

Inquiry into Actions of Sector Agencies in Relation to Contamination of Infant Formula with Enterobacter Sakazakii

March 2005

**Dr P G Tuohy
Dr M Jacobs**

**Chief Advisor Child and Youth Health
Director of Public Health**

Ministry of Health 133 Molesworth Street Wellington



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Addendum:

Following the publication of this report the Ministry of Health has been informed of three earlier cases of *Enterobacter sakazakii* infection in New Zealand neonates. In 1986 a premature infant contracted *E.sakazakii* septicemia, but survived, apparently without serious sequelae. In 1991 premature twins contracted *E.sakazakii* meningitis. One twin suffered serious permanent neurological effects, and the other recovered fully.

The subsequent reports of these cases do not affect the findings or recommendations made in the report, but serve to highlight the importance of the recommendation that infection with this organism be made a notifiable disease.

Executive summary

In July 2004, a premature Waikato infant contracted *Enterobacter sakazakii* meningitis, and died. This tragic event led to an investigation which found that four other babies in the NICU were colonised with this organism, but did not become unwell. The investigation attributed the source of the organism to powdered infant formula used in the nursery.

E.sakazakii is a gram-negative rod-shaped bacterium which was first associated with neonatal deaths in 1958. Over the last 40 years about 50 cases of infection with this organism have been reported worldwide.

In April 2002 the Centre for Disease Control (CDC) and the U.S. Food and Drug Administration (USFDA) reported on a fatal case of *E.sakazakii* that had occurred the previous year. The USFDA made a number of recommendations to American health care providers. They recommended that powdered infant formulas not be used in neonatal intensive care settings unless there is no alternative available. They also recommended that if a powdered formula had to be used, that risks of infection could be reduced by preparing only a small amount of reconstituted formula for each feeding, minimizing the holding time before a reconstituted formula is fed, and minimizing the time over which the formula is administered by feeding tube (hang-time) to less than 4 hours. The New Zealand Ministry of Health (MoH) became aware of this information in mid 2002. The USFDA notification seemed to be related to a rare organism contaminating a brand of infant formula that was unavailable in New Zealand. We could not find any record that this information was passed on to hospitals or the public at that stage.

Over the next year and a half there was little public discussion about *E.sakazakii* but research continued, and in January 2004 WHO and FAO convened an international workshop in Geneva on the risk posed by this organism. The Ministry of Health, and the newly formed New Zealand Food Safety Authority became aware of the report from this workshop the following month and began to consider a New Zealand response to the recommendations. On the basis that this was a rare infection, and no known cases had occurred in New Zealand, it was not considered that this process was urgent. Unfortunately within a few months of this work being commenced a cluster of cases occurred in New Zealand with one fatality.

This report considers the recent emergence of information about *E.sakazakii* and the recommendations regarding prevention of infection with this organism. The findings of the report are:

- a) Given the information available at the time, the Ministry of Health and the NZFSA acted reasonably in relation to the risks posed by *E.sakazakii*.
- b) The initial response to the issue of *E.sakazakii* following the USFDA recommendations in 2002 was reasonable, in the context of the rareness of the condition and the fact that no known infections had occurred in New Zealand. The issue was at least partially portrayed as relating to one specific brand of product, which was not available in New Zealand.

- c) Although the health sector in New Zealand generally relies more on WHO advice than that emanating from the USFDA, the Ministry of Health could have, at this stage, facilitated the dissemination of the 2002 USFDA recommendations to hospitals with Neonatal intensive care units. Further, although it was reasonable in the context not to make the adoption of RTF feeds mandatory, a recommendation to review milk room practices and hang time could have been made.
- d) The Ministry of Health and the NZFSA acted reasonably when informed of the WHO/FAO report in January 2004. Given the rareness of the infection and the ongoing discussion among overseas regulatory agencies, the issue was given an appropriate priority and was being addressed through interagency collaboration, but unfortunately the process was not completed prior to the infant's death.
- e) The Ministry of Health reacted appropriately to the death of the infant at Waikato Hospital, and information was provided to the sector and to the public in a timely and professional fashion.

