	1.1	1.6	2.6	4.8	10.2	24.0	64.2
48	0.8	1.6	3.8	12.3	50.4	264.8	$1.8x10^3$

BRIEF DISCUSSION: REFRIGERATED STORAGE

The estimation of relative risk is based upon prediction of the temperature of the formula through stages of rehydration, preparation, cooling, storage, warming and feeding. Figure 1 shows the temperature-time profiles for prepared formula across a variety of storage durations for a refrigeration temperature of 6°C. As the figure demonstrates, refrigeration (if any) of formula occurs after preparation and continues for the specified amount of time (e.g., 1, 2, 4, …, 48 hours). The formula is then warmed (rapidly, e.g., through immersion in a water bath) raising the temperature of the formula. The temperature then reaches a plateau at the room temperature at which feeding occurs, in this instance 27°C.

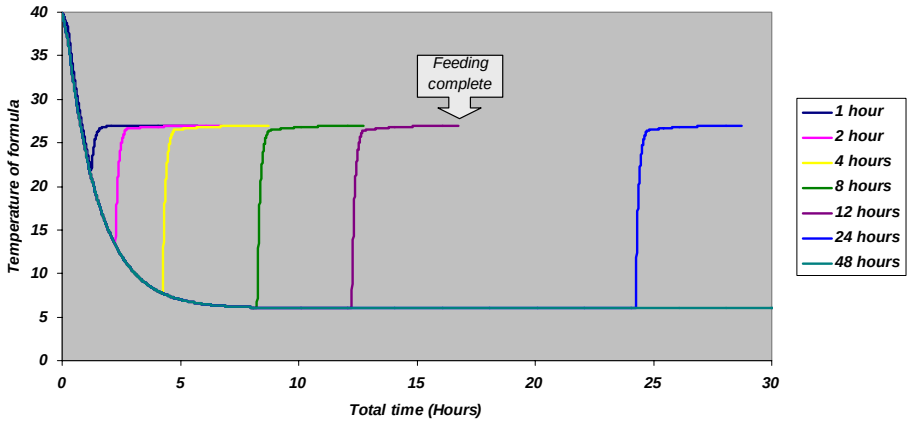

Figure 1: (Note: This graph is best viewed in colour). Temperature-time profiles of prepared formula through a range of refrigerated storage times (1, 2, 4, 8, 12, 24 and 48 hours), warming, and feeding. Refrigeration temperature is 6°C, re-hydration liquid is 40°C. Note that cooling profiles overlap, 48 hours is off the scale of the graph.

Based upon the predictions of the temperature-time profile of the formula, the extent of growth or inactivation that might occur in any contaminating *E. sakazakii* population is predicted, and is accumulated to give a final estimate of the dose at the point of feeding. The extent of growth is heavily dependent upon the refrigeration temperature. This is most noticeable when the refrigeration temperature is 10°C, where the risk at 10°C is more than 1000 times larger than the risk at 4°C for a storage time of 48 hours. Figure 2 shows the cumulative log change in populations of *E. sakazakii* that occurs during cooling, storage, warming and feeding of the formula. A positive log change indicates growth. This figure illustrates, as expected, that the total log change is greatest for refrigerated storage at higher temperatures, with the difference in the log change at 10°C compared to 4°C increasing with longer storage durations.

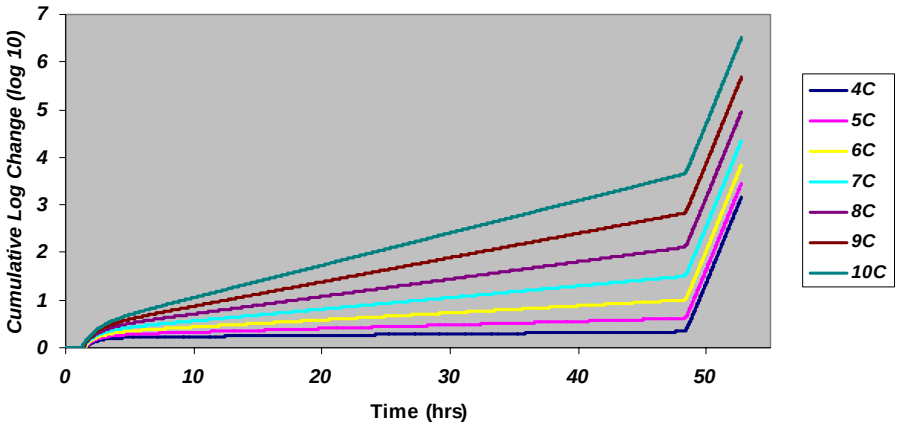

Figure 2: (Note: graph is in colour). Cumulative log change occurring over time in contaminating populations of E. sakazakii as predicted by the risk assessment model for a variety of refrigeration temperatures. In this scenario, after 48 hours, the formula is warmed to room temperature for feeding. Positive log changes indicate growth.

