INFANT NUTRITION COUNCIL OF AMERICA

Powdered Infant Formula Preparation Recommendations

Key Points

- Powdered infant formula (PIF) is a convenient and cost-effective source of infant nutrition.
- PIF is not sterile and may contain microorganisms, such as *Cronobacter. Cronobacter* illness is extremely rare, but can cause blood infections, sepsis, or meningitis, especially in premature, low birthweight and immunocompromised infants.
- Parents and caregivers should follow manufacturer instructions for preparing infant formula to help prevent possible *Cronobacter* contamination.

Overview

Powdered infant formula (PIF) is a convenient and cost-effective source of infant nutrition. PIF is reconstituted by mixing the powder with water prior to feeding.

PIF is not a sterile product, so microorganisms such as *Cronobacter* bacteria may be introduced through improper preparation techniques. *Cronobacter* bacteria (also known as *Enterobacter sakazakii)* are common in the environment and may be found in many substances including food, water, soil, human hands and on household surfaces. [1,2,3,4] *Cronobacter* has also been found in and around opened cans of PIF. *Cronobacter* illness is extremely rare but can cause blood infections, sepsis, or meningitis, especially in premature, low birthweight and immunocompromised infants. As *Cronobacter* illness can be extremely harmful to infants, it is critical that caregivers take great care when preparing PIF.

Infant formula manufacturers include instructions for how to prepare and handle PIF on product labels, which takes into account microbiological safety and water quality. However, government agencies, health organizations and other stakeholders have differing opinions regarding the preparation of PIF, including the temperature of the water to be used to reconstitute the powder. The Infant Nutrition Council of America (INCA) believes recommendations should align in support of manufacturer instructions to avoid continued consumer and healthcare professional confusion and possible harm to infants, parents and caregivers.

Current recommendations on use of hot water to prepare infant formula

Beginning in 2002, the U.S. Food and Drug Administration (FDA) recognized that preparing infant formula with hot water had the potential for: 1) loss of heat sensitive nutrients; 2) changes in physical characteristics of some formulas; 3) inability to assure adequate destruction of *E. sakazakii*; and 4) injury to hospital staff preparing formula. However, FDA has never recommended preparing PIF with hot water. Rather the FDA recommends caregivers "follow the manufacturer's directions on the printed label" and also states that

"In most cases, it's safe to mix formula using ordinary cold tap water that's boiled for one minute and cooled. Remember that formula made with hot water needs to be cooled quickly to body temperature—about 98 degrees Fahrenheit—if it is to be fed to the baby immediately. If the formula is not being fed immediately, refrigerate it right away and keep refrigerated until feeding."

In 2004, the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) expressed concern that hot water may inactivate vitamins in PIF and kill probiotic strains contained in the formula. Therefore, they recommended that formula should only be reconstituted with water >70 °C if formula manufacturers are certain that the nutritional aspects of the formula will be maintained[5].

However, it is known that some ingredients, including probiotics and some vitamins, are heat labile[6,7] and hot water would negatively impact the nutrient stability of PIF. Furthermore, as an emulsion, infant formulas are temperature sensitive[8] and risk becoming instable at >70 °C which could result in an increased risk of clogged nipples and/or tubes and negatively impact an infant's nutritional intake. Nonetheless, in 2007 the World Health Organization (WHO) began recommending that PIF should be reconstituted with water that has been boiled and allowed to cool slightly, but not below 70 °C.

In 2012, the U.S. Centers for Disease Control and Prevention (CDC) supported the WHO recommendation to use hot water (158 °F/70 °C and above) to make formula for use at home. The CDC responded to concerns raised by the International Formula Council that nutrient and probiotics stability could be negatively impacted, that these concerns were clinically insignificant. This disregard for nutrient and ingredient stability seems to have been taken into consideration by the FDA which has noted "Infant formula is unique in comparison to almost all other foods in that it is often the sole source of nutrition in a rapidly growing and developing vulnerable population. Unlike foods that are included in a mixed diet, nutrient inadequacies in a product that constitutes the only source of nutriture in a diet cannot be compensated for by nutrients in other foods in the diet."