A number of recommendations are made by this report. These address systemic issues which the investigation has brought to light, and suggest changes to processes and future actions which should reduce the likelihood of similar problems recurring. The recommendations are:

1. That the Ministry of Health and NZFSA review their MOU in order to clarify the roles and responsibilities of each organisation with respect to food borne infectious diseases, and disseminate the MOU throughout relevant areas of each organisation.
2. That a formal letter should follow all email correspondence between the NZFSA and Ministry of Health when joint review of a food safety topic is necessary. This should be copied to the Deputy Director General – Public Health. Audit trails for incoming correspondence should be reviewed.
3. That the Ministry of Health identify a process through which relevant WHO/FAO, USFDA, CDC and other international health authority decisions and recommendations relating to clinical safety are identified, and passed on to the relevant Directorates. The process should ensure that “new risks” are on the standing agenda of key committees with clear reporting arrangements to the highest level of the food safety governance framework.
4. That all relevant current Ministry of Health health information and health promotion material relating to infant feeding is reviewed by the end of May 2005 to ensure that it is consistent with the current recommendations.
5. That the current recommendations made by the Ministry of Health and the NZFSA regarding this organism be reviewed in light of emerging information, at latest by October 2005 and going forward on a regular basis as international developments emerge over time.

6. That in order to monitor adequacy of the implementation of the advice to NICUs, and to support health international agencies, infections with *E.sakazakii* be made a notifiable disease under the Health (Infectious and Notifiable Diseases) Regulations 1966. A retrospective review of notifications should be performed, and any isolates properly typed to permit proper identification of the source of outbreaks.

Terms of Reference

1 Issue which led to the Inquiry

In July 2004, a baby died following *Enterobacter sakazakii* (*E.sakazakii*) infection while in a Neonatal Intensive Care Unit in the Waikato region.

2 Terms of Reference

The Director-General by letter dated 11 February 2005 appointed Drs Pat Tuohy and Mark Jacobs to investigate this issue as follows:

- I. To determine the information available on the safety of infant formula in respect to contamination by *E.sakazakii*.
- II. To investigate what actions the responsible government agencies undertook to ensure public safety.
- III. Report to the Director-General of Health on the results of the inquiry making recommendations as appropriate regarding the appropriateness and timeliness of actions and any changes required to improve processes and procedures.
- IV. The report is to be completed by 11 March 2005.

Determine the information available on the safety of infant formula in respect to contamination by *E.sakazakii*.

Introduction

Enterobacter sakazakii is a gram-negative rod-shaped bacterium classified in the *Enterobacteriaceae* family and was first associated with neonatal deaths in 1958. The organism was previously called "yellow-pigmented *Enterobacter cloacae*" but was renamed *Enterobacter sakazakii* in 1980.

Over the last 40 years about 50 cases of infection with this organism have been reported worldwide. *E.sakazakii* has disproportionately affected preterm neonates with sepsis, meningitis, or necrotizing enterocolitis the most commonly described sites of infection, however some term and older infants have been infected and died or suffered permanent brain damage. This is well documented in the Annex 2 to the Codex Alimentarius paper of January 2004, which is attached as Appendix A (www.codexalimentarius.net/ccfh36/fh04_01e.htm). The case-fatality rate among infected neonates is high with figures between 33% and 50% reported. *E.sakazakii* is also a rare cause of bacteremia and osteomyelitis in adults.

The organism is ubiquitous in the environment, but milk-based powdered infant formulas have served as the source in many cases of neonatal infection. Levels of *E.sakazakii* in milk-based powdered infant formula that are within the 1994 Codex Alimentarius limit for coliforms have been shown to cause infection.

