

## **2006 IBFAN ARTICLE FOR MIDDLE EAST FOOD**

### **Intrinsic contamination of powdered infant formula by pathogenic microorganisms**

The risk of illness and death linked to *Enterobacter sakazakii* infections is a well-documented problem inherent in the use of powdered infant formulas, including follow-on formulas and milk-based cereal food. The deaths of 2 premature infants in France in December, 2004 from severe infections caused by powdered infant formula contaminated by *Enterobacter sakazakii* illustrate the seriousness of this recently recognised public health concern. Other deaths before have occurred in Belgium and the US.

In February, 2004, the Food and Agricultural Organization (FAO) and World Health Organization (WHO) organised the first Joint Expert Meeting to provide scientific advice for the revision of the Codex Alimentarius Recommended International Code of Practice for Foods for Infants and Children. Consistent with the need to provide safe feeding for all infants, the Expert Meeting examined the problem of *Enterobacter sakazakii* and other microorganisms in powdered infant formula, concluding that "intrinsic contamination of powdered infant formula with *Enterobacter sakazakii* and *Salmonella* has been a cause of infection and illness in infants, including severe disease which can lead to serious developmental sequelae and death"(1).

#### **Severity of infection**

*E. sakazakii*, a highly virulent pathogen, can be the cause for bacterial meningitis and cerebritis, sepsis and bacteraemia. Meningitis is the most frequently reported condition in *E. sakazakii* infection and can result in brain abscesses in around 90% of cases, causing quadriplegia and severe developmental delay. *E. sakazakii* meningitis leads to "an acute inflammation of the meninges surrounding the brain and spinal cord and frequently results in mortality". Infant mortality for *E. sakazakii* meningitis is 40-80%, with death often occurring within hours of infection (2). Scientific studies report that babies fed only infant formula rather than breastmilk are ten times more likely to contract necrotizing enterocolitis, a severe disease which leads to death in 10-55% of cases in premature neonates, and which some studies have attributed to *E. sakazakii* in the formula (2).

### **Populations at Risk**

The Expert Meeting noted that *E. sakazakii* has caused disease in all age groups and that among infants, those at greatest risk for *E. sakazakii* infection are neonates (less than 28 days old), particularly pre-term, low birth-weight or immuno-compromised infants. Infants of HIV positive mothers are also at risk, because they may require infant formula and they may be more susceptible to infection. The proportion of such infants, and low birth-weight infants, is higher in developing countries (1).

*E. sakazakii* infections have rarely been documented. In the USA, the rate of infection in low birth-weight babies was estimated at 8.7 per 100 000. Testing methods are slow to improve and it is only recently that *E. sakazakii* has been suspected and detected in infections in newborns in industrialised countries. Few developing countries have testing facilities capable of establishing the causal link between bacterial infection in the baby and the bacteria present in the formula. As the Expert Meeting noted: "There is a dearth of information on contamination of powdered infant formula sold in developing countries, and there has also been no surveillance on the disease burden resulting from consumption of contaminated powdered formula". A significant emerging problem is antibiotic resistance to the drugs used to treat suspected *E. sakazakii* infection(1), (2).

### **Cause of infections in newborns**

The Expert meeting "considered, on the basis of the information available, that in between 50 and 80% of cases, powdered infant formula is both the vehicle and the source (indirect or direct) of *E. sakazakii* induced illness" (1). Research on improved new testing protocols that was conducted in 2004 by the Nestlé Research Center concluded that contamination levels in milk powder factories are higher than previously detected: "A survey was carried out with 192 environmental samples from four different milk powder factories. Using this new protocol, *E. sakazakii* was isolated from almost 40% of the samples, whereas the reference procedure ... only yielded 26% positive results". (3).

### **Susceptibility of newborn babies to infections**

" The newborn infant is so susceptible to infections that powdered infant formula requires a high level of microbiological quality control during production, distribution and storage". (4) The Infant Food Manufacturers Advisory Committee on Child Health and Nutrition explains that "The immunophysiology of human milk cannot be reproduced in an infant

formula": the formula-fed infant is not protected by the anti-infective (anti-bacterial, anti-viral and anti-parasitic) agents present in breastmilk. Nor does this infant receive breastmilk to stimulate the development of the immature immune system. The formula-fed infant thus lacks protection against the risk of contracting meningitis or necrotizing enterocolitis caused by pathogens in the milk powder. (Note 1)

## **Recommendations to Manufacturers**

The Report of the 2004 Expert Meeting recommends that the infant food industry should be encouraged to reduce the concentration and prevalence of *E. sakazakii* in both the manufacturing environment and powdered infant formula. Industry should consider implementing an effective environmental monitoring programme, using the Enterobacter family as an indicator of hygienic control in factory production lines. There is currently no requirement to test for *E. sakazakii* and the current specifications for this pathogen are under review by the Codex Alimentarius Commission. Specific recommendations include employing a supplier assurance scheme and monitoring for raw materials, especially for ingredients not undergoing additional heat treatment prior to mixing. The processing of ingredients (drying of wet ingredients in large spray dryers, mixing dry minor ingredients in large blenders) requires strict adherence both to Good Manufacturing Practices (GMPs) as well as to Hazard Analysis Critical Control Point (HACCP) principles<sup>1</sup>. Effective separation of wet and dry processing operations is recommended, and industry should monitor and test the concentration and prevalence of the Enterobacteriaceae in finished products and at different points of the manufacturing process. "However, given the large quantity of the product consumed and the fact that even one contaminating bacteria is capable of growing in large numbers, a combination of risk reduction measures may be required for the effective management of the risk" (1).

