

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



DISTRICT II NEW YORK STATE

BOARD OF DIRECTORS

District Chairperson
Henry Schaeffer, MD
Brooklyn, NY

District Vice Chairperson
Danielle Laraqe, MD
New York, NY

District Treasurer
Anne Francis, MD
Rochester, NY

National Nominating Committee
Paul Yellin, MD
New York, NY

Chapter Forum Representative
Sanford Mayer, MD
Rochester, NY

President, NY Chapter 1
Jacob Felix, MD
Horseheads, NY

Vice President, NY Chapter 1
Jonathan Klein, MD
Rochester, NY

President, NY Chapter 2
Anthony Battista, MD
Mineola, NY

Vice President, NY Chapter 2
Ishvar S. Patel, MD
Flushing, NY

President, NY Chapter 3
Benard Dreyer, MD
New York, NY

Vice President, NY Chapter 3
Sheila L. Palevsky, MD, MPH
New York, NY

DISTRICT OFFICES

Executive Director
George Dunkel
Email: gdunkel@aap.org

□ 240 Washington Ave. Ext.
Suite 505
Albany, NY 12203
Phone: 518/456-0951
Fax: 518/456-8573

Administrative Coordinator
Jessica Geslani
Email: jgeslani@aap.org

□ 420 Lakeville Road
Suite 244
Lake Success, NY 11042
Phone: 516/326-0310
Fax: 516/326-0316

<http://www.aapdistrictii.org>

April 11, 2007

Rena Bryant
Secretary to the Board of Health
Board of Health
Department of Health and Mental Hygiene
125 Worth Street CN-31
New York, NY 10013

Dear Secretary Bryant:

We applaud the revision of the New York City Health Code Article 115 to reflect current guidelines for the preparation of prescription formulae as described in *Infant Feedings: Guidelines for Preparation of Formula and Breast Milk in Health Care Facilities*, Pediatric Nutrition Practice Group, American Dietetic Association, 2004, and as regulated by the United States Food and Drug Administration.

Prescriptions for such special formulae may be written by those health care providers who are authorized to write prescriptions by the New York State Department of Education which, to our understanding, does not include dietitians.

We look forward to continuing our collaboration with the New York City Department of Health and Mental Hygiene. Please feel free to contact us at any time.

Sincerely,

Benard P. Dreyer, MD
President, NY Chapter 3

Anthony J. Battista, MD
President, NY Chapter 2

Sheila L. Palevsky MD, MPH
Vice President, NY Chapter 3

Ishvar S. Patel, MD
Vice President, NY Chapter 2



2

ROSS PRODUCTS DIVISION • ABBOTT LABORATORIES

625 CLEVELAND AVENUE • COLUMBUS, OHIO 43215-1724 • (614) 624-7677

April 18, 2007

Ms. Rena Bryant
Secretary to the Board of Health, New York City
125 Worth Street CN-31
New York, NY 10013

Re: Proposed repeal and reenactment of Article 115 of the New York City Health Code

Dear Ms. Bryant:

We applaud the Board of Health for moving to update Article 115 of the New York City Health Code. While Article 115 had been amended since its first publication, it did not reflect current recommendations and standards of practice regarding the preparation and handling of specialized formula products.

Abbott's Ross Products Division manufactures a wide range of nutritional formula products in both powdered and liquid forms, for use by infants, children, and adults. As a manufacturer we do not recommend that terminal heating or pasteurization be used in the routine preparation of any of our nutritional products. This same recommendation is reflected in the most recent 2004 guidelines of the American Dietetic Association for institutional infant feeding preparation. The excessive heat used in terminal pasteurization can cause physical and chemical changes, which may compromise product quality as well as lead to potential nutrient losses.

Therefore, we recommend that section 115.21(d) of the proposed provisions of Article 115 be changed as follows:

"Containers of prescription formula shall be sterilized in an autoclave unless the physician or dietitian's order states that such formula shall not be sterilized or if the label on a container of a commercially manufactured infant formula base advises that such formula should not be sterilized after preparation per manufacturer's recommendation it is advised formula shall not be sterilized after preparation."

Thank you for your consideration of this change. We would be happy to discuss it with you further.

Sincerely,

Mary Beth Arensberg, PhD, RD, LD
Director, Health Policy and Programs

Martha Robinson

From: Michelle Robinson
Sent: Wednesday, April 18, 2007 1:11 PM
To: Ming-Chin Yeh
Cc: Rena Bryant; Martha Robinson
Subject: RE: Proposal to amend Article 115 of the New York City Health Code
Importance: High

Thank you very much for your comment.

From: Ming-Chin Yeh [mailto:myeh@hunter.cuny.edu]
Sent: Wednesday, April 18, 2007 12:43 PM
To: Michelle Robinson
Subject: RE: Proposal to amend Article 115 of the New York City Health Code

Hi- I am delighted to see that in the proposal, dietitians, in addition to physicians, are allowed to make nutrition prescriptions. People with a RD (Registered Dietitian) credential have in-depth nutritional knowledge. In my opinion they are well qualified to perform this task.

Thanks for providing me an opportunity to review the proposal.

Best,
Ming

Ming-Chin Yeh, PhD
Assistant Professor
Nutrition and Food Science Track
Program in Urban Public Health
Hunter College, City University of New York
425 East 25th street
New York, NY 10010
212-481-4134
myeh@hunter.cuny.edu

5

From: Alice Lenihan [mailto:Alice.Lenihan@ncmail.net]
Sent: Friday, April 20, 2007 1:33 PM
To: Lauren Kotch
Cc: Noble, Larry
Subject: Re: Fwd: Re: Proposal to amend Article 115 of the New York City Health Code

I did review the Code change recommendation and it looks like they were going to allow the formula post preparation 48 hours before destroying. We typically say destroy within 24 hours. The American Dietetic Association group will be looking at what may need revision in their guidelines document. At this point USDA does not provide any guidance on use of powdered formula for VLBW or immune compromised infants.

I have attached a new WHO document on powdered infant formula. Maybe we can discuss this issue when we meet next weekend.

Alice

**Safe preparation, storage and
handling
of powdered infant formula**

GUIDELINES

World Health Organization
in collaboration with
Food and Agriculture Organization of the United Nations
2007

CONTENTS

Executive Summary	iii
Acknowledgements	v

PART 1: INTRODUCTION

1.1	Background	1
1.2	Illness associated with PIF	1
1.2.1	<i>E. sakazakii</i>	2
1.2.2	<i>Salmonella</i>	2
1.3	Populations at greatest risk of infection	3
1.4	Contamination of PIF	3
1.5	Breastfeeding recommendation	4
1.6	Purpose	4
1.7	Scope	5
1.8	Assumptions behind the recommendations	5
1.9	Training	6

PART 2: IN CARE SETTINGS

2.1	Recommendations	7
2.1.1	<i>Use of infant formula</i>	7
2.1.2	<i>General requirements</i>	7
2.1.3	<i>Cleaning and sterilization of feeding and preparation equipment</i>	8
2.1.4	<i>Preparing a feed using PIF</i>	8
2.1.5	<i>Preparing feeds in advance for later use</i>	9
2.1.6	<i>Re-warming stored feeds</i>	10
2.1.7	<i>Transporting feeds</i>	10
2.1.8	<i>Holding and feeding times</i>	10
2.2	Rationale behind recommendations	11
2.2.1	<i>Choice of infant formula</i>	11
2.2.2	<i>General requirements</i>	11
2.2.3	<i>Good hygienic practice</i>	11
2.2.4	<i>Cleaning and sterilizing feeding and preparation equipment</i>	11
2.2.5	<i>Temperature of reconstitution water</i>	12
2.2.6	<i>Volume of container for preparing batches</i>	12
2.2.7	<i>Holding and feeding times</i>	12

2.2.8	<i>Labelling of feed</i>	13
2.2.9	<i>Storage of prepared feeds</i>	13
2.2.10	<i>Re-warming stored feeds</i>	13
2.2.11	<i>Transporting prepared feeds</i>	13

PART 3: IN THE HOME

3.1	Recommendations	15
3.1.1	<i>Cleaning and sterilizing feeding and preparation equipment</i>	15
3.1.2	<i>Preparing a feed using powdered infant formula</i>	16
3.1.3	<i>Preparing feeds in advance for later use</i>	16
3.1.4	<i>Re-warming stored feeds</i>	17
3.1.5	<i>Transporting feeds</i>	17
3.2	Rationale behind recommendations	17
3.2.1	<i>Good hygienic practice</i>	17
3.2.2	<i>Cleaning and sterilizing feeding and preparation equipment</i>	18
3.2.3	<i>Temperature of water for reconstitution</i>	18
3.2.4	<i>Storage of prepared feeds</i>	18
3.2.5	<i>Re-warming and use of stored feeds</i>	19
3.2.6	<i>Transporting feeds</i>	19
3.2.7	<i>Holding and feeding times</i>	19
	Appendix 1	21
	Appendix 2	23
	Appendix 3	25
	References cited in the text	27

EXECUTIVE SUMMARY

Powdered infant formula (PIF) has been associated with serious illness and death in infants due to infections with *Enterobacter sakazakii*. During production, PIF can become contaminated with harmful bacteria, such as *Enterobacter sakazakii* and *Salmonella enterica*. This is because, using current manufacturing technology, it is not feasible to produce sterile PIF. During the preparation of PIF, inappropriate handling practices can exacerbate the problem.