It has been reported anecdotally (J. Bhatia personal communication) that cases of *E.sakazakii* infection have occurred in NICUs using ready to feed (RTF) formula, possibly because the use of powdered formula for rare metabolic conditions, and because of the addition of 'fortifier' powdered formula to expressed breast milk (EBM) to increase caloric density. Recent research suggests that a 'hang time' of less than 4 hours is unlikely to permit sufficient bacterial growth to cause infection.

A timeline of *E.sakazakii* related reports and activities

| | |
|---------------|---|
| 1961 | First report of <i>E.sakazakii</i> infection in a neonate. |
| 1980 | Name change from <i>E.cloacae</i> (<i>yellow pigmented</i>) to <i>E.sakazakii</i> |
| 2001 April | Outbreak in a neonatal nursery in Tennessee |
| 2002 April | CDC publish review in MMWR |
| 2002 April | ANZFA contacts NZ MoH about product recall due to <i>E.sakazakii</i> |
| 2002 May | MoH contacted by National Womens' Hospital about <i>E.sakazakii</i> risk |
| 2002 July | Health Canada issue warning to health professionals |
| 2002 October | USFDA recommend changing to RTF formula and other measures |
| 2003 April | Food safety functions transferred from MoH to NZFSA |
| 2004 January | MoH alerted to UK study on <i>E.sakazakii</i> implicating infant formula |
| 2004 February | WHO/FAO joint workshop on <i>E.sakazakii</i> , MoH alerted to recommendations |
| 2004 February | MoH requests NZFSA to consider public announcement on <i>E.sakazakii</i> risk |
| 2004 March | Codex Alimentarius Committee meeting on <i>E.sakazakii</i> held in Ottawa |
| 2004 April | NZFSA commence work on <i>E.sakazakii</i> |
| 2004 May | MoH invited to comment on NZFSA draft report |
| 2004 May | NZFSA place <i>E.sakazakii</i> report on website |
| 2004 July | Infant dies at Waikato hospital from <i>E.sakazakii</i> meningitis |
| 2004 October | ESPGHAN report |
| 2005 January | INFOSAN report |
| 2005 March | Codex Committee meeting in Buenos Aires |

2002 – 2004 International reports

On the 12th of April 2002 the Centre for Disease Control (CDC) reported on a fatality associated with an outbreak of *E.sakazakii* in a NICU in Tennessee in their weekly review paper, Morbidity and Mortality Weekly Report (MMWR), which is attached as Appendix B (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5114a1.htm>). The Ministry of Health would have received this information at the time as a library subscription to MMWR has been in place for several years. .

The CDC made a number of recommendations that were simultaneously promulgated to American health practitioners by the U.S. Food and Drug Administration (USFDA). However USFDA alerts are not routinely sent to overseas regulatory agencies, such as the Ministry of Health, unless specifically requested. On October 10th 2002 the USFDA wrote again to update American health practitioners about the risk *E.sakazakii* posed to neonates fed milk-based powdered infant formulas. (<http://www.cfsan.FDA.gov/~dms/inf-ltr3.html>). The revised letter (Appendix C) deleted the initial recommendation regarding preparation of infant formula with boiling water due to potential for loss of heat sensitive nutrients, changes in physical characteristics of some formulas, inability to assure adequate destruction of *E.sakazakii*, and injury to hospital staff preparing formula.

The USFDA noted in their October letter that clusters of *E.sakazakii* infections have been reported among infants fed milk-based powdered infant formula products from various manufacturers. Studies showed that the bacterium was present in small amounts in up to 15% of samples tested.

Although there has been considerable bacteriological interest and clinical concern about this organism, infections remain extremely rare and are not currently subject to mandatory reporting in the USA or elsewhere.

Powdered infant formulas, unlike RTF formulas, are not subjected to high temperatures for sufficient time to make the final packaged product commercially sterile. The USFDA noted in their October 2002 letter that infant formulas nutritionally designed for consumption by premature or low birth weight infants are available in commercially sterile liquid form. Some other specialty infant formulas, and milk fortifier are only available in powder form. These are still used in NICUs worldwide.