### **Thermo-resistance of *E. sakazakii* strains**

It has been suggested that the high thermal resistance of *E. sakazakii* strains, compared to other members of the *Enterobacter* family, can possibly explain their high prevalence in powdered and prepared formula milk. Even low

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<sup>1</sup> Quality of raw materials, air and liquid filters, sifter screens, magnets/metal detectors, pasteurisation and storage temperatures are among such important control points and must be addressed specifically.

numbers of bacteria present in the tin may multiply exponentially at room temperature when the formula is reconstituted. Based on currently available knowledge, the Expert Meeting noted that sterilization of the final product in its dry form in a processing environment in cans or sachets seems only possible using irradiation. However, with the doses that are likely to be required to inactivate *E. sakazakii* in the dry state, the technology does not appear to be feasible due to nutritional changes and organoleptic deterioration of the product.

The 2004 Expert Meeting therefore concluded that "It is important to note that powdered infant formula meeting current standards is not a sterile product and may occasionally contain pathogens". The Meeting "did not identify a feasible method, using current technology, to produce commercially sterile powders or completely eliminate the potential of contamination".

### **The World Health Assembly**

For these reasons, in May 2005 the World Health Assembly (Note 2) adopted a resolution to address the problem by urging member States "to ensure that clinicians and other health-care personnel, community health workers and families, parents and other caregivers, particularly of infants at high risk, are provided with enough information and training by health-care providers, in a timely manner on the preparation, use and handling of powdered infant formula in order to minimize health hazards; are informed that powdered infant formula may contain pathogenic micro-organisms and must be prepared and used appropriately; and, where applicable, that this information is conveyed through an explicit warning on packaging."

In the USA, it is mandatory for other non-pasteurised food products such as apple juice to carry a warning on the packaging: "This product has not been pasteurised and, therefore, may contain harmful bacteria that may cause serious illness in children, the elderly, and persons with weakened immune systems".

### **The Codex Alimentarius Commission**

The Codex Committee on Food Hygiene has established a working group to consider the implications of the 2004 Risk Profile introduced by Canada and the USA documenting the severe life-threatening nature of *E. sakazakii* infections in susceptible neonates, and the sporadic low levels of pathogens

found in implicated formula products. These implicated products were general in conformity with the microbiological requirements of the current Codex Code of Hygienic Practices for Foods for Infants and Children, dating from 1979. The Working Group will review the risk assessment model for accuracy and validity, and will estimate the potential risk reduction associated with tightened microbiological criteria and the need to revise product labelling. The Proposed Draft Revision of the International Code of Practice for Food for Infants and Young Children is being discussed. The two parent bodies of the Codex Alimentarius Commission, FAO and WHO, convened a second Joint Expert Meeting in January 2006 to provide advice on how to minimise the risk of *E. sakazakii* and *Salmonella* in powdered infant formula, given that this risk cannot be eliminated. The product remains high risk for use in developing countries, where there is a higher number of vulnerable infants. The Report of this Expert Meeting will be made available on the FAO website in April 2006.

#### **References:**

(1) *Enterobacter sakazakii* and other microorganisms in powdered infant formula. FAO/WHO Expert Meeting Report: Microbiological Risk Assessment Series number 6, WHO, Geneva 2004: <http://www.who.int/foodsafety/publications/micro/mra6/en/print.html>  
Also available in Spanish on this site.

(2) Gurtler J, Kornacki J, Beuchat L. *Enterobacter sakazakii*: A coliform of increased concern to infant health. International Journal of Food Microbiology 2005; 104: 1-34

(3) Guillaume-Gentil O. et al. A simple and rapid cultural method for detection of *Enterobacter sakazakii* in environmental samples. Journal of Food Protection, 2005; 68 (1): 64-69

(4) Forsythe SJ. *Enterobacter sakazakii* and other bacteria in powdered infant milk formula. Blackwell Publishing Ltd. 2005. Maternal and Child Nutrition 1, pp. 44-50

(5) Wharton B. Infant Nutrition: Possible Future Developments in Developed Countries, IFM web site, October 2005: [www.ifm.net/industry/future.htm](http://www.ifm.net/industry/future.htm)

#### **Notes**

Note 1: As a global public health recommendation, infants should be exclusively breastfed for the first six months of life to achieve optimal growth, development and health. Infants who are not breastfed require a suitable breastmilk substitute, for example an infant formula prepared in accordance with applicable Codex Alimentarius standards. Information provided in this connection to mothers and other family members who need to use it should include adequate instructions for appropriate preparation and the health hazards of inappropriate preparation and use (WHO 2002 The Global Strategy for Infant and Young Child Feeding).

Note 2: The World Health Assembly is composed of the Ministers of Health of all the countries in the world and constitutes the highest policy-setting body in the field of international public health.