Recognizing the need to address such hazards in PIF, Codex Alimentarius decided to revise the Recommended International Code of Hygienic Practice for Foods for Infants and Children. In doing so it requested specific scientific advice from the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO). FAO and WHO have provided this advice in the reports of two expert meetings held in 2004 and 2006 on *Enterobacter sakazakii* and other microorganisms in powdered infant formula (PIF). Part of this advice included recommendation to develop guidelines for the preparation of PIF.

The World Health Assembly (WHA) of WHO requested in 2005 the Organization to develop such guidelines on the safe preparation, handling and storage of PIF in order to minimize the risk to infants.

The FAO/WHO advice on *E. sakazakii* in PIF includes a quantitative microbiological risk assessment of *E. sakazakii* in PIF. One of the aspects of the risk assessment was to determine relative risk reduction associated with different preparation, storage and handling scenarios. The recommendations made in the present guideline document are largely based on the findings of the quantitative risk assessment. No risk assessment was carried out for *Salmonella*, but the group reported that the basic risk control principles for *E. sakazakii* would also hold true for *S. enterica*.

In general, sterile liquid infant formula is recommended for infants at the highest risk of infection. Where sterile liquid infant formula is not available, preparation of PIF with water at a temperature of no less than 70 °C dramatically reduces the risk. Minimizing the time from preparation to consumption also reduces the risk, as does storage of prepared feed at temperatures no higher than 5 °C.

Users of PIF are made aware that powdered infant formula is not a sterile product and may be contaminated with pathogens that can cause serious illness. Correct preparation and handling of PIF reduces the risk of illness.

The present guidelines are presented in two parts. One part provides guidance for the preparation of PIF in care settings where professional care providers are involved in the preparation of large quantities of PIF for a large number of infants. The second part provides guidance for the preparation of PIF in a home environment, aimed at parents and those involved in the care of infants in the home environment.

The document provides specific guidance on the most appropriate practices in the different steps during the preparation of PIF in these two types of settings. Cleaning and sterilization of feeding and preparation equipment is an important prerequisite to the safe preparation of PIF. The specific guidance focuses on the most important parameters during preparation such as the temperature of reconstitution, the cooling, holding and feeding times,

as well as the storage and transportation of prepared PIF. The rationale behind the recommendations is provided in both sets of guidance.

ACKNOWLEDGEMENTS

The World Health Organization would like to express its appreciation to all those who contributed to the preparation of these guidelines. Special appreciation is extended to the Food Safety Authority of Ireland and particularly to Judith O'Connor and Alan Reilly for their time, efforts and expertise provided in the elaboration of these guidelines. Appreciation is also extended to the many people in more than 20 countries as well as several stakeholder associations who have provided their comments and suggestion following a call for comments issued through the International Food Safety Authorities Network (INFOSAN).

The preparation of these Guidelines was coordinated by WHO in collaboration with FAO, with contributions from Peter Karim Ben Embarek, Jaap Jansen, Margaret Miller, Jenny Bishop, Janis Bernat, Françoise Fontannaz and Jørgen Schlundt in WHO, with Sarah Cahill and Maria de Lourdes Costarrica in FAO.

PART 1: INTRODUCTION

1.1 Background

In 2004, the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) met jointly in Geneva to convene an expert meeting on *Enterobacter sakazakii* and other microorganisms in powdered infant formula (PIF). This meeting was organized in response to a request from the Codex Committee on Food Hygiene (CCFH) for input into the revision of the Recommended International Code of Hygienic Practice for Foods for Infants and Children (CAC, 1979).

Based on the literature reviewed, the expert meeting concluded that *E. sakazakii* and *Salmonella enterica* were the organisms of most concern in PIF. The expert meeting conducted a preliminary risk assessment for *E. sakazakii*, which established that the inclusion of a pathogenic lethal step at the point of preparation (e.g. reconstituting PIF with water at no less than 70 °C) and a decrease in the holding time and feeding times would effectively reduce risk. Based on this preliminary risk assessment, the expert group made recommendations to FAO, WHO, Codex, member countries, nongovernmental organizations and the scientific community for minimizing the risk (Appendix 1). One recommendation was that “Guidelines should be developed for the preparation, use and handling of infant formula to minimize the risk”.

The World Health Assembly (WHA) of WHO, in 2005, in its Resolution WHA 58.32 (WHA, 2005), requested the Organization to develop such guidelines on the safe preparation, handling and storage of PIF in order to minimize the risk to infants.

A second meeting of the FAO/WHO expert group was convened in January 2006, to address additional requests from the CCFH taking into consideration new scientific data (on *E. sakazakii* and *S. enterica*), and to apply a quantitative microbiological risk assessment model for *E. sakazakii* in PIF. This model had been developed since the first meeting in 2004. One of the aspects of the risk assessment was to determine relative risk reduction associated with different preparation, storage and handling scenarios. The recommendations made in this guidance document are largely based on the findings of the quantitative risk assessment.

No risk assessment was carried out for *Salmonella*, but the group reported that the basic risk control principles for *E. sakazakii* would also hold true for *S. enterica*. However, the specific risk reductions achieved would vary to some degree, based on the mode and sources of *Salmonella* contamination and its growth and survival characteristics.

A first draft of the present guidelines was developed based on existing national guidelines and on the outcome of the risk assessment. Extensive consultation on the draft guidelines was undertaken through the International Food Safety Authorities Network (INFOSAN). Comments received from more than 20 INFOSAN Member countries and International Organizations representing stakeholders were considered and appropriate modifications were made to the draft guidelines.

1.2 Illness associated with PIF

PIF is not a sterile product, even if it has been manufactured to meet current hygiene standards. This means that it may occasionally contain pathogens that can cause serious illness.

The FAO/WHO expert working groups (2004 & 2006) concluded that *E. sakazakii* and *Salmonella enterica* are the pathogens of most concern in PIF. Severe illness and sometimes death in infants has been attributed to PIF that has been contaminated with *E. sakazakii* or *Salmonella*, at either the manufacturing or preparation stage. Because the manufacture of commercially sterile PIF is not feasible using current processing technology, there is a potential risk of infection to infants through consumption of PIF. This risk is increased when prepared feeds are handled or stored incorrectly.

Extrinsic contamination of PIF is possible from the person preparing the formula and the environment the formula is prepared in. Specific food hygiene control measures have been included in these guidelines to help address these issues.

1.2.1 *E. sakazakii*

E. sakazakii was first implicated in a case of neonatal meningitis in 1958, and since then there have been around 70 reported cases of *E. sakazakii* infection (Drudy et al., 2006). However, it is likely that *E. sakazakii* is significantly under-reported in all countries. Although *E. sakazakii* can cause illness in all age groups, infants are believed to be at greatest risk of infection.

In 2004, PIF was microbiologically linked to two *E. sakazakii* outbreaks, in New Zealand and in France (FAO/WHO, 2006). The French outbreak involved nine cases, and resulted in the death of two infants. While eight of the cases were in premature infants of low birth weight (<2 kg), one case was in an infant born at 37 weeks and weighing 3.25 kg. The outbreak involved five hospitals, and a review of practices in the hospitals revealed that one hospital was not following recommended procedures for the preparation, handling and storage of feeding bottles, and four were storing reconstituted formula for >24 hours in domestic-type refrigerators, with no temperature control or traceability.