The USFDA also noted that a substantial percentage of premature neonates in neonatal intensive care units were being fed reconstituted non-sterile infant formula. In light of the epidemiological findings and the fact that powdered infant formulas are not commercially sterile products, the USFDA recommended that powdered infant formulas not be used in neonatal intensive care settings unless there is no alternative available. If the only option available to address the nutritional needs of a particular infant is a powdered formula, the USFDA advised that risks of infection could be reduced by:

- Preparing only a small amount of reconstituted formula for each feeding to reduce the quantity and time that formula is held at room temperature for consumption; Recognizing differences in infant formula preparation among

hospitals, individual facilities should identify and follow procedures appropriate for that institution to minimize microbial growth in infant formulas;

- Minimizing the holding time, whether at room temperature or while under refrigeration, before a reconstituted formula is fed; and
- Minimizing the "hang-time" (i.e., the amount of time a formula is at room temperature in the feeding bag and accompanying lines during enteral tube feeding), with no "hang-time" exceeding 4 hours. Longer times should be avoided because of the potential for significant microbial growth in reconstituted infant formula.

These recommendations were also provided to Canadian health professionals by Health Canada in July 2002 and published on the Health Canada Website (http://www.hc-sc.gc.ca/food-aliment/mh-dm/mhe-dme/e_enterobacter_sakazakii.html) Appendix D.

There is no available literature which indicates the level of compliance with the USFDA's recommendations in any country, or which provides any information about subsequent incidence of *E.sakazakii* infection in the USA, as cases are not subject to mandatory reporting.

In February 2004 a Joint FAO/WHO Workshop was held in Geneva on 'Enterobacter Sakazakii and Other Microorganisms in Powdered Infant Formula'. Attendance was by invitation to specific experts, rather than by national representation, and no Ministry of Health or NZFSA officials were invited to attend this expert group meeting.

A number of recommendations were made at that meeting and published on the WHO website (<http://www.who.int/foodsafety/micro/meetings/feb2004/en/print.html>) The report is attached as Appendix E, and was made available to the Ministry of Health and NZFSA in February.

The relevant recommendations are extracted below.

8.2 Recommendations made by FAO and WHO from February 2004 workshop

8.2.1 To member countries, NGOs, FAO and WHO

- *Encourage health professionals to investigate and report sources and vehicles (including powdered infant formula) of infection by E.sakazakii and other Enterobacteriaceae.*
- *In situations where the mother cannot breastfeed or chooses not to breastfeed for any reason, alert caregivers of infants – both in the home and in healthcare facilities (particularly those at high risk) – to the fact that powdered infant formula is not a sterile product and that even a product meeting existing Codex standards can be contaminated with pathogens that can cause serious illness.*
- *Develop guidelines for the preparation, use and handling of infant formulas to minimize the risks.*
- *In situations where the mother cannot breastfeed or chooses not to breastfeed for any reason, encourage caregivers of infants, particularly those at high risk, to use, whenever possible and appropriate, commercially sterile formula (e.g. liquid) or formula which has undergone an effective point-of-use decontamination procedure (e.g. heating reconstituted formula).*
- *Encourage industry to develop a greater range of alternative formula products that are commercially sterile for high-risk groups.*

- Encourage industry to reduce the concentration and prevalence of *E.sakazakii* in the manufacturing environment and powdered infant formula (in a context of risk reduction options).
- Nutritional and other factors need to be considered, e.g. alteration of nutritional content, risk from burns due to handling boiling or hot water or formula, and potential for increased risk from germination of bacterial spores. The formula should thereafter be cooled and handled properly.
- Encourage industry to use an effective environmental monitoring programme as an important component to an effective environmental management programme.
- Promote the use of Enterobacteriaceae rather than coliform testing as an indicator of hygienic control in factories.

