



International Food Safety Authorities Network (INFOSAN)

13 January 2005

INFOSAN Information Note No. 1/2005 - *Enterobacter sakazakii*

Enterobacter sakazakii in powdered infant formula

SUMMARY NOTES

- *Enterobacter sakazakii* is a pathogen present in low frequency in powdered infant formula and emerging as a public health concern
- Member States of WHO and of the FAO/WHO Codex Alimentarius Commission have expressed concern of this problem and are urging for action at national and international level
- WHO and FAO have convened an expert meeting on this subject with clear recommendations
- WHO and Codex are presently actively working towards preparing advice for Member States

Introduction

Member States of the World Health Organization as well as of the FAO/WHO Codex Alimentarius Commission (CAC) have expressed concerns regarding the recent findings of disease risk related to *Enterobacter sakazakii* (*E. sakazakii*) and other microorganisms in powdered infant formula. At its meeting in June 2003 the CAC noted the need to address concerns with pathogens that may be present in infant formula. In March, 2004 the Codex Committee for Food Hygiene (CCFH) agreed to proceed as quickly as possible with the revision of the International Code of Hygienic Practice for Foods for Infants and Children, including, as appropriate, microbiological criteria on *E. sakazakii* as well as other relevant microorganisms (<http://www.who.int/foodsafety/micro/jemra/meetings/feb2004/en/>). The proposed revised code will be considered at the 37th Session of the CCFH, 14-19 March 2005 (ftp://ftp.fao.org/codex/ccfh37/fh37_04e.pdf). In May 2004 at the Fifty-Seventh World Health Assembly (WHO's governing body), a draft resolution on this subject was proposed by several Member States. Because of time limitations it was decided to work further on a resolution text to be discussed at the WHO Executive Board (http://www.who.int/gb/ebwha/pdf_files/EB115/B115_7-en.pdf) at its meeting on 17-23 January 2005. The final draft resolution will be forwarded for consideration by the Fifty-eighth World Health Assembly in May 2005.

In February 2004 FAO and WHO convened an expert meeting¹ on *E. sakazakii* to provide pertinent scientific information to Member States and Codex as well as other interested parties on this issue.

The purpose of this Information Note is to inform: 1) all national food safety authorities about this issue including potential preventative measures and 2) all such authorities about the ongoing normative work related to this issue

¹ *Enterobacter sakazakii* and other microorganisms in powdered infant formula. Geneva, FAO/WHO, 2004. (Microbiological Risk Assessment Series, No. 6., ISBN: 92 4 156262 5.). <http://www.who.int/foodsafety/publications/micro/en/es.pdf>

The problem and its magnitude

Enterobacter sakazakii in powdered infant formula has been implicated in outbreaks causing sepsis, meningitis or necrotising enterocolitis, especially in infants less than 2 months old. Cases of *E. sakazakii* infections due to contaminated infant formula have been reported in a number of developed countries. It is likely that there is a significant underreporting of infections in all countries. The overall incidence of disease caused by *E. sakazakii* seems to be low. In the few outbreaks investigated mortality rates of from 20% to in some cases higher than 50% have been reported. For survivors, severe lasting complications occurred, including neurological disorders. Recent outbreaks in 2004 include the death of a preterm infant in July in New Zealand, and an outbreak in France (9 infected, 4 diseased, 2 deaths) in October-December (<http://www.sante.gouv.fr/htm/actu/pregestimil/sommaire.htm>).

In general *E. sakazakii* has caused disease in all age groups. From the age distribution of reported cases, infants (children less than 1 year old) appear to be mainly at risk. Among infants the greatest risk for *E. sakazakii* infection are among neonates (first 28 days), particularly pre-term, low birth-weight or immunocompromised infants. Infants of HIV-positive mothers are also at high risk both because they may specifically require infant formula and because they may be more susceptible to infection. This, and low birth weight, may present a particular concern for some developing countries, where the proportion of such infants is higher than in developed countries. Higher ambient temperatures and lack of refrigeration to store rehydrated formula will also increase the risk, due to relatively rapid growth of the organism once reconstituted.

While *E. sakazakii* has been detected in different types of food, only powdered infant formula has been linked to outbreaks of disease. There are two main routes by which *E. sakazakii* can enter reconstituted infant formula: a) *through intrinsic contamination* - either through contaminated ingredients added after drying or from the processing environment after drying and before packing or b) *through external contamination* of the formula during reconstitution and handling e.g. through poorly cleaned utensils. Based on the available information, in 50-80 % of cases, powdered infant formula is both the source and the vehicle of *E. sakazakii* induced illness, and in 20-50% of the cases the formula was the vehicle but poor hygiene during reconstitution and handling was the source. It should be noted that powdered infant formula has also been shown to cause Salmonella infection in infants.

Considering the limitations of current surveillance systems in most countries and the fact that infant formula is widely used, the presence of *E. sakazakii* in infant formula and its potential effects in infants could well be a significant public health problem in many countries. However, the true magnitude of the problem is still unknown. A review of English scientific literature from 1961 to 2003 found 48 cases of *E. sakazakii*-induced illness among infants. In order to further reinforce risk management options, it is recommended to countries to improve surveillance systems for these diseases in order to assess the level of potential underreporting.