INFLUENCE OF TEMPERATURE OF THE RE-HYDRATING LIQUID FOR REFRIGERATED STORAGE

The relative risk estimates presented in Table 1 assumed the liquid used to re-hydrate the formula was at 40°C. However, the temperature of the re-hydrating fluid influences the overall profile of risk. Table 2 shows the relative risk according to the temperature of the re-hydrating liquid and the length of refrigerated storage. These results are based upon refrigeration of the formula for the specified durations (1, 2, 4, 8, 12, 24 and 48 hours) at 6°C. For these scenarios the baseline scenario (e.g., assigned a relative risk of 1) employs re-hydration with a liquid temperature of 10°C and refrigerated storage at 6°C for 1 hour. The

shaded cells of the table highlight the combinations of temperature and time that present a risk at least two-fold that of re-hydration with a liquid temperature of 10°C and refrigerated storage for 1 hour. This table shows that using re-hydration temperatures of between 40°C and 50°C represent scenarios with the uppermost risk estimates.

Table 2: The risk resulting from storage for a range of refrigerated storage times (1, 2, 4, 8, 12, 24 and 48 hours) at 6°C for 1 hour and a range of temperatures of re-hydrating liquid.

	Re-hydrating liquid temperature (°C)						
Time (hours)	***10°C***	***20°C***	***30°C***	***40°C***	***50°C***	***60°C***	***65°C***
1	**1**	1.8	4.4	10.5	7.4	0.1	<0.01
2	1.1	2.0	5.0	13.9	15.7	1.0	<0.01
4	1.1	2.2	5.9	17.3	20.9	1.5	<0.01
8	1.2	2.3	6.3	19.0	23.2	1.6	<0.01
12	1.3	2.5	6.7	20.3	24.8	1.8	<0.01
24	1.5	3.0	8.2	24.8	30.3	2.2	<0.01
48	2.2	4.3	12.2	37.0	45.3	3.2	<0.01

BRIEF DISCUSSION: INFLUENCE OF TEMPERATURE OF THE RE-HYDRATING LIQUID FOR REFRIGERATED STORAGE

The temperature of the re-hydration liquid influences the risk in two key ways. First, there is the inactivation effect of adding the liquid. At temperatures above 49°C inactivation begins to occur, however, appreciable inactivation occurs above 55°C. Second, the temperature of the re-hydrating liquid influences the temperature-time profile of the prepared formula. The lower the temperature of the re-hydrating fluid, the sooner the formula will reach refrigeration temperatures during cooling such that growth will be minimized. Conversely, the warmer the rehydrating liquid is when added, the longer the formula will provide favourable temperature conditions for growth. Table 3 shows the time the prepared formula will be less than 25°C, between 25 and 49°C and above 49°C. The most favourable range for growth is between 25 and 49°C. From Table 3 it can be seen that the higher the re-hydrating liquid temperature, the longer the period of time spent in the range 25 and 49°C.

Table 3: Period of time (hours) prepared formula will be less than 25°C, between 25 and 49°C and above 49°C – considers preparation, refrigeration at 6°C for 8 hours, warming and feeding.

	Re-hydrating liquid temperature (°C)						
Time (hours)	***10°C***	***20°C***	***30°C***	***40°C***	***50°C***	***60°C***	***65°C***
Temp <25°C	8.56	8.56	8.1	7.66	7.32	7.06	6.94
Temp 25-49°C	4.18	4.18	4.64	5.08	5.38	5.3	5.3
Temp >49°C	0	0	0	0	0.04	0.38	0.5
Total time	12.74	12.74	12.74	12.74	12.74	12.74	12.74

