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DECLARATIONS OF INTEREST

Two out of the 16 experts which participated in this meeting declared an interest in the topics under consideration:

Dr Forsythe: His research is related to a commercially available tool for diagnosis of *Enterobacter sakazakii* in infant formula.

Dr Zwietering: His unit at the University of Wageningen performs scientific research which is financially supported by a company producing powdered infant formula.

FOREWORD

The Members of the Food and Agriculture Organization of the United Nations (FAO) and of the World Health Organization (WHO) have expressed concern regarding the level of safety of food at both national and international levels. Increasing food-borne disease incidence over the last decades seems, in many countries, to be related to an increase in disease caused by microorganisms in food. This concern has been voiced in meetings of the Governing Bodies of both Organizations and in the Codex Alimentarius Commission. It is not easy to decide whether the suggested increase is real or an artefact of changes in other areas, such as improved disease surveillance or better detection methods for microorganisms in foods. However, the important issue is whether new tools or revised and improved actions can contribute to our ability to lower the disease burden and provide safer food. Fortunately new tools which can facilitate actions seem to be on their way.

Over the past decade, risk analysis – a process consisting of risk assessment, risk management and risk communication – has emerged as a structured model for improving our food control systems with the objectives of producing safer food, reducing the numbers of food-borne illnesses and facilitating domestic and international trade in food. Furthermore, we are moving towards a more holistic approach to food safety, where the entire food chain needs to be considered in efforts to produce safer food.

As with any model, tools are needed for the implementation of the risk analysis paradigm. Risk assessment is the science-based component of risk analysis. Science today provides us with in-depth information on life in the world we live in. It has allowed us to accumulate a wealth of knowledge on microscopic organisms, their growth, survival and death, even their genetic make-up. It has given us an understanding of food production, processing and preservation, and of the link between the microscopic and the macroscopic world and how we can benefit from as well as suffer from these microorganisms. Risk assessment provides us with a framework for organizing all this data and information and to better understand the interaction between microorganisms, foods and human illness. It provides us with the ability to estimate the risk to human health from specific microorganisms in foods and gives us a tool with which we can compare and evaluate different scenarios, as well as identify the types of data necessary for estimating and optimizing mitigating interventions.

Microbiological risk assessment (MRA) can be considered as a tool that can be used in the management of the risks posed by food-borne pathogens and in the elaboration of standards for food in international trade. However, undertaking a microbiological risk assessment, particularly quantitative MRA, is recognized to be a resource-intensive task requiring a multidisciplinary approach. Yet food-borne illness is one of the most widespread public health problems, creating social and economic burdens as well as human suffering, making it a concern that all countries need to address. As risk assessment can also be used to justify the introduction of more stringent standards for imported foods, a knowledge of MRA is important for trade purposes, and there is a need to provide countries with the tools for understanding and, if possible, undertaking MRA. This need,

combined with that of the Codex Alimentarius for risk-based scientific advice, led FAO and WHO to undertake a programme of activities on MRA at international level.

The Food Quality and Standards Service, FAO, and the Food Safety Department, WHO, are the lead units responsible for this initiative. The two groups have worked together to develop the area of MRA at international level for application at both national and international level. This work has been greatly facilitated by the contribution of people from around the world with expertise in microbiology, mathematical modelling, epidemiology and food technology, to name but a few.

This Microbiological Risk Assessment Series provides a range of data and information to those who need to understand or undertake MRA. It comprises risk assessments of particular pathogen-commodity combinations, interpretative summaries of the risk assessments, guidelines for undertaking and using risk assessment, and reports addressing other pertinent aspects of MRA.

We hope that this series will provide a greater insight into MRA, how it is undertaken and how it can be used. We strongly believe that this is an area that should be developed in the international sphere, and have already from the present work clear indications that an international approach and early agreement in this area will strengthen the future potential for use of this tool in all parts of the world, as well as in international standard setting. We would welcome comments and feedback on any of the documents within this series so that we can endeavour to provide member countries, Codex Alimentarius and other users of this material with the information they need to use risk-based tools, with the ultimate objective of ensuring that safe food is available for all consumers.

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ABBREVIATIONS

a_w	Water activity
BAM	Bacteriological Analytical Manual (USFDA)
BfR	Federal Institute for Risk Assessment (Germany)
BHI	Brain Heart Infusion
BPW	Buffered peptone water
BSI	Bloodstream infection
CAC	Codex Alimentarius Commission
CCFH	Codex Committee on Food Hygiene
CCNFSDU	Codex Committee on Nutrition and Foods for Special Dietary Uses
CCP	Critical control point
cfu	Colony forming unit
EE	*Enterobacteriaceae* enrichment
FAO	Food and Agriculture Organization of the United Nations
FSMP	Formula for special medical purposes
g	Gram(s)
GHP	Good hygienic practice
GMP	Good manufacturing practice
HACCP	Hazard Analysis Critical Control Point (System)
HEPA	High efficiency particle air
HIV	Human immunodeficiency virus
ISO	International Organization for Standardization
JEMRA	Joint FAO/WHO Expert Meetings on Microbiological Risk Assessment
LBW	Low birth weight
MPN	Most probable number
MRA	Microbiological risk assessment
NEC	Necrotizing enterocolitis
NGO	Non-governmental organization
PC	Contamination from the infant formula
PE	Contamination from the environment
PFGE	Pulsed field gel electrophoresis
PIF	Powdered infant formula
RAPD	Random amplified polymorphic DNA
RCP	Recommended Code of Practice
RIVM	National Institute of Public Health and the Environment (the Netherlands)
SIDS	Sudden infant death syndrome
TTC	Time to consumption
ULPA	Ultra low particle air
USFDA	United States Food and Drug Administration
VHPSS	Victorian Hospital Pathogen Surveillance Scheme
VLBW	Very low birth weight
VRBG	Violet red bile glucose
WHO	World Health Organization

EXECUTIVE SUMMARY

Consistent with the need to provide safe feeding for all infants,[1] the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) jointly convened an expert meeting on *Enterobacter sakazakii* and other microorganisms in powdered infant formula (WHO, Geneva, 2-5 February 2004). The meeting was organized in response to a specific request to FAO/WHO for scientific advice from the Codex Committee on Food Hygiene to provide input for the revision of the Recommended International Code of Hygienic Practice for Foods for Infants and Children. It also aimed to provide pertinent information to the member countries of both organizations.