International normative action

Powdered infant formula has been consumed by millions of infants for many years and constitutes the great majority of infant formula used routinely worldwide. However, it is important to note that powdered infant formula meeting current standards is not a sterile product and may occasionally contain low levels of pathogens. Present technology does not seem to allow for the production of commercially sterile powders.

Current Codex advisory microbiological specifications for powdered infant formula allow approximately 1-10 coliform bacteria per gram formula; *E. sakazakii* belongs to the group of coliforms. While this limit probably helps reducing the number of outbreaks, it does not provide a sufficient level of safety as evidenced by outbreaks caused by powdered formula with *E. sakazakii* concentrations below this limit. Specific limits for *E. sakazakii* are presently being considered in CCFH's deliberations. Codex guidance will also cover hygiene requirements specific to the manufacturing of powdered products using different technological processes, as well as hygiene related to the plant environment during production. It will also provide labelling guidance for consumers for handling and storing of the product after the reconstitution.

Reduction of the risk:

While the inclusion of future revised Codex guidance in national regulations will contribute to a reduction in the risk related to *E. sakazakii* a number of other factors are also important. *A full list of recommendations from the WHO/FAO expert meeting is available in the report section 8.2.*³

As a global public health recommendation, **infants should be exclusively breastfed for the first 6 months of life** to achieve optimal growth, development and health. Thereafter, to meet their evolving nutritional requirements, infants should receive nutritionally adequate and safe complementary foods while breastfeeding continues until up to 2 years of age or beyond. **Infants who are not breastfed and who do not have access to banked donor milk, require a suitable breast-milk substitute**, for example an infant formula produced and prepared in accordance with applicable standards. Information provided in this connection to mothers and other family members who need to use infant formula should include adequate instructions for appropriate preparation and the health hazards of inappropriate preparation and use².

While currently available technology does not seem to be able to produce sterile powdered infant formula, recommendations are being directed to the industry to improve its safety. It is estimated³ that a significant reduction in the frequency of contamination of powdered infant formula, e.g. from reducing the level of Enterobacteriaceae in the production environment, could reduce the disease risk significantly. It is also estimated that the inclusion of a lethal step, e.g. the use of hot water (70°-90°C) during the reconstitution of powder as well as a decrease in the holding time before feeding as well as the feeding time itself will effectively reduce the existing risk. A combination of such intervention measures would have the greatest impact. While *E. sakazakii* appears not to be found in drinking water supplies in the developed world; it is plausible that it can occur in drinking water of poor quality. Safe drinking water (see WHO Guidelines for Drinking Water Quality, 3rd edition - http://www.who.int/water_sanitation_health/publications/cdrom/en/) should always be used to reconstitute the powder. **Water should be brought to a rolling boil and be cooled for a few minutes to reach a temperature ensuring pasteurization but avoiding clumping (70°-90°C) before it is added to the formula.** It is very important to emphasize that the formula should be cooled to body temperature before feeding.

It is also recommended that **caregivers to infants, and especially infants at high risk, should be alerted, through labelling or other means, to the fact that powdered infant formula is not a sterile product.** Many consumers, including those directly involved in caring for infants, are not aware that powdered infant formula is not a sterile product and may be contaminated with extremely low levels of pathogens that can cause serious illness. Educational programmes targeted to caregivers of infants in the home, daycare and healthcare facilities and health care providers for infants, in combination with labelling procedures, should focus on **enabling caregivers to i) understand the importance of product labelling information, ii) follow the instructions accompanying products, and iii) make informed choices.** In particular, it should be stressed that improper storage of contaminated reconstituted powdered infant formula can support the rapid growth of pathogens and will significantly increase the risk of disease. It will be advisable to **avoid storage of reconstituted formula by preparing enough for one feed at a time.** It should also be noted that the addition, in hospitals or at home, of ingredients such as cereals or sugar may present an additional source of contamination.

It will be important for WHO and FAO to address the particular needs of developing countries, in minimizing risk in the use of breast-milk substitutes for vulnerable infants, e.g. infants of HIV-positive mothers, and low-

² WHO 2002. *The global strategy for infant and young child feeding.* Available at http://www.who.int/child-adolescent-health/New_Publications/NUTRITION/gs_icyf.pdf.

³ *Enterobacter sakazakii* and other microorganisms in powdered infant formula. Geneva, FAO/WHO, 2004. (Microbiological Risk Assessment Series, No. 6., ISBN: 92 4 156262 5.). <http://www.who.int/foodsafety/publications/micro/en/es.pdf>

birth weight infants. Specifically it should be realized that some of the current recommendations for use and preparation of powdered infant formulas might not in all cases be achievable where refrigeration is unavailable, fuel is expensive and where there are high levels of illiteracy.

Investigation and reporting of sources and vehicles of infection by *E. sakazakii*, including powdered infant formula, should be encouraged in all countries. This could include consideration of the establishment of an international laboratory-based network. In addition research should be promoted to gain a better understanding of the ecology, taxonomy, virulence and other characteristics of *E. sakazakii* and on ways to reduce its levels in reconstituted powdered infant formula.