

3. HAZARD IDENTIFICATION

The microorganisms or microbial toxins of concern with powdered infant formula, and the strength of the evidence of a causal association between their presence in powdered infant formula and illness in infants, were categorized as follows:

3.1 CATEGORY “A” ORGANISMS – CLEAR EVIDENCE OF CAUSALITY

Enterobacter sakazakii and *Salmonella enterica* are in category “A” because both are well-established causes of illness in infants (e.g. systemic infection, necrotizing enterocolitis [NEC] and severe diarrhoea), and they have been found in powdered infant formula. Contaminated powdered infant formula has been convincingly shown, both epidemiologically and microbiologically, to be the vehicle and source of infection in infants.

The presence of *E. sakazakii* in powdered infant formula (and its association with illness in infants) is more likely than other Enterobacteriaceae or other *Enterobacter* species to be detected, because of the paucity of other vehicles or modes of transmission for *E. sakazakii* in this age group, and because it is facilitated by the use of molecular fingerprinting detection techniques. In other words, there may in fact be more instances of powdered infant formula-borne infection with Enterobacteriaceae than with *E. sakazakii*, but the former elude detection. Although there are clearly some differences in the microbial ecology of *S. enterica* and *E. sakazakii*, many of the risk-reduction strategies aimed at controlling *E. sakazakii* are also likely to control other Enterobacteriaceae, especially other *Enterobacter* species.

3.2 CATEGORY “B” ORGANISMS – CAUSALITY PLAUSIBLE, BUT NOT YET DEMONSTRATED

Other Enterobacteriaceae are in category “B” because they are well-established causes of illness in infants (e.g. systemic infection, NEC and severe diarrhoea) and have been found in powdered infant formula, but contaminated powdered infant formula has not been convincingly shown, either epidemiologically or microbiologically, to be the vehicle and source of infection in infants. These organisms include, for example: *Pantoea agglomerans* and *Escherichia vulneris* (both formally known as *Enterobacter agglomerans*), *Hafnia alvei*, *Klebsiella pneumoniae*, *Citrobacter koseri*, *C. freundii*, *Klebsiella oxytoca* and *Enterobacter cloacae*.

These organisms are increasing in importance as neonatal pathogens and, being Enterobacteriaceae (known to be present in low levels in powdered infant formula), are potential candidates as powdered infant formula-borne pathogens. For example, infant formula has been implicated as the vehicle of infection in an outbreak of *C. freundii* infection (Thurm and Gericke, 1994). In this event, however, it was not shown how the feed became contaminated.

3.3 CATEGORY “C” ORGANISMS – CAUSALITY LESS PLAUSIBLE OR NOT YET DEMONSTRATED

Other microorganisms are in category “C”, either because, despite causing illness in infants (e.g. systemic infection, NEC and severe diarrhoea), they have not been identified in powdered infant formula, or, although having been identified in powdered infant formula, they have not been implicated as causing such illness in infants. These organisms include *Bacillus cereus*, *Clostridium difficile*, *C. perfringens*, *C. botulinum*, *Staphylococcus aureus* and *Listeria monocytogenes*.

Bacillus cereus, a spore-forming gram-positive rod commonly found in the environment, is an acknowledged enteropathogen. Enterotoxigenic *B. cereus* has been isolated from reconstituted milk-based formula (Rowan and Anderson, 1998). Although one confirmed common source outbreak associated with infant formula has been reported in Chile (Cohen et al., 1984), no evidence of intrinsic contamination of the infant formula with *B. cereus* was provided. Thus, a causal association between powdered infant formula and *B. cereus* infection was not demonstrated.

Clostridium difficile is a frequent colonizer of newborns, usually without clinical manifestations. One study, sparked by the finding of stools positive for *C. difficile* in two infants dying of sudden infant death syndrome (SIDS), showed significantly greater colonization of newborns fed on formula than breastfed infants (Cooperstock et al., 1982). However, no direct link with powdered infant formula was established.