Limited information was available on the numbers of *E. sakazakii* organisms that ill patients were exposed to in any of the various outbreaks. It is therefore not possible to develop a dose-response curve for *E. sakazakii* (FAO/WHO, 2006). However, it is possible that a small number of cells present in PIF could cause illness. This risk increases rapidly when bacteria in the reconstituted formula are allowed to multiply, such as by holding at inappropriate temperatures for an extended period.

In the United States of America, an incidence rate of 1 per 100 000 infants for *E. sakazakii* infection has been reported. This incidence rate increases to 9.4 per 100 000 in infants of very low birth weight, i.e. <1.5 kg (FAO/WHO, 2006).

1.2.2 *Salmonella*

At least six PIF-associated salmonellosis outbreaks have been described since 1995, across Canada, France, Korea, Spain, UK and USA (FAO/WHO, 2006). The most recent was an outbreak of *S. agona* that occurred in France in 2005. This outbreak involved 141 infants, all of whom were under 12 months of age.

Although the infectious dose for infants, or specific groups of infants, is not known, information from outbreak investigations indicates that at least some *Salmonella* serotypes have potential to cause illness at very low doses. This may be a specific concern for infants, particularly those in the higher susceptibility category (premature; low birth weight; immunocompromised).

The United States of America reported a salmonellosis incidence rate of 139.4 cases per 100 000 infants in 2002. The incidence rate for infants was more than eight times higher than that of the general population (16.2 per 100 000) (CDC, 2002).

1.3 Populations at greatest risk of infection

Although *E. sakazakii* can cause illness in all age groups, infants (children <1 year) are at most risk with neonates and infants under two months at greatest risk. The groups of infants at greatest risk includes in particular pre-term infants, low-birth-weight (<2.5 kg) infants or immunocompromised infants. However, infants who are compromised for any other reason may also be at greater risk of *E. sakazakii* infection. Infants of HIV-positive mothers are also at risk because they may be immunocompromised and may specifically require PIF (FAO/WHO, 2004). There appear to be two distinct infant risk groups for *E. sakazakii* infection: premature infants who develop bacteraemia after one month of age, and term infants who develop meningitis during the neonatal period. Therefore, the FAO/WHO expert working group (2006) concluded that while infants appear to be the group at particular risk, neonates and also those less than two months of age are at greatest risk (FAO/WHO, 2006).

It is very important to note that, although high-risk groups of infants have been identified, *E. sakazakii* infection has occurred in previously healthy infants outside the neonatal period (Gurtler, Kornacki and Beuchat, 2005). Furthermore, infections have occurred in both hospital and outpatient settings. For this reason, educational messages on the safe preparation and handling of PIF are required for health-care workers, parents and other infant carers.

In the case of salmonellosis, infants are more likely than the general population to experience severe illness or death. Immunocompromised infants are particularly vulnerable. While infants who are breastfed are 50% less likely to contract salmonellosis, a few reports have described the transmission of *Salmonella* via expressed breast milk (FAO/WHO, 2006).

1.4 Contamination of PIF

Current manufacturing processes cannot achieve the production of sterile PIF. Contamination of PIF with *E. sakazakii* and *Salmonella* can occur intrinsically, or from extrinsic sources. Intrinsic contamination occurs at some stage during its manufacture (e.g. from the manufacturing environment, or from raw ingredients).

Recent data point to differences in the microbial ecology of *Salmonella* spp. and *E. sakazakii*. *E. sakazakii* is more commonly found in the manufacturing environment than *Salmonella*. Surveys have identified *E. sakazakii* in 3–14% of PIF samples (FAO/WHO, 2006), but the levels of contamination reported have been low: 0.36–66.0 cfu/100 g (Forsythe, 2005). In contrast, *Salmonella* is rarely found in PIF. In one survey, no *Salmonella* were found in samples from 141 different formulas (Muytjens, Roelofs-Willemsse and Jasper, 1988). The current Codex specification for *Salmonella* is the absence of organisms in 60 samples of 25 g each. Specific criteria for *E. sakazakii*, however, are not included, but come under the general category of coliforms (CAC, 1979). The standard requires a minimum of 4 to 5 samples with <3 coliforms/g and a maximum of 1 in 5 control samples with levels >3 but <20 coliforms/g. This is currently under review in the Codex Committee on Food Hygiene.

Extrinsic contamination can occur when contaminated utensils (e.g. spoons, blenders, bottles, teats) are used for preparing or feeding PIF, or contamination may occur from the preparation environment.

While *E. sakazakii* and *Salmonella* do not grow in dry PIF, they can survive for long periods. *E. sakazakii* has been shown to survive up to and beyond one year in dry PIF (Forsythe, 2005). Reconstituted PIF, however, provides an ideal environment for the growth of pathogens. Storage of reconstituted PIF at temperatures not more than 5 °C will prevent the growth of *Salmonella* and *E. sakazakii*. However, held above this temperature (e.g. at room temperature), there is the potential for rapid growth of *E. sakazakii* or *Salmonella*, particularly if held for extended periods.

1.5 Breastfeeding recommendation

WHO recommends that infants should be exclusively breastfed for the first six 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 for up to two years of age or beyond (WHO/UNICEF, 2003).

It is important to support breastfeeding and promote its benefits to infants and young children. There are, however, instances where breast milk is not available, where the mother is unable to breastfeed, where they have made an informed decision not to breastfeed, or where breastfeeding is not appropriate, e.g. where the mother is taking medication that is contraindicated for breastfeeding or the mother is HIV-positive.¹ Similarly, some very low-birth-weight babies may not be able to breastfeed directly, and in some cases expressed breast milk may not be available at all or available in insufficient quantities.

Infants who are not breastfed require a suitable breast-milk substitute, for example, an infant formula prepared in accordance with the present guidelines.

1.6 Purpose

The purpose of this document is to deliver recommendations on the safe preparation, storage and handling of PIF, in order to reduce the risk of infection from *E. sakazakii* and *S. enterica*. In principle, infant formula should be used only when medically indicated² in accordance with the 10 Steps of the WHO/UNICEF Baby-Friendly Hospital Initiative (BFHI) (Appendix 2).

These present guidelines are considered to be a generic document that will provide guidance and support for countries and governments. When adapted at the country level, conditions (i.e. climatic and socioeconomic differences, etc.) within the country should be

¹ Exclusive breastfeeding is recommended for HIV-infected women for the first 6 months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants before that time. When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected women is recommended. http://www.who.int/child-adolescent-health/publications/NUTRITION/consensus_statement.htm

² The marketing of PIF should meet the requirements of the WHO/UNICEF International Code of Marketing of Breast-Milk Substitutes (WHO, 1981) and all relevant resolutions of the World Health Assembly. The aim of the Code is to contribute to the provision of safe and adequate nutrition for infants, by the protection and promotion of breastfeeding, and by ensuring the proper use of breast-milk substitutes, when these are necessary, on the basis of adequate information and through appropriate marketing and distribution.

reflected. Individual countries should outline minimum training requirements for parents, caregivers, and staff in hospitals and day-care centres.

Specific details of illness associated with PIF, sources of contamination, characteristics of *E. sakazakii* and *Salmonella* have been covered in full in FAO/WHO reports (FAO/WHO, 2004, 2006) and are therefore only summarized in this document (Sections 1.2–1.4).

1.7 Scope

These guidelines provide recommendations for the preparation of PIF in care settings and in the home.

The guidelines in this document apply only to the preparation of PIF for infants no more than 12 months (as defined in Codex ALINORM 07/30/26) (CAC, 2007). Follow-up formula (as defined in Codex Standard 156-1987) (CAC, 1987) and formula for special medical purposes intended for infants (as defined in Codex Alinorm 07/30/26, Appendix II) (CAC, 2007) are considered outside the scope of this document. However, it should be noted that, in the absence of other guidance, the preparation of these formulas should follow that of PIF for infants no more than 12 months.

1.8 Assumptions behind the recommendations

As PIF may contain pathogens, one of the recommendations from the joint FAO/WHO meeting in Geneva, 2004 (FAO/WHO, 2004), and the basis for the WHA resolution request, was that guidance on the preparation, use and handling of PIF is required because many people who prepare PIF (both general public and health professionals) are not aware of the risks associated with this product, nor are they familiar with best practice for its reconstitution.