8.2.2 To Codex Commission on Food Hygiene (CCFH)

- Revise the code of practice and related text including the microbiological specifications to better address the microbiological risks of powdered infant formula.
- Establish appropriate microbiological specifications for *E.sakazakii* in powdered infant formula.

8.2.3 To member countries, FAO, WHO, Codex and NGOs

- Enhance risk communication, training, labeling and educational activities and approaches to ensure awareness of the issue and appropriate point of use procedures for preparation, storage and use of infant formula.
- Address the capability of adults to implement control measures in the process of preparation and administration of formula and the capability of laboratory technicians to identify *E.sakazakii*.

8.2.4 To FAO, WHO and the scientific community

- Promote the use of internationally validated detection and molecular typing methods for *E.sakazakii* and related organisms.
- Establish a laboratory-based network to alert authorities of *E.sakazakii* outbreaks based on standardized reference methods with supporting central laboratory resources and training facilities.
- Promote research on ways to reduce the levels of *E.sakazakii* in reconstituted powdered infant formula, e.g. strict time-temperature control on rehydration, decreasing the time of feeding, addition of inhibitors, use of biopreservatives and acidification and combining treatments.
- Promote research to gain a better understanding of the ecology, taxonomy, characteristics and virulence of *E.sakazakii*.

In March 2004 the issue of *E.sakazakii* in infant formula was brought to the attention of the 35th session of the CCFH by two separate processes. The 24th session of the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) requested the CCFH to revise the Recommended International Code of Hygienic Practices for Foods for Infants and Children (CAC/RCP 21-1979) in order to address concerns raised by pathogens that may be present in infant formula.

At the same time, the United States of America and Canada introduced a risk profile (Appendix A) for *E.sakazakii* in powdered infant formula for consideration by the committee. (www.codexalimentarius.net/ccfh36/fh04_01e.htm)

The profile documented the severe life-threatening nature of *E.sakazakii* infections in susceptible neonates and infants and the sporadic, low levels of pathogen found in implicated formula products. Implicated products were generally in conformance with the microbiological requirements of the current Codex Alimentarius Code of Hygienic Practices for Foods for Infants and Children.

As a result, the 35th Session of the CCFH:

1. set up a drafting group led by Canada to initiate revision of this code;
2. noted that, as well as *E.sakazakii*, there were a number of other pathogen of concern that may be present in powdered infant formula such as *Clostridium botulinum*, *Staphylococcus aureus* and other *Enterobacter* species;
3. requested the United States and Canada to update the risk profile to include other pathogens of concern, and
4. requested FAO and WHO to convene an expert consultation on pathogens of concern in powdered infant formula, at the earliest opportunity.

In November 2004 the working group met in Ottawa, Canada to consider the issues raised in the March meeting, and to revise the International Code for Hygienic Practice for Foods for Infants and Children. It was suggested that the Code be replaced by a Draft Recommended International Code for Hygienic Practice for Powdered Infant Formula.

In September 2004 the European Food Safety Authority debated the international response to *E.sakazakii* and recommended that:

1. A Performance Objective (PO) for powdered infant formula and follow-on formula, aiming at very low levels of Salmonella and *E.sakazakii* (e.g. absence in 1, 10 or 100 kg) is introduced.
2. That verification of compliance with the PO is confirmed by testing for Enterobacteriaceae in the environment and in the product
3. That guidelines for preparation, handling, storage and use of infant formula in the home and in hospitals are developed.

http://www.efsa.eu.int/science/biohaz/biohaz_opinions/691_en.html

In October 2004 the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGAN) published an article in the Journal of Paediatric Gastroenterology and Nutrition in entitled "Preparation and Handling of Powdered Infant Formula: A Commentary by the ESPGHAN Committee on Nutrition." This article is attached as Appendix F. An abstract is available from the following website.