In 2011, the American Dietetic Association (ADA; now the Academy of Nutrition and Dietetics, AND) began recommending that commercially prepared, chilled, sterilized water be used for reconstitution of infant formula.[9] AND recommends referring to the powdered formula can for preparation of standard formula recipes using a scoop when making recommendations for households.[9]

A more recent U.S. FDA rule for the current good manufacturing practices (CGMPs) specifically designed for infant formula, includes required testing for both *Salmonella* and *Cronobacter*. A public comment published in response to the interim GMP rule noted that significant progress has been made in clarifying sources of and risk groups for *Cronobacter*, particularly *C. sakazakii,* and supported the FDA's proposed *Cronobacter* limit (neg/10 g based on 30 samples).

Recommendations for PIF Preparation with Hot Water are Problematic

Recommendations for healthcare/facility and home preparation of PIF are inconsistent, contradictory, and problematic.[10,11]

The WHO guidelines for hygienic preparation of PIF aim to reduce the number of bacteria in the reconstituted product by using hot water. However, reducing the bacterial load of reconstituted PIF does not necessarily reduce the risk of infection to infants. For example, previously reported concerns include the colonization of opportunistic pathogens including, but not limited to *Cronobacter* to feeding tubes, including enteral and nasogastric tubes. Additionally this risk has been identified regardless of the type of feed, including breast milk.[10] This identifies a modifiable practice in feeding time and frequency for infants that is not addressed by current WHO guidelines.

Additionally, the WHO guidelines introduce the potential for contamination from sources other than PIF. For example, Silano et al. mention the inherent risk of contamination with determining water temperature by dipping a thermometer into reconstituted formula.[11]

The use of hot water for reconstitution precludes the inclusion of probiotic bacterial cultures (e.g. *Lactobacillus fermentum* and *L. reuteri*) in PIFs that are known heat labile ingredients. [6,11]

Recommendations to boil water and cool for 30 minutes prior to use do not account for the variation in cooling curves according to volume of water and type of kettle or the frequency and small volumes of formula needed for some infants, particularly premature infants.[11]

Critical considerations for safe preparation of infant formula

"Hygienic practices and avoidance of temperature abuse are of vital importance, regardless of the type of feed."[10] It is essential to communicate that, regardless of the type of infant nutrition, sanitary/hygienic practices for preparing nutrition, bottles, nipples, and tube feeds, feeding the infant immediately or storing at < 5 °C is critical. This will minimize the risk of several pathogens, including *Cronobacter*.

Many mothers do not follow safe practices when preparing infant formula. A 2008 study of mothers participating in the 2005–2007 Infant Feeding Practices Study II who fed their infant formula showed that the majority of formula-feeding mothers did not receive instruction on formula preparation (77%) or storage (73%) from a health professional. Thirty percent did not read some of the safe-use directions on the formula package label; an approximately equal percentage (38%) thought that both powdered (which is not sterile) and ready-to-feed (which is sterile) formula were unlikely to contain germs; and 85% believed that following safe-storage directions was very important. Among the mothers of the youngest infants analyzed, 55% did not always wash their hands with soap before preparing infant formula, 32% did not adequately wash bottle nipples between uses, 35% heated formula bottles in a microwave oven, and 6% did not always discard formula left standing for >2 hours. The prevalence of these unsafe practices was similar among mothers of older infants. No consistent pattern of maternal characteristics was associated with unsafe practices.[12]

An assessment of neonatal exposure of pathogens, including *Cronobacter spp*., has been suggested for a holistic approach to reduce the risk of infections.[13] This approach is warranted since several other sources of *Cronobacter* have been identified. Previous research has shown that the use of centralized feeding preparation rooms in hospital settings reduces the incidence of microbial contamination.[14]

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