The recommendations are largely based on the findings of a FAO/WHO risk assessment on *E. sakazakii* in PIF, conducted in January 2006 (FAO/WHO, 2006). The quantitative risk assessment model that was developed calculates the increase or decrease in the relative risk associated with different feeding practices, compared to a baseline scenario.

These recommendations apply to persons preparing and handling PIF in care settings and in the home. In general, a dramatic reduction in risk is achieved when PIF is reconstituted with water that is no less than 70 °C. Risk is controlled by minimizing the time from preparation to consumption.

These recommendations are made under the assumption that the person preparing PIF has access to safe water; soap; a clean preparation environment; boiling water; and refrigeration. Where water quality is poor, boiling, chlorination and filtration are important means to inactivate microbial pathogens and make the water safe. To disinfect water: bring to a rolling boil; add 3–5 drops of bleach to 1 litre of water; or physically remove pathogens with the appropriate filter.

In certain circumstances (e.g. developing countries, or in the case of emergencies) one or more of these resources may be unavailable. In these cases, the simplest, most effective measures for reducing the risk of illness from the use of PIF are:

- Reconstitution with boiling water and consumption as soon as the formula is cool.
- Where boiling water is not available, reconstitute PIF with safe water at room temperature, and consume immediately.

1.9 Training

All persons preparing feeds from PIF should be informed about the risk associated with PIF and trained in or informed about its safe preparation according to these guidelines. As these guidelines recommend the use of very hot water, additional information or training, or both, should be provided on the safe handling of hot water. The present guideline document is divided into two main sections. Part 2 provides guidance for the preparation of PIF in care settings, and part 3 provides guidance for the preparation of PIF in the home environment. Both sections include a rationale for the recommendations provided. Both environments have many similarities and therefore part of the guidance and rationale is very similar between the two sections. Depending on the targeted end user, specific guidance material using either part 2 or part 3 should be developed.

PART 2: IN CARE SETTINGS

PIF is not a sterile product and may be contaminated with pathogens that can cause serious illness. Correct preparation and handling reduces the risk of illness.

Where available, commercially sterile ready-to-feed liquid infant formula should be used for infants at greatest risk. Sterile liquid infant formula does not contain pathogenic microorganisms and so does not pose a risk of infection. However, its use may not always be an option, and the use of PIF may be required.

PIF is not a sterile product and may contain harmful bacteria. Reconstituted PIF provides an ideal environment for the growth of these pathogens. Even if present in powdered formula at very low levels, inappropriate preparation and handling of reconstituted PIF provides ideal conditions for these pathogens to multiply, which greatly increases the risk of infection. However, the risk of illness can be reduced if PIF is prepared safely and handled correctly.

Care settings include hospitals and day-care centres such as crèches. Hospitals, especially intensive care units, that provide care for vulnerable infants are at greatest risk of *E. sakazakii* infection, as discussed earlier.

Hospitals and day-care centres may also be required to prepare large batches of PIF in advance, for later use. This practice may increase the risk of *E. sakazakii* infection if not carried out correctly.

Because PIF is not a sterile product, there is an innate risk of infection with bacteria such as *E. sakazakii*. The recommendations below outline best practice for the preparation, storage and handling of PIF in care settings in order to reduce the risk of infection with *E. sakazakii*. These recommendations are also appropriate for reducing the risk of infection with *Salmonella*.

2.1 Recommendations

2.1.1 Use of infant formula

1. Infant formula should be selected based on the medical needs of the infant.
2. Where available, use commercially sterile liquid infant formula for infants at greatest risk.

2.1.2 General requirements

1. Each institution should establish written guidelines for the preparation and handling of PIF.
2. The implementation of guidelines should be monitored.
3. Personnel preparing PIF should be fully trained according to the guidelines and trained in hygiene requirements for food preparation.
4. There should be full traceability of PIF prepared in care settings.
5. There should be a clean dedicated area for preparation and storage of PIF. Additional guidance on the layout of the preparation room should be communicated at country level.

2.1.3 Cleaning and sterilization of feeding and preparation equipment

It is very important that all equipment used for feeding infants and for preparing feeds has been thoroughly cleaned and sterilized before use.

1. Hands should always be washed thoroughly with soap and water before cleaning and sterilizing feeding and preparation equipment (as described below). In care settings, a dedicated hand-washing sink is recommended.
2. Cleaning: wash feeding and preparation equipment (e.g. cups, bottles, teats and spoons) thoroughly in hot soapy water. Where feeding bottles are used, clean bottle and teat brushes should be used to scrub inside and outside of bottles and teats to ensure that all remaining feed is removed.
3. After washing feeding and preparation equipment, rinse thoroughly in safe water.
4. Sterilizing: if using a commercial sterilizer, follow manufacturer's instructions. Feeding and preparation equipment can also be sterilized by boiling:
 - a. fill a large pan with water and completely submerge all washed feeding and preparation equipment, ensuring that there are no trapped air bubbles;
 - b. cover the pan with a lid and bring to a rolling boil, making sure the pan does not boil dry; and
 - c. keep the pan covered until the feeding and preparation equipment is needed.
5. Hands should be washed thoroughly with soap and water before removing feeding and preparation equipment from a sterilizer or pan. The use of sterilized forceps for handling sterilized feeding and preparation equipment is recommended.
6. To prevent recontamination, it is best to remove feeding and preparation equipment just before it is required for use. If equipment is removed from the sterilizer and not used immediately, it should be covered and stored in a clean place. Feeding bottles can be fully assembled to prevent the inside of the sterilized bottle and the inside and outside of the teat from becoming contaminated.

2.1.4 Preparing a feed using PIF

It is best to prepare feeds fresh each time and to feed immediately. Hospitals and other care settings will be required to prepare feeds for many infants. Ideally, each feed should be prepared in an individual feeding cup or bottle. However, in certain circumstances, feeds are mixed in larger containers, and then transferred into individual feeding cups or bottles. This practice poses a risk because PIF is more susceptible to contamination in large, open containers. Also, large volumes of feed take much longer to cool, leaving the potential for growth of harmful bacteria. The recommendations below outline the safest practice for preparing feed in individual containers or in batches for immediate consumption:

1. Clean and disinfect a surface on which to prepare the feed.
2. Wash hands with soap and water, and dry using a clean cloth or a single-use napkin.
3. Boil a sufficient volume of safe water. If using an automatic kettle, wait until the kettle switches off; otherwise make sure that the water comes to a rolling boil. Note: bottled water is not sterile and must be boiled before use. Microwave ovens should never be used in the preparation of PIF as uneven heating may result in 'hot spots' that can scald the infant's mouth.

4. Taking care to avoid scalds, pour the appropriate amount of boiled water, which has been allowed to cool slightly, but not below 70 °C, into a cleaned and sterilized feeding cup or bottle. The temperature of the water should be checked using a sterile thermometer.
 - a. If making a batch in a larger container: the container should have been cleaned and sterilized. It should be no larger than 1 litre, be made from food-grade material and be suitable for pouring hot liquids.
5. To the water, add the exact amount of formula as instructed on the label. Adding more or less powder than instructed could make infants ill.
 - a. If using feeding bottles: assemble the cleaned and sterilized parts of the bottle according to the manufacturer's instructions. Shake or swirl gently until the contents are mixed thoroughly, taking care to avoid scalds.
 - b. If using feeding cups: mix thoroughly by stirring with a cleaned and sterilized spoon, taking care to avoid scalds.
 - c. If preparing a batch in a larger container: stir formula using a cleaned and sterilized spoon to ensure even mixing. Immediately pour into individual feeding cups or bottles, taking care to avoid scalds.
6. Cool feeds quickly to feeding temperature by holding under a running tap, or placing in a container of cold water or iced water. Ensure that the level of the cooling water is below the top of the feeding cup or the lid of the bottle.
7. Dry the outside of the feeding cup or bottle with a clean or disposable cloth and label with appropriate information, such as type of formula, infant's name or ID, time and date prepared, and preparer's name.
8. Because very hot water has been used to prepare the feed, it is essential that the feeding temperature is checked before feeding in order to avoid scalding the infant's mouth. If necessary, continue cooling as outlined in step 6 above.
9. Discard any feed that has not been consumed within two hours.

2.1.5 Preparing feeds in advance for later use

It is best to make PIF fresh for each feed and to consume immediately, as reconstituted PIF provides ideal conditions for the growth of harmful bacteria. For practical reasons, feeds may need to be prepared in advance. In care or institutional settings, feeds may have to be prepared in batches and stored until required. The steps below outline the safest practice for preparing feeds in advance and storing for later use. If refrigeration is not available, feeds should be prepared fresh and consumed immediately. They should not be prepared in advance for later use.