ROOM TEMPERATURE STORAGE

To study the impact of room temperature storage, the relative risk was estimated for storage durations from 1 to 10 hours at a range of room temperatures, specifically 15, 20, 25, 30 and 35°C. This range of room temperatures is considered here to represent a range of possible climates, and therefore variation in room temperatures in which holding may occur. All results are based upon the following preparation conditions, which are constant for all room temperature holding scenarios considered:

- Preparation occurs at room temperature and lasts ¼ hour
- There is no refrigerated cooling or deliberate warming
- Temperature of re-hydrating fluid is 40°C

In these scenarios, each holding temperature has its own baseline scenario (i.e., 1 hour of holding at that temperature is assigned a relative risk of 1). To investigate the impact of storage duration at each room temperature (15, 20, 25, 30 and 35°C) the risk (relative to holding for 1 hour at that temperature) is estimated and presented in Table 4. It can be seen that as the duration of holding increases then so does the risk, with the effect being far more pronounced at warmer room temperatures.

Table 4: Risk posed from holding at room temperature for 1 to 10 hours. Risk estimate is relative to the risk resulting from holding for 1 hour for each room temperature scenario. In this table, the estimates of relative risk are only valid within columns.

	Room Temperature (°C) – liquid mixing temp 40°C				
Time (hours)	***15°C***	***20°C***	***25°C***	***30°C***	***35°C***
1	**1**	**1**	**1**	**1**	**1**
2	2.5	3.6	5.4	7.7	9.1
3	4.8	10.5	24.2	52	78.1
4	8.2	26.8	98.3	337.2	681.9
6	20.3	147.8	$1.4x10^3$	$1.3x10^4$	$5.1x10^4$
8	47.3	762.8	$2.0x10^4$	$5.0x10^5$	$3.9x10^6$
10	108.5	$3.9x10^3$	$2.7x10^5$	$1.9x10^7$	$2.9x10^8$

BRIEF DISCUSSION: ROOM TEMPERATURE STORAGE

During holding at room temperature, the prepared formula is cooling from 40°C until it reaches temperature equilibrium with its surroundings. Therefore, the higher the room temperature, the higher the temperature of the formula will be when equilibrium is reached. This is illustrated in Figure 3. At all temperatures considered, holding for extended times increases the opportunity for growth to occur. At warmer room temperatures, conditions for growth are more favourable, and therefore the extent of growth that may occur is amplified. Both of these factors result in an increase in risk.

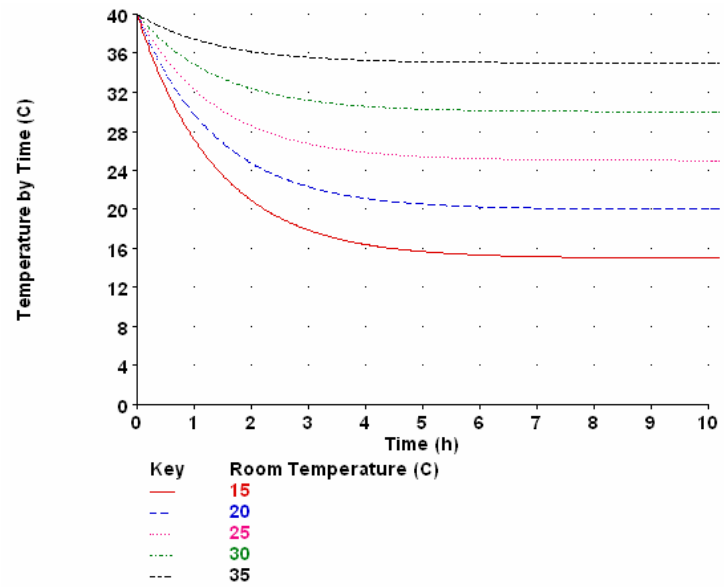

Figure 3: (Note: graph is in colour). Temperature profile of prepared formula held at a range of room temperatures for up to 10 hours, with a re-hydrating liquid temperature of 40 °C.

INFLUENCE OF TEMPERATURE OF THE RE-HYDRATING LIQUID WHILE HOLDING AT ROOM TEMPERATURE

The relative risk estimates presented in Table 4 assumed the liquid used to re-hydrate the formula was at 40°C. However, as for refrigerated storage, the temperature of the re-hydrating fluid influences the overall profile of risk for holding at room temperature. Table 5 shows the relative risk according to the temperature of the re-hydrating liquid and the duration of holding at a room temperature of 25°C. The estimates are relative to the risk following re-hydration with a liquid temperature of 10°C and holding at room temperature (25°C) for 1 hour. The shaded cells of the table highlight the combinations of temperature and time that present a risk at least two-fold greater relative to re-hydration with a liquid temperature of 10°C and holding at room temperature (25°C) for 1 hour. This table shows that re-hydration temperatures of between 40°C and 50°C have the highest associated risk estimates.

