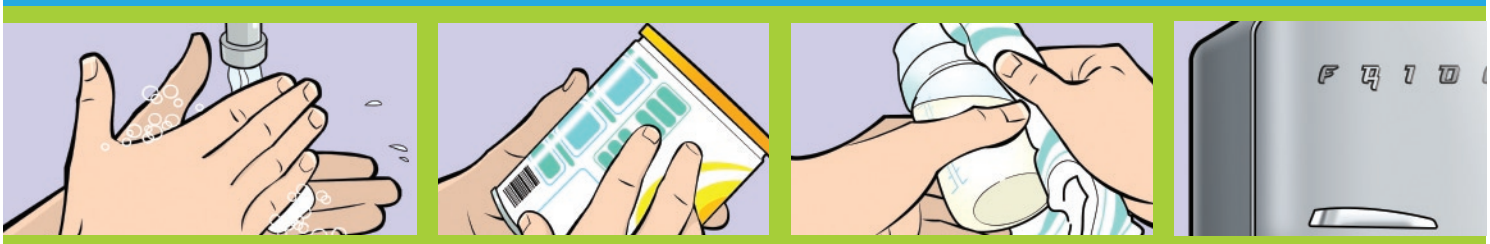
Safe preparation, storage and handling of powdered infant formula

Guidelines



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Contents

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

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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, Jenny Murcott and Jørgen Schlundt in WHO, with Sarah Cahill and Maria de Lourdes Costarrica in FAO.

Part 1: Introduction

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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.

Part 1: Introduction (continued)

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).

Part 1: Introduction (continued)

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-Willemse and Jasper, 1988). The current Codex specification for *Salmonella* is the absence of organisms in 60 samples of 25 g each. Specific criteria for