1. Follow steps 1 to 7 in Section 2.1.4. If using feeding cups, a batch of formula should be prepared in a clean, sterilized jar or container that is no larger than 1 litre and has a lid. The prepared PIF can be refrigerated in the lidded container and dispensed into cups as needed.
2. Place cooled feeds in a dedicated refrigerator. The temperature of the refrigerator should be no higher than 5 °C and should be monitored daily.
3. Feeds can be stored in the refrigerator for up to 24 hours.

It is not recommended that batches of formula are cooled and stored in large volumes as large volumes can promote inadequate cooling and hence lead to the growth of harmful bacteria.

2.1.6 Re-warming stored feeds

1. Remove feeds from the refrigerator just before they are needed.
2. Re-warm for no more than 15 minutes.
3. To ensure that the feed heats evenly, periodically shake or swirl the feed in its covered container. Note: microwave ovens should never be used for re-warming feeds as uneven heating may result in 'hot spots' that may scald the infant's mouth.
4. Check feeding temperature in order to avoid scalding the infant's mouth.
5. Discard any re-warmed feed that has not been consumed within two hours.

2.1.7 Transporting feeds

In many care settings, feeds are prepared in a central preparation area, and transported to different wards, etc. Transporting prepared feeds poses a risk as it increases the time from preparation to consumption, providing the opportunity for growth of harmful bacteria. If feeds will not be consumed within two hours of preparation, they should be refrigerated before transportation, transported under refrigerated (or cool) conditions, and reheated at the destination. The recommendations below outline the safest practice for transporting prepared feeds:

1. If feed will be consumed within two hours of preparation:
 - a. prepare feeds as in Section 2.1.4; and
 - b. transport and use immediately.
2. If feed will not be consumed within two hours of preparation:
 - a. prepare feed and place in the refrigerator as outlined in Section 2.1.5;
 - b. ensure that feed is cold before transporting;
 - c. to transport, only remove from the refrigerator immediately before transporting;
 - d. transport the cold feed to its destination (for transport taking over 30 minutes, refrigeration or cool bags are recommended); and
 - e. re-warm at the destination, as in Section 2.1.6; or
 - f. alternatively, feeds transported under cool or refrigerated conditions can be returned to a refrigerator at the destination and used within 24 hours from preparation. Feeds that have been warmed up or feeds that have been partially consumed must not be returned to the refrigerator and should be discarded if not consumed within 2 hours.

2.1.8 Holding and feeding times

1. Discard any feed that has not been consumed within two hours from preparation (unless refrigerated).
2. Prepared feeds can be held in the refrigerator ($\leq 5^{\circ}\text{C}$) for up to 24 hours.
3. Discard all leftover feed.

4. Preferably, the hang-time for continuous or bolus feeds should be no more than two hours at room temperature.
5. Continuous or bolus feeds should not be warmed during feeding.

2.2 Rationale behind recommendations

2.2.1 Choice of infant formula

Infant formula should be selected based on the medical needs of the infant.

Where feasible, sterile liquid infant formula should be used in care settings, especially when feeding high-risk infants. These feeds do not contain harmful bacteria. Care settings, such as neonatal intensive care units, provide care for infants at greatest risk of *E. sakazakii* infection, i.e. neonates and those less than two months of age. However, sterile liquid infant formula is not always available (e.g. for infants who have special dietary needs), and PIF might be used instead.

2.2.2 General requirements

The preparation of feeds in institutions such as hospitals should be carefully controlled. This is because large volumes of feeds may need to be prepared, and the infants consuming feeds in these settings may be at particular risk of infection.

In order to help control the preparation of feeds from PIF, a dedicated area for preparation and storage of feeds should be provided to reduce the risk of cross-contamination with harmful bacteria. Each institution should establish written guidelines for the preparation and handling of feeds prepared from PIF, the implementation of which should be monitored. This ensures consistent and safe handling. Full training should be given to staff preparing feeds, so that they understand the risks involved with PIF and know what steps to take to ensure these risks are reduced or controlled.

2.2.3 Good hygienic practice

Poor hygiene has been reported as the probable cause of some *E. sakazakii* outbreaks (Forsythe, 2005). The person preparing the feed should clean and disinfect the preparation surface and wash hands with soap and water before preparing a feed. This is because harmful bacteria can be carried on hands and can also be present on surfaces. Washing hands and cleaning and disinfecting surfaces reduces the risk of feeds becoming contaminated during preparation.

Hands must also be washed after using the toilet and after diaper changing because harmful bacteria, including *E. sakazakii* (Drudy et al., 2006), have been found in the urine and stools of infants. These bacteria can easily be carried on the hands and contaminate feed during its preparation.

2.2.4 Cleaning and sterilizing feeding and preparation equipment

Outbreaks of *E. sakazakii* infection have been attributed to equipment used for preparing feeds (Gürtler et al., 2005). *E. sakazakii* is widespread in the environment and has been shown to attach and grow (form 'biofilms') on surfaces commonly used in infant feeding equipment, such as latex, silicon and stainless steel. It is therefore important that all infant feeding and preparation equipment (e.g. feeding cups, bottles, rings and teats) has been thoroughly cleaned and sterilized before use, since the formation of biofilms on such

equipment may result in reservoirs of infection that can continually contaminate feeds (Iversen, Lane and Forsythe, 2004).

2.2.5 Temperature of reconstitution water

According to the FAO/WHO risk assessment (FAO/WHO, 2006), risk is dramatically reduced when PIF is reconstituted with water that is no less than 70 °C, as this temperature will kill any *E. sakazakii* in the powder. This level of risk reduction holds even if feeding times are extended (i.e. up to two hours), and even if ambient room temperature reaches 35 °C. Consequently, Reconstituting PIF with water no less than 70 °C dramatically reduces the risk to all infants, even slow feeding infants and infants in warm climates where refrigeration for the prepared formula may not be readily available (e.g. developing countries).

When PIF is prepared with water that is less than 70 °C, it does not reach a high enough temperature to completely inactivate *E. sakazakii* present in the powder. This is a concern for the two following reasons: a) A small number of cells may cause illness, therefore it is important that cells present in the PIF are destroyed; and b) there is potential for surviving cells to multiply in the reconstituted formula. This risk is increased when the reconstituted formula is held for extended periods above refrigeration temperature.

Concerns have been raised over the use of very hot water for reconstituting PIF, but risk of *E. sakazakii* is only dramatically reduced when water at a temperature of no less than 70 °C is used (see appendix 3). Currently, the instructions on many PIF products lead to PIF being reconstituted with water that is around 50 °C. But, according to the FAO/WHO risk assessment, reconstitution with 50 °C water generally results in the greatest increase in risk, unless the reconstituted formula is consumed immediately. Under no circumstances is risk reduced when PIF is reconstituted with 50 °C water. Manufacturer's instructions should be reviewed in the light of the findings of the risk assessment.

2.2.6 Volume of container for preparing batches

Often in care settings, a number of feeds are prepared in a single, large container, mixed and then transferred into bottles or feeding cups. Anecdotal evidence suggests that large volumes are prepared, and left to cool for long periods in the preparation container (refrigerated or not).

Preparation in larger containers increases the risk of infection, as:

- the feed is more likely to become contaminated; and
- large volumes may take a long time to cool down, meaning that the formula remains for extended periods at a temperature that supports the growth of harmful bacteria.

The FAO/WHO risk assessment found that the use of larger containers (25 litre) for preparing and cooling feeds was associated with increased risk as a result of the slower cooling of formula, and therefore feeds should be cooled in small containers where possible.

2.2.7 Holding and feeding times

According to the FAO/WHO risk assessment for *E. sakazakii* in PIF, increased feeding durations are generally associated with increased risk due to possible bacterial growth. This risk is increased for warmer ambient temperatures (30 °C and 35 °C). However, when PIF is reconstituted with ≥ 70 °C water, risk is dramatically reduced, and this risk reduction remains valid for feeding times of two hours. This finding has practical implications for the reduction

of risk of *E. sakazakii* infection for slow-feeding infants and for infants in warm climates where ambient room temperature may be around 35 °C.