Table 5: The risk resulting from holding at room temperature (25°C) for durations of 1, 2, 3, 4, 6, 8, and 10 hours for a range of temperatures of re-hydrating liquid.

	Re-hydrating liquid temperature (°C) – Room temperature 25°C						
Time (hours)	*10°C*	*20°C*	*30°C*	*40°C*	*50°C*	*60°C*	*65°C*
1	1	1	1	1.8	1.1	0.8	0.1
2	1	1.3	3.9	10.5	8.1	0.8	0.1
3	1.5	4.3	15.2	46.7	41.5	1.2	0.1
4	4.9	15.2	58	190.2	180.9	5.4	0.1
6	61.3	200.5	803.8	$2.8x10^3$	$2.8x10^3$	86.4	0.1
8	815.3	$2.7x10^3$	$1.1x10^4$	$3.8x10^4$	$3.8x10^4$	$1.2x10^3$	0.1
10	$1.1x10^4$	$3.6x10^4$	$1.5x10^5$	$5.2x10^5$	$5.2x10^5$	$1.7x10^4$	0.1

BRIEF DISCUSSION: INFLUENCE OF TEMPERATURE OF THE RE-HYDRATING LIQUID: HOLDING AT ROOM TEMPERATURE

The temperature of the re-hydration liquid influences this profile of risk. The warmer the liquid when added, the greater the increase in risk is for longer holding times. During holding at room temperature, the prepared formula will cool or warm to room temperature. At rehydration temperatures that are lower than room temperature, the formula will warm to room temperature. At temperatures greater than room temperature, the formula will cool to room temperature. This is illustrated in Figure 4.

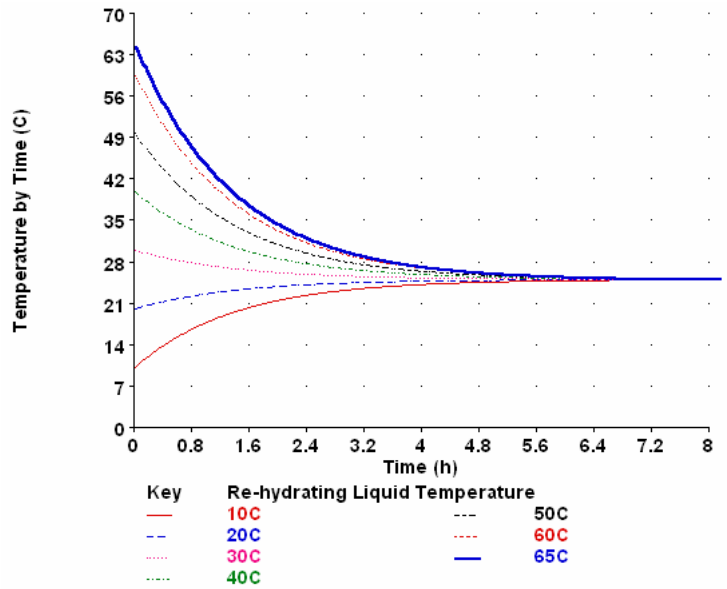

Figure 4: (Note: graph is in colour). Temperature profiles of prepared formula mixed with different re-hydration liquid temperatures held at a room temperature 25°C for 8 hours.

Table 6 shows the duration of time in which prepared formula will be a) less than 25°C, b) between 25 and 49°C and c) above 49°C according to the re-hydration temperatures when formula is held for 8 hours at 25°C. From Table 3 it can be seen that the higher the re-hydrating liquid temperature, the longer the period of time spent in the range of 25 to 49°C, and therefore the greater the opportunity for growth to occur.

Table 6: Period of time (hours) prepared formula will be less than 25°C, between 25 and 49°C and above 49°C when held at a room temperature of 25°C for 8 hours.