<http://www.jpagn.org/pt/re/jpagn/abstract.00005176-200410000-00002.htm;jsessionid=CZhDLOwy7D2hQNbumnzpUK3f4hgQ8qCimEcap3ScpjWPb11Q151H!2131737664!-949856031!9001!-1>

ESPGHAN noted the following:

- Powdered infant formulae are not sterile and may contain pathogenic bacteria. Milk products are excellent media for bacterial proliferation.
- Multiplication of *E.sakazakii* in prepared formula feeds can cause devastating sepsis, particularly in the first 2 months of life.
- In approximately 50 published case reports of severe infection, there are high rates of meningitis, brain abscesses and necrotizing enterocolitis, with an overall mortality from 33% to 80%.
- Breastfeeding provides effective protection against infection, one of the many reasons why it deserves continued promotion and support.

ESPGHAN made the following recommendations to minimize the risk of infection in infants not fully breastfed.

- Powdered formulae for children younger than 2 months should be freshly prepared for each feed.
- Any milk remaining should be discarded rather than used in the following feed. Infant feeds should never be kept warm in bottle heaters or thermoses.
- In hospitals and other institutions written guidelines for preparation and handling of infant formulae should be established and their implementation monitored.
- If formula needs to be prepared in advance, it should be prepared on a daily basis and kept at 4°C or below.
- Manufacturers of infant formulae should make every effort to minimize bacterial contamination of powdered products

2004 Australian reports

In July 2004 the Australian Food Safety Centre, a joint Government/industry body, published a summary of the advance report from the Geneva workshop on the Food Safety Centre's website. It is attached as Appendix G, and available from <http://www.foodsafetycentre.com.au/fsh/fshbull36a.htm>

This report contained a number of risk reduction strategies for formula fed infants .

The principal measures identified were:

- reduce initial levels of the organism in raw materials on receipt;
- reduce levels during heat treatment of raw milk related ingredients and reconstituted powdered
- infant formula prior to use;
- prevent an increase in levels by avoiding post-processing contamination;
- apply microbiological criteria. In order to implement effective microbiological criteria, it will be necessary to validate the recommended and newly developed detection methods; and
- provide appropriate information and preparation instructions.

The report noted that in a number of UK studies, *E.sakazakii* grew between 6°C and 45°C in all media tested with one strain being able to grow at 47 °C but only in infant formula milk. They concluded that the standard high-temperature short-time pasteurisation process of 15 seconds at 72 °C will inactivate the organism.

The authors also recommend that all bottles and utensils should be cleaned thoroughly as soon as possible after use to deter *E.sakazakii* biofilm formation, which could become a source of infection.

2004 New Zealand reports

In May 2004 the New Zealand Food Safety Authority placed a draft report from its Dairy Technical Consultation Committee on its website in response to commercial concerns regarding the presence of *E.sakazakii* in New Zealand milk powder.

The report, which is attached as Appendix H, identified the risk to infants of *E.sakazakii* in powdered milk formula and commented that "...WHO recommends the use of commercially sterile liquid formula or the careful preparation of powdered formula".

<http://www.nzfsa.govt.nz/dairy/publications/information-papers/enterobacter-sakazakii/>

2005 International reports

The International Food Safety Authorities Network (INFOSAN)

INFOSAN represents a number of European regulatory agencies. In their Information Note 1/2005 on the 13th of January 2005 (Appendix I) they made a number of recommendations about infant formula preparation, which included:

- *Use of hot (70 degree Celsius) water to make up infant feeds.*
- *Make up the feed just before feeding baby – one feed at a time.*
- *Consumers should be alerted through labeling or other means that powdered infant formula is not a sterile product.*

The report is available on the following website:

No recommendations were made by INFOSAN on the use of prepackaged liquid formula in NICUs.