It is recommended that formula is not held at room temperature for more than two hours, even if water at no less than 70 °C is used to reconstitute PIF. This is because the feed may have become contaminated during preparation, or harmful bacteria may have been introduced into the cup or feeding bottle from the infant's mouth. Also, hot water (70 °C) may have activated bacterial spores of harmful bacteria in the formula. Holding prepared feeds above refrigeration temperature for extended periods provides the opportunity for such bacteria to grow.

2.2.8 Labelling of feed

Prepared feeds should be labelled with details of the infant formula, patient's name, preparer's name and preparation time and date. As care institutions look after many infants, feeds tend to be prepared in bulk. Adequate labelling will ensure traceability of all feeds.

2.2.9 Storage of prepared feeds

If feeds are not to be consumed within two hours after preparation, they should be quickly cooled immediately after preparation, and stored in a refrigerator (at a maximum temperature of 5 °C). Refrigerated storage, at temperatures lower than 5 °C, prevents or slows down growth of harmful bacteria. The FAO/WHO assessment showed a less than 1.3-fold increase in risk when prepared feeds were refrigerated properly.

Feed stored in the refrigerator should be used within 24 hours of preparation. Even if water no less than 70 °C was used to reconstitute PIF, spoilage bacteria may have survived that can grow at refrigeration temperatures and can cause feeds to spoil. The quality of reconstituted PIF may also deteriorate on prolonged storage. If there is an increased risk of microbial contamination in the preparation area or environment, then storage times should be reduced, or feeds made fresh and consumed immediately.

The refrigerator should be capable of bringing the formula to a temperature of no more than 5 °C within 1 hour of preparation. The temperature of the refrigerator should be monitored daily. Feeds should be cooled quickly before placing into the refrigerator as hot feeds will increase the refrigerator's temperature. Feeds can be rapidly cooled by placing under cold running water or in a bowl of cold water.

2.2.10 Re-warming stored feeds

Because of the possibility of growth of harmful bacteria at temperatures above 5 °C, stored formula should only be removed from the refrigerator and re-warmed immediately before feeding. Feeds should not be left warming for more than 15 minutes as re-warming for extended periods means that the feed will be held at a temperature that is ideal for the growth of harmful bacteria. Holding feed in bottle warmers for lengthy periods was reported as one of the probable causes of an outbreak of *E. sakazakii* infection (Gurtler, Kornacki and Beuchat, 2005).

2.2.11 Transporting prepared feeds

In many care settings, feeds are prepared in a central preparation area, and transported to different wards or areas of the facility. Transporting prepared feeds poses a risk of infection

as it increases the time from preparation to consumption, providing the opportunity for growth of harmful bacteria.

Because of this potential for growth, feeds that will not be consumed within two hours of preparation should be quickly cooled and refrigerated until the temperature of the feed is reduced to a temperature of no more than 5 °C. The cooled formula can then be transported to its destination. At the destination, feeds can be re-warmed for feeding (Section 2.2.10). Alternatively, feeds can be returned to a refrigerator and used within 24 hours from preparation.

If transport takes longer than 30 minutes, it is recommended that feeds are transported under refrigerated conditions in order to prevent feeds from warming up. If refrigerated transport is not available, feeds can be transported in a cooled container, such as a cool bag containing ice-packs.

PART 3: IN THE HOME

3.1 Recommendations

PIF is not a sterile product and may be contaminated with pathogens that can cause serious illness. Correct preparation and handling reduces the risk of illness.

Where available, commercially sterile ready-to-feed liquid infant formula should be used for infants at greatest risk.

PIF is not a sterile product and can pose a risk to infants, particularly if it is prepared and handled inappropriately. Reconstituted PIF provides an ideal environment for the growth of harmful bacteria. Even if present in powdered formula at very low levels, inappropriate preparation and handling of feeds provides ideal conditions for the growth of harmful bacteria, which greatly increases the risk of infection. However, the risk can be reduced if feeds are prepared and handled correctly.

The recommendations below outline the best practice for the safe preparation, storage and handling of PIF in the home in order to reduce the risk of infection with *E. sakazakii*. These recommendations are also appropriate for reducing the risk of infection with *Salmonella*.

It is recommended healthcare professionals ensure that parents and caregivers are instructed in the safe preparation, storage and handling of PIF.

3.1.1 Cleaning and sterilizing feeding and preparation equipment

It is very important that all equipment used for feeding infants and for preparing feeds has been thoroughly cleaned and sterilized before use.

1. Hands should always be washed thoroughly with soap and water before cleaning and sterilizing feeding and preparation equipment (as described below).
2. Cleaning: wash feeding and preparation equipment (e.g. cups, bottles, teats and spoons) thoroughly in hot soapy water. Where feeding bottles are used, clean bottle and teat brushes should be used to scrub inside and outside of bottles and teats to ensure that all remaining feed is removed.
3. After washing the feeding and preparation equipment, rinse thoroughly in safe water.
4. Sterilizing: if using a commercial home sterilizer (e.g. electric or microwave steam sterilizer, or chemical sterilizer), follow manufacturer's instructions. Feeding and preparation equipment can also be sterilized by boiling:
 - a. fill a large pan with water and completely submerge all washed feeding and preparation equipment, ensuring there are no trapped air bubbles;
 - b. cover the pan with a lid and bring to a rolling boil, making sure the pan does not boil dry; and
 - c. keep the pan covered until the feeding and preparation equipment is needed.
5. Hands should be washed thoroughly with soap and water before removing feeding and preparation equipment from a sterilizer or pan. The use of sterilized kitchen tongs for handling sterilized feeding and preparation equipment is recommended.
6. To prevent recontamination, it is best to remove feeding and preparation equipment just before it is to be used. If equipment is removed from the sterilizer and not used

immediately, it should be covered and stored in a clean place. Feeding bottles can be fully assembled to prevent the inside of the sterilized bottle and the inside and outside of the teat from becoming contaminated.

3.1.2 Preparing a feed using powdered infant formula

It is best to make PIF fresh for each feed and to consume immediately, as reconstituted PIF provides ideal conditions for the growth of harmful bacteria. The steps below outline the safest way to prepare individual feeds of PIF in bottles or in feeding cups for immediate consumption.

1. Clean and disinfect a surface on which to prepare the feed.
2. Wash hands with soap and water, and dry using a clean cloth or a single-use napkin.
3. Boil a sufficient volume of safe water. If using an automatic kettle, wait until the kettle switches off; otherwise make sure that the water comes to a rolling boil. Note: bottled water is not sterile and must be boiled before use. Microwaves should never be used in the preparation of PIF as uneven heating may result in 'hot spots' that can scald the infant's mouth.
4. Taking care to avoid scalds, pour the appropriate amount of boiled water that has been allowed to cool to no less than 70 °C, into a cleaned and sterilized feeding cup or bottle. To achieve this temperature, the water should be left for no more than 30 minutes after boiling.
5. To the water, add the exact amount of formula as instructed on the label. Adding more or less powder than instructed could make infants ill.
 - a. If using bottles: assemble the cleaned and sterilized parts of the bottle according to the manufacturer's instructions. Shake or swirl gently until the contents are mixed thoroughly, taking care to avoid scalds.
 - b. If using feeding cups: mix thoroughly by stirring with a cleaned and sterilized spoon, taking care to avoid scalds.
6. Immediately after preparation, quickly cool feeds to feeding temperature by holding the bottle or feeding cup under running tap water, or by placing in a container of cold or iced water. Ensure that the level of the cooling water is below the top of the feeding cup or the lid of the bottle.
7. Dry the outside of the feeding cup or bottle with a clean or disposable cloth.
8. Because very hot water has been used to prepare the feed, it is essential that the feeding temperature is checked before feeding in order to avoid scalding the infant's mouth. If necessary, continue cooling as outlined in step 6.
9. Discard any feed that has not been consumed within two hours

3.1.3 Preparing feeds in advance for later use

It is best to make PIF fresh for each feed and to consume immediately, as reconstituted PIF provides ideal conditions for the growth of harmful bacteria. For practical reasons, however, feeds may need to be prepared in advance. The steps below outline the safest way to prepare and store feeds for later use. If refrigeration is not available, feeds should be prepared fresh and consumed immediately rather than prepared in advance for later use.

1. Follow steps 1 to 7 of Section 3.1.2. If using feeding cups, a batch of formula should be prepared in a clean, sterile jar that is no larger than 1 litre, with a lid. The prepared PIF can be refrigerated and dispensed into cups as needed.
2. Place cooled feeds in a refrigerator. The temperature of the refrigerator should be no higher than 5 °C.
3. Feeds can be stored in the refrigerator for up to 24 hours.