After reviewing the available scientific information, the expert meeting concluded that intrinsic contamination of powdered infant formula with *E. sakazakii* and *Salmonella* has been a cause of infection and illness in infants, including severe disease which can lead to serious developmental sequelae and death. No link has been established between illness and other microorganisms in powdered infant formula, although such a link was considered plausible for other Enterobacteriaceae.

E. sakazakii has caused disease in all age groups. From the age distribution of reported cases, it is deduced that infants (children <1 year) are at particular risk. Among infants, those at greatest risk for *E. sakazakii* infection are neonates (≤28 days), particularly pre-term infants, low-birth-weight infants or immunocompromised infants. Infants of HIV-positive mothers are also at risk, because they may specifically require infant formula and they may be more susceptible to infection.[2] This, and low birth weight, may be of particular concern for some developing countries where the proportion of such infants is higher than in developed countries.

It is important to note that powdered infant formula meeting current standards is not a sterile product and may occasionally contain pathogens. The meeting did not identify a feasible method, using current technology, to produce commercially sterile powders or completely eliminate the potential of contamination.

E. sakazakii is an opportunistic pathogen emerging as a public health concern. Little is known about its ecology, taxonomy, virulence and other characteristics. Recent data, however, point to differences in the microbial ecology of *Salmonella* and *E. sakazakii*.

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[1] As a global public health recommendation, infants should be exclusively breastfed for the first 6 months of life to achieve optimal growth, development and health. Thereafter, to meet their evolving nutritional requirements, infants should receive nutritionally adequate and safe complementary foods while breastfeeding continues until up to 2 years of age or beyond. Infants who are not breastfed require a suitable breastmilk substitute, for example an infant formula prepared in accordance with applicable Codex Alimentarius standards. Information provided in this connection to mothers and other family members who need to use it should include adequate instructions for appropriate preparation and the health hazards of inappropriate preparation and use (WHO, 2002).

[2] The UN guidance for these infants is that where replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding is recommended, and powdered infant formula may be an option. Some of these infants may be HIV-positive and thus immunocompromised.

Data from the infant food industry and national control authorities indicate that the detection of *Salmonella* in finished powdered infant formula is rare. The current Codex specification for *Salmonella* is the absence of organisms in 60 samples of 25 g each. *E. sakazakii* is more commonly found than *Salmonella* in the manufacturing environment, which is a potential source of post-heat-treatment contamination. Specific criteria for *E. sakazakii* are not included in the current Codex Code.

Even low levels of contamination of *E. sakazakii* in powdered infant formula were considered to be a risk factor, given the potential for multiplication during the preparation and holding time prior to consumption of reconstituted formula.

Based on a preliminary risk assessment, the inclusion of a lethal step at the point of preparation and a decrease in the holding and feeding times effectively reduced risk. A combination of intervention measures had the greatest impact.

Summary of recommendations

The expert meeting made recommendations to FAO, WHO, Codex, their member countries, NGOs and the scientific community. These are summarized below.

- In situations where infants are not breastfed, caregivers, particularly of infants at high risk, should be regularly alerted that powdered infant formula is not a sterile product and can be contaminated with pathogens that can cause serious illness; they should be provided with information that can reduce the risk.

- In situations where infants are not breastfed, caregivers of high-risk infants, should be encouraged to use, whenever possible and feasible, commercially sterile liquid formula or formula which has undergone an effective point-of-use decontamination procedure (e.g. use of boiling water to reconstitute or by heating reconstituted formula).[3]

- Guidelines should be developed for the preparation, use and handling of infant formula to minimize risk.

- The infant food industry should be encouraged to develop a greater range of commercially sterile alternative formula products for high-risk groups.

- The infant food industry should be encouraged to reduce the concentration and prevalence of *E. sakazakii* in both the manufacturing environment and powdered infant formula. To this end, the infant food industry should consider implementing an effective environmental monitoring programme and the use of Enterobacteriaceae rather than coliform testing as an indicator of hygienic control in factory production lines.

[3] Nutritional and other factors need to be considered, e.g. alteration of nutritional content, risk from burns due to handling boiling or hot water/formula, and potential for germination of bacterial spores. The formula should thereafter be cooled and handled appropriately.

- In revising its code of practice, Codex should better address the microbiological risks of powdered infant formula and, if deemed necessary, include the establishment of appropriate microbiological specifications for *E. sakazakii* in powdered infant formula.

- FAO/WHO should address the particular needs of some developing countries and establish effective measures to minimize risk in situations where breastmilk substitutes may be used in exceptionally difficult circumstances, e.g. feeding infants of HIV-positive mothers or low-birth-weight infants.

- The use of internationally validated detection and molecular typing methods for *E. sakazakii* and other relevant microorganisms should be promoted.

- Investigation and reporting of sources and vehicles, including powdered infant formula, of infection by *E. sakazakii* and other Enterobacteriaceae should be encouraged. This could include the establishment of a laboratory-based network.

- Research should be promoted to gain a better understanding of the ecology, taxonomy, virulence and other characteristics of *E. sakazakii* and of ways to reduce its levels in reconstituted powdered infant formula.