	Re-hydrating liquid temperature (°C)						
Time (hours)	***10°C***	***20°C***	***30°C***	***40°C***	***50°C***	***60°C***	***65°C***
Temp <25°C	8.25	8.25	0	0	0	0	0
Temp 25-49°C	0	0	8.25	8.25	8.21	7.73	7.55
Temp >49°C	0	0	0	0	0.04	0.52	0.70
Total time	8.25	8.25	8.25	8.25	8.25	8.25	8.25

SUMMARY

- For refrigeration temperatures of 4 to less than 6°C, storage up to 48 hours has a relatively low impact on risk (i.e., risk increases less than 4-fold). For storage at 6°C for 48 hours the associated risk becomes ~4-fold greater than the risk for storage at 4°C for 1 hour.

- Refrigeration temperatures up to 10°C have a relatively low impact on risk (i.e., less than 4-fold increase) provided storage time is less than 4 hours. Storage for 4 hours at 10°C is associated with a 4-fold increase in risk relative to storage at 4°C for 1 hour.

- Storage at refrigeration temperatures greater than 6°C for extended periods of time generates larger associated risk estimates. Storage for 24 hours at 10 °C is associated with a ~65-fold increase, and storage for 48 hours at 10 °C is associated with a >1,000-fold increase in risk. Note that, in some handling situations, the capacity to cool large volumes of warm liquid may be more important than the temperature of the refrigeration itself. Slow cooling rates combined with warm rehydration represents a relatively high risk scenario.

- Increased periods of holding of prepared formula at room temperature increases the risk significantly. For example, for a room temperature of 25°C the population (and therefore the risk) increases 5-fold with 2 hours of holding, and 24-fold with 3 hours of holding relative to holding for 1 hour. The temperature of the room significantly amplifies this impact of holding time.

- Very warm ambient temperatures combined with the absence of refrigeration, as may be the norm in many developing countries, constitutes a very high (e.g., more than 1000-fold higher) risk scenario, when compared to the combination of moderate room temperatures with refrigerated storage of rehydrated formula. Recommendations for handling would need to consider this distinct high-risk scenario. As an example, much of the excess relative risk can be mitigated by having a correspondingly shorter time between rehydration and consumption.

- The temperature of the re-hydrating liquid influences the profile of risk, with re-hydrating temperatures of 40-50°C having the greater estimates of relative risk (e.g., due to rehydration at near-optimal growth temperatures).

- Risk estimates are sensitive to lag time, growth rate and other predictive microbiology parameters. These parameters remain uncertain due to limited data. However, this report's use of relative risk estimates should limit the impact of this sensitivity.

Annex 2: Concept note for the FAO/WHO consultation on the Development of Practical Risk Management Strategies based on Microbiological Risk Assessment Outputs

Background: In 1999, following the request of the Codex Alimentarius Commission, FAO and WHO began work in the area of microbiological risk assessment (MRA). This new area of work sought to facilitate the development of, and to support new risk management strategies to address the problem of microbiological food safety. Although the previous decade saw great advancement in this area with the application of Good Hygienic Practices (GHPs) and the Hazard Analysis Critical Control Point (HACCP) system these are not always sufficiently effective and new approaches are needed to enhance these systems or support the implementation of other/additional microbiological risk management strategies. For example, the application of HACCP is limited or non-existent in the primary production of food, although the abundance of microbial agents in this environment sometimes seriously endangers product safety. Risk management also needs to provide solutions in this area and this may be achieved through the identification of effective intervention schemes based on risk assessment.

Risk assessment, as a tool, can be used to thoroughly examine a food production system, to give a better insight of its strengths and weaknesses in terms of microbial control and provide an estimate of the risk to the consumer, based on an existing system or as a result of simulated changes to a system. Therefore, as a tool, risk assessment has the potential to allow the user develop targeted and effective risk management strategies.

To date FAO and WHO have jointly developed risk assessments on *Salmonella* in eggs and broiler chickens, *Listeria monocytogenes* in ready-to-eat foods, *Vibrio* spp. in seafood and *Campylobacter* spp. in poultry. These were undertaken in response to specific requests from the Codex Committee on Food Hygiene (CCFH). Despite the fact that the risk assessments have addressed specific questions posed by Codex, the international risk management task to convert the output of these risk assessments into effective risk management strategies has proved to be difficult. There are a number of possible reasons for this. MRA is a new tool and has only recently been used at the national level. This limited experience of its use in countries has hindered the comprehension of how it could be used at the international or Codex level. In the past couple of years some experience has been gained at the international level as efforts to incorporate risk assessment outputs into Codex risk management texts are ongoing. It is now important to learn from this limited experience and aim to develop guidance for the future.