3.1.4 Re-warming stored feeds

1. Remove stored feed from the refrigerator just before it is needed.
2. Re-warm for no more than 15 minutes. To ensure that the feed heats evenly, periodically shake the covered jar or container.
3. Microwave ovens should never be used to re-warm a feed as uneven heating may result in 'hot spots' that can scald the infant's mouth.
4. Check feeding temperature in order to avoid scalding the infant's mouth.
5. Discard any re-warmed feed that has not been consumed within two hours.

3.1.5 Transporting feeds

Because of the potential for growth of harmful bacteria during transport, feeds should first be cooled to no more than 5 °C in a refrigerator and then transported.

1. Prepare the feed and place in the refrigerator, as outlined in Section 3.1.3.
2. Ensure feed is cold before transporting.
3. Do not remove feed from the refrigerator until immediately before transporting.
4. Transport feed in a cool bag with ice packs.
5. Feeds transported in a cool bag should be used within two hours as cool bags do not always keep foods adequately chilled.
6. Re-warm at the destination, as in Section 3.1.4.
7. If you reach the destination within two hours, feeds transported in a cool bag can be placed in a refrigerator and held for up to 24 hours from the time of preparation.
8. Alternatively, if you are going out for the day, individual portions of PIF can be transported in washed and sterilized containers. At the destination, hot water no less than 70 °C can be used to prepare the feed, using washed and sterilized feeding and preparation equipment.

3.2 Rationale behind recommendations

3.2.1 Good hygienic practice

Poor hygiene has been reported as the probable cause of some *E. sakazakii* outbreaks (Forsythe, 2005). The person preparing the feed should clean and disinfect the preparation surface and wash hands with soap and water before preparing a feed. This is because harmful bacteria can be carried on hands and can also be present on surfaces. Washing hands and cleaning and disinfecting surfaces reduces the risk of feeds becoming contaminated during preparation.

Hands must also be washed after using the toilet and after diaper changing because harmful bacteria, including *E. sakazakii* (Drudy et al., 2006), have been found in the urine and stools of infants. These bacteria can easily be carried on the hands and contaminate feed during its preparation.

3.2.2 Cleaning and sterilizing feeding and preparation equipment

Outbreaks of *E. sakazakii* infection have been attributed to equipment used for preparing feeds (Gürtler et al., 2005). *E. sakazakii* is widespread in the environment and has been shown to attach and grow (form 'biofilms') on surfaces commonly used in infant feeding equipment, such as latex, silicon and stainless steel. It is therefore important that all infant feeding and preparation equipment (e.g. feeding cups, bottles, rings and teats) has been thoroughly cleaned and sterilized before use, since the formation of biofilms on such equipment may result in reservoirs of infection that can continually contaminate feeds (Iversen, Lane and Forsythe, 2004).

3.2.3 Temperature of water for reconstitution

According to the FAO/WHO risk assessment, risk is dramatically reduced when PIF is reconstituted with water that is no less than 70 °C, as this temperature will kill any *E. sakazakii* in the powder. This level of risk reduction holds even if feeding times are extended (i.e. up to two hours), and even if ambient room temperature reaches 35 °C. Consequently, reconstituting PIF with water no less than 70 °C dramatically reduces the risk to all infants, even slow feeding infants and infants in warm climates where refrigeration may not be readily available (e.g. developing countries).

When PIF is prepared with water cooler than 70 °C, it does not reach a high enough temperature to completely inactivate *E. sakazakii* present in the powder. This is a concern for two reasons: a) a small number of cells may cause illness, therefore it is important that cells present in the PIF are destroyed; and b) the potential for surviving cells to multiply in the reconstituted formula. This risk is increased when the reconstituted formula is held for extended periods above refrigeration temperature.

Concerns have been raised over the use of very hot water for reconstituting PIF, but risk of *E. sakazakii* is only dramatically reduced when water at a temperature of no less than 70 °C is used. Currently, the instructions on many PIF products lead to PIF being reconstituted with water that is around 50 °C. But, according to the FAO/WHO risk assessment, reconstitution with 50 °C water generally results in the greatest increase in risk, unless the reconstituted formula is consumed immediately. Under no circumstances is risk reduced when PIF is reconstituted with 50 °C water. Manufacturer's instructions should be reviewed in the light of the findings of the risk assessment.

3.2.4 Storage of prepared feeds

Because PIF may contain harmful bacteria, it is best to prepare it fresh for each feed. However, in practical terms this is not always possible. Feeds may need to be prepared in advance, e.g. for the crèche, babysitter, or if you are going out for the day. In these circumstances, feeds should be prepared using water no less than 70 °C, cooled quickly immediately after preparation, and stored in the refrigerator (at 5 °C or colder) for no more than 24 hours.

Feed stored in the refrigerator should be used within 24 hours of preparation. Even if water no less than 70 °C was used to reconstitute PIF, spoilage bacteria may have survived that can grow at refrigeration temperatures and can cause feeds to spoil. The quality of reconstituted PIF may also deteriorate on prolonged storage.

Feeds should be cooled quickly before placing into the refrigerator, as hot feeds will increase the refrigerator's temperature. Feeds can be rapidly cooled by placing under cold running water or in a bowl of cold water.

3.2.5 Re-warming and use of stored feeds

Because of the possibility of growth of harmful bacteria at temperatures above 5 °C, stored formula should not be removed from the refrigerator and re-warmed until immediately before feeding. Feeds should not be left warming for more than 15 minutes as re-warming for extended periods means that the feed will be held at a temperature that is ideal for the growth of harmful bacteria. Holding feed in bottle warmers for lengthy periods was reported as one of the probable causes of an outbreak of *E. sakazakii* infection (Gurtler, Kornacki and Beuchat, 2005).

3.2.6 Transporting feeds

Transporting prepared feeds poses a risk as it increases the time from preparation to consumption, providing the opportunity for growth of harmful bacteria. Because of this potential for growth, feeds that need to be transported should be quickly cooled and refrigerated until they are cold before transporting.

In order to minimize growth of harmful bacterial, cooled feeds should only be removed from the refrigerator at the last minute and transported in a cool bag. At the destination, feeds can be re-warmed for feeding. Feeds held in a cool bag should be used within two hours. Alternatively, if transported feeds are returned to a refrigerator within two hours, they can be stored for up to 24 hours from preparation. By following these steps, feeds will be kept cool, which will slow down or prevent the growth of harmful bacteria.

3.2.7 Holding and feeding times

Minimizing the time from preparation to consumption is an effective measure for controlling the risk of infection with *E. sakazakii*. Prepared feed should be discarded after two hours, unless it has been stored in the refrigerator since preparation (see Section 3.1.3). Leftover feed should never be saved for later, or added to a freshly prepared feed, as harmful bacteria may have had the chance to grow during the feeding period.

It is recommended that formula is not held at room temperature for more than two hours, even if water at no less than 70 °C is used to reconstitute PIF. This is because the feed may have become contaminated during preparation, or harmful bacteria may have been introduced into the cup or feeding bottle from the infant's mouth. Also, hot water (70 °C) may have activated bacterial spores of harmful bacteria in the formula. Holding prepared feeds above refrigeration temperature for extended periods provides the opportunity for such bacteria to grow.

APPENDIX 1

Summary of recommendations made by the joint FAO/WHO expert meeting (FAO/WHO, 2004):

- In situations where infants are not breastfed, caregivers, particularly of infants at high risk, should be regularly alerted that PIF 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 that has undergone an effective point-of-use decontamination procedure (e.g. use of boiling water to reconstitute or by heating reconstituted formula).
- 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 PIF. 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.
- In revising its code of practice, Codex should better address the microbiological risks of PIF and, if deemed necessary, include the establishment of appropriate microbiological specifications for *E. sakazakii* in PIF.
- FAO/WHO should address the particular needs of some developing countries and establish effective measures to minimize risk in situations where breast-milk 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 PIF, 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 PIF.