Codex Alimentarius commission – Committee on food hygiene

The commission met on March 14th 2005 in Buenos Aires to discuss a number of food hygiene issues including the proposed revised code prepared by Canada. The agenda is attached as Appendix J, and available from the website: http://www.codexalimentarius.net/ccfh36/fh04_01e.htm

Current international recommendations

1. Use of Ready to Feed (RTF) formula in NICUs.

Sterile RTF formula should be used instead of powdered infant formula where possible and appropriate, especially in high risk infants. (CDC, USFDA and WHO/FAO) This recommendation was not mentioned by ESPGHAN or INFOSAN.

2. Use of powdered formula (general)

Preparing only a small amount of reconstituted formula for each feeding to reduce the quantity and time that formula is held at room temperature for consumption. (USFDA) (ESPGHAN - infants <2 months) (INFOSAN).

- *Individual facilities should identify and follow procedures appropriate for that institution to minimize microbial growth in infant formulas; (USFDA)*
- *Minimizing the holding time, whether at room temperature or while under refrigeration, before a reconstituted formula is fed; (USFDA) (ESPGHAN)*
- *If formula needs to be prepared in advance, it should be prepared on a daily basis and kept at 4°C or below. (ESPGHAN)*
- *Minimizing the "hang-time" (i.e., the amount of time a formula is at room temperature in the feeding bag and accompanying lines during enteral tube feeding), with no "hang-time" exceeding 4 hours. (USFDA)*
- *Health professionals should investigate and report sources and vehicles (including powdered infant formula) of infection by *E.sakazakii* and other Enterobacteriaceae. (WHO/FAO)*

- *Health providers should advise parents and caregivers about the risk of ES in powdered milk formula. (WHO/FAO)*
- *Develop guidelines for the preparation, use and handling of infant formulas to minimize the risks. (WHO/FAO), (ESPGHAN)*
- *Consider the use of boiled water cooled to 70 degrees C to reconstitute powdered infant formula. (WHO/FAO), (INFOSAN). This was initially suggested by the CDC but is not recommended by the USFDA and was removed from the health professional advisory letter of October 2002. This process is opposed by the food industry groups.*

Any milk remaining should be discarded rather than used in the following feed. Infant feeds should never be kept warm in bottle heaters or thermoses. (ESPGHAN)

Investigate what actions the responsible government agencies undertook to ensure public safety

Ministry of Health Actions

On the 17th April 2002 the Australian and New Zealand Food Authority (ANZFA) contacted the Ministry of Health about the recall of a specific infant formula because of the outbreak of *E.sakazakii* in Tennessee in 2001 which led to the 2002 CDC report and the USFDA letter to health practitioners. In the ANZFA email there was no reference to any USFDA or other recommendations about the use of powdered infant formula in a NICU setting.

On the 6th of May 2002, a Dietician at the National Womens' Hospital contacted the food group of the Ministry of Health about the issue. In response to the hospital the Ministry of Health determined that the relevant product was not for sale in New Zealand, and did not consider an advisory necessary. The email in response said:

"There has been no identifiable problem with such formulas in New Zealand, therefore the Ministry of Health has not issued any guidelines. However as a precautionary measure hospitals may decide to adopt procedures such as those outlined by the USFDA."

There is no record as to whether or not the USFDA precautionary measures were communicated by the Ministry of Health to any other hospitals at this time.

In January 2004 the Ministry of Health was alerted to a media article from the BBC on *E.sakazakii* in commercial foods (including infant formula) in the Netherlands, and contacted ESR to determine whether there had been any cases in New Zealand. No cases were identified, but there was a comment that the bacteria had been detected in a meat rendering plant and a milk processing plant in New Zealand.

In February 2004 the summary report of the Joint WHO/FAO Workshop was released and distributed within the nutrition group of the Ministry of Health. In March 2004 the Ministry of Health brought this report to the attention of NZFSA, and in email correspondence requested NZFSA to consider what measures needed to be put in place *"to prevent cases in New Zealand"* and asked *"Whether [NZFSA] had any plans to inform practitioners/public about the