Difficulties also exist because the outputs of MRA are different to those from chemical assessments, which have been underway for many years. The "bright-line" numerical outputs of chemical assessments, often related to a definable levels or doses below which no symptoms appear, are used directly to develop standards. With MRA, dealing with a living agent which can react differently in different conditions, leads to a more complex assessment. MRA can provide a lot of valuable and insightful information but not the "bright-line" numerical outputs many risk managers are familiar with. Compounding this complexity is the fact that for infectious microorganisms no minimum infectious dose applies, even one single organism can cause disease. Some other complicating factors include data gaps relating microbial epidemiology and ecology, and the complexities of the dose-response relationships, influenced by many human and environmental conditions. All these factors have contributed to a basic conceptual problem as to how MRA can be used.

In 2002 FAO and WHO convened a meeting in Kiel[2] to develop guidelines for the Application of Microbiological Risk Assessment in the elaboration of standards, guidelines and related texts. While this meeting provided some very useful outcomes and advice on undertaking risk assessment, primarily because there was some good experience in that area at the national level and a number of lessons had been learned, the outcome in terms of guidance on using the outputs of the risk assessment in risk management was less

[2] FAO/WHO, 2002. Principles and guidelines for incorporating microbiological risk assessment in the development of food safety standards, guidelines and related texts. Report of a Joint FAO/WHO Consultation, 18 – 22 March 2002, Kiel, Germany.

concrete. Also, the present Codex draft Principles and Guidelines for Microbiological Risk Management[3] despite their significant merits and developmental benefits, do not provide specific and useful practical guidance.

The struggle at both the national and international levels to effectively and efficiently use microbiological risk assessment as a tool to support risk management has highlighted the need to revisit this area in more detail and to look at the experiences in the countries that are using MRA with the objective of developing practical guidance that would facilitate the work of national and international risk managers.

Purpose and scope: This consultation aims to delineate the different ways in which MRA can contribute to the enhancement of current, or the development of new and effective risk management strategies for implementation at different steps along the food chain. The final output of the meeting will be a guidance document for the preparation of risk management strategies using MRA and associated scientific information that would serve both national and international microbiological risk management.

In doing the above a number of issues, as mentioned below, will have to be considered.

- What difficulties or stumbling blocks have been encountered so far in developing practical Risk Management (RM) Guidance based on the outputs of MRA and associated or relevant scientific information? What is missing? What can be done to overcome these?

- What kind of risk management actions can be developed using MRA in combination with other scientific and technological information.

- How can MRA be used together with other RM support tools to develop better risk management strategies at practical level such as Codes of Hygienic Practice and HACCP systems with interventions for risk reduction at primary production and processing level?

- MRAs are developed both nationally and internationally. While national or one country risk assessments are usually for use only in that country, international risk assessments preferably should be set up to be used both at the international level by Codex and at country level, although not necessarily in the same way. Therefore the consultation will also examine how a risk assessment can be used under different circumstances as the basis for risk management actions. (See Figure 1)

- Due to regional, cultural and geographical differences across the world, risk management guidance produced, particularly at the international level will have limitations in terms of its specificity and is usually more generic in nature. Therefore, the risk management guidance will need to be adapted to country or regional situations. The level of adaptation required will vary depending on the specificity of the guidance document. How can MRA and other scientific information be used to make such management guidance as useful as possible and facilitate its adaptation at the national level?.

- MRAs may be qualitative or quantitative in nature so it will be necessary to consider how the type of MRA will impact the way it is used in risk management. The same question applies to the use of information from Risk Profiles as a basis for microbiological risk management.

- Technical and economic feasibility and data availability are also issues that have to be considered in the risk management process. While this is recognized the current consultation will not address these in detail but focus on the optimal use of MRA outputs and associated scientific information in developing risk management strategies.

[3] Proposed Draft Principles and Guidelines for the Conduct of Microbiological Risk Management (MRM), Codex Committee on food Hygiene, 37th Session Buenos Aries, Argentina, 14- 19 March 2005 (CX/FH 05/37/6)

Figure 1: Practical Guidance for Risk Management at national and international level, based on interactive application of MRA