APPENDIX 2

Ten steps to successful breastfeeding

(Taken from the WHO/UNICEF Baby-Friendly Hospital Initiative (BFHI))

1. Have a written breastfeeding policy that is routinely communicated to all health care staff.
2. Train all health care staff in skills necessary to implement this policy.
3. Inform all pregnant women about the benefits and management of breastfeeding.
4. Help mothers initiate breastfeeding within one half-hour of birth.
5. Show mothers how to breastfeed and maintain lactation, even if they should be separated from their infants.
6. Give newborn infants no food or drink other than breast milk, unless medically indicated.
7. Practice rooming in – that is, allow mothers and infants to remain together 24 hours a day.
8. Encourage breastfeeding on demand.
9. Give no artificial teats or pacifiers (also called dummies or soothers) to breastfeeding infants.
10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic.

APPENDIX 3

The use of very hot water for the reconstitution of PIF has been questioned because of concerns over the loss of heat-sensitive nutrients; the risk of scalding for infants and the preparer; activation of *Bacillus cereus* or other bacterial spores; and clumping of powder (FAO/WHO, 2006). The ESPGHAN³ Committee on Nutrition disagreed with the use of boiling water and of heating reconstituted formula to temperatures close to boiling point, because of the possible adverse effects on nutrients such as vitamins (Agostoni et al., 2004). In October 2002, the US Department of Agriculture revised its recommendation to Health Professionals to use boiling water to reconstitute PIF because of: the potential for the loss of heat sensitive nutrients; changes in physical characteristics of some formulas; the inability to assure adequate destruction of *E. sakazakii*; and injury to hospital staff preparing formula (US FDA, 2002). However, the UK has recently updated advice on preparation of PIF, recommending reconstitution with water that is greater than 70 °C to reduce the risk associated with using PIF (FSA, 2006).

The FAO/WHO expert meeting (2006) did note these concerns. Data presented at the meeting on the reduction in vitamin levels on reconstitution with boiling water showed that vitamin C is the only vitamin that is significantly affected (reduction ranging from 5.6 to 65.6% in the four powders tested). However, to offset the loss of vitamins during the shelf-life of the product, all dry formulas actually contained higher levels of vitamin C than was labelled. After reconstituting with boiling water, three of the four formulas still contained higher levels than labelled. The fourth, after a vitamin C reduction of 65.6%, contained 9.0 mg/100 calories. This level is still greater than the minimum level of vitamin C (8 mg/100 calories) required by the Codex Standard for Infant Formula (CAC, 1981).

This study appears to indicate that reduction in vitamin levels from use of water at >70 °C is not significant. However, as the results of only one study were discussed, the meeting did not agree to make any specific recommendations on this issue, but it was noted that the option of fortifying formulas to accommodate any reduction in vitamins could be possible if the practice of preparing formula with very hot water were to be recommended.

In addressing the other concerns concerning the use of very hot water, the expert meeting concluded that the risk of scalding can be addressed through educational messages on the label and training of those preparing and feeding PIF. Although re-activation of spores may be an issue with the use of very hot water, using the formula immediately, after cooling to a suitable feeding temperature, or refrigerating if it is to be used later, should address this issue. Results of studies reported in a recent risk assessment (Food Standard Australia New Zealand, 2003) show that the level of *Bacillus cereus* in the formula is not affected by the temperature of water used (either 56°C or 90°C) or the subsequent cooling conditions. The assessment also indicates that the present guidance provided does not lead to a risk of *Bacillus cereus*. Finally, clumping does not occur with all formulas when reconstituted with very hot water, and current technology could be applied to address this issue for products where it does occur.

³ European Society for Paediatric Gastroenterology, Hepatology and Nutrition

REFERENCES CITED IN THE TEXT

- Agostoni, C., Axelsson, I., Goulet, O., Koletzko, B., Michaelsen, K.F., Puntis, J.W.L. et al. 2004. Preparation and handling of powdered infant formula: a commentary by the ESPGHAN Committee on Nutrition. *Journal of Pediatric Gastroenterology and Nutrition*, 39:320–322.
- CAC [Codex Alimentarius Commission]. 1979. Recommended international code of hygienic practice for foods for infants and children (CAC/RCP 21-1979). See: http://www.codexalimentarius.net/web/standard_list.do?lang=en
- CAC. 1981. Codex Standard for Infant Formula (Codex Stan 72-1981). See: http://www.codexalimentarius.net/web/standard_list.do?lang=en
- CAC. 1987. Codex Standard for Follow-up Formula (Codex Stan 156-1987). See: http://www.codexalimentarius.net/web/standard_list.do?lang=en
- CAC. 2007. Codex Standard for Infant Formula and formulas for special medical Purposes Intended for Infants (Codex Alinorm 07/30/26, Appendix II). (To be adopted in July 2007). See: http://www.codexalimentarius.net/download/report/669/al30_26e.pdf
- CAC. 2004. Report of the 25th Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses, Bonn, Germany, 3–7 November 2003. Codex Alinorm 04/27/26. Document J1464e. Available from: <http://www.fao.org/docrep/meeting/008/j1464e/j1464e00.htm>
- CDC [Centres for Disease Control and Prevention (USA)]. 2002. FoodNet annual report, 2002. Available from: http://www.cdc.gov/foodnet/annual/2002/2002AnnualReport_tables&graphs.pdf
- Drudy, D., Mullane, N.R., Quinn, T., Wall, P.G. & Fanning, S. 2006. *Enterobacter sakazakii*: an emerging pathogen in powdered infant formula. *Clinical Infectious Diseases*, 42(7):996–1002.
- FAO [Food and Agriculture Organization of the United Nations]/WHO [World Health Organization]. 2004. *Enterobacter sakazakii* and other microorganisms in powdered infant formula. Meeting report. Geneva, Switzerland, 2–5 February 2004. [FAO/WHO] *Microbiological Risk Assessment Series*, No. 6
- FAO/WHO. 2006. *Enterobacter sakazakii* and *Salmonella* in powdered infant formula. Meeting Report. Joint FAO/WHO Technical Meeting on *Enterobacter sakazakii* and *Salmonella* Powdered Infant Formula, Rome, Italy, 16–20 January 2006. [FAO/WHO] *Microbiological Risk Assessment Series*, No. 10.
- Forsythe, S. 2005. *Enterobacter sakazakii* and other bacteria in powdered infant milk formula. *Maternal and Child Nutrition*, 1(1):44–50.
- FSA [Food Standards Agency, UK]. 2006. Guidance on preparing infant formula. Article first posted 13 February 2006; accessed 25 November 2006. Available at: <http://www.food.gov.uk/news/newsarchive/2005/nov/infantformulastatementnov05>
- FSANZ [Food Standard Australia New Zealand]. 2003. *Bacillus cereus* in infant formula. Microbiological risk assessment report.
- Gurtler, J.B., Kornacki, J.L. & Beuchat, L.R. 2005. *Enterobacter sakazakii*: A coliform of increased concern to infant health. *International Journal of Food Microbiology*, 104(1):1–34.
- Gürtler, M., Adler, T., Kasimir, S. & Fehlhäber, K. 2005. The importance of *Campylobacter coli* in human campylobacteriosis: prevalence and genetic characterization. *Epidemiology and Infection*, 133(6):1081–1087.

- Iversen, C., Lane, M. & Forsythe, S.J. 2004. The growth profile, thermotolerance and biofilm formation of *Enterobacter sakazakii* grown in infant formula milk. *Letters in Applied Microbiology*, 38(5):378–382.
- Muytjens, H.L., Roelofs-Willemse, H. & Jasper, G.H.J. 1988. Quality of powdered substitutes for breast milk with regard to members of the family Enterobacteriaceae. *Journal of Clinical Microbiology*, 26:743–746.
- US FDA [U.S. Food and Drug Administration]. 2002. Health Professionals Letter on *Enterobacter sakazakii* infections associated with use of powdered (dry) infant formulas in neonatal intensive care units. 16-3-2006. See: <http://www.cfsan.fda.gov/~dms/inf-ltr3.html>
- WHA [World Health Assembly]. 2005. Resolution WHA 58.32 on Infant and young-child nutrition. See: http://www.who.int/gb/ebwha/pdf_files/WHA58/WHA58_32-en.pdf or http://www.who.int/gb/e/e_wha58.html
- WHO [World Health Organization]. 1981. International Code of Marketing of Breast-Milk Substitutes. Available at: <http://whqlibdoc.who.int/publications/9241541601.pdf>
- WHO/UNICEF [United Nations Children's Fund]. 2003. The Global Strategy for Infant and Young Child Feeding. WHO, Geneva. See: www.who.int/child-adolescent-health/New_Publications/NUTRITION/gs_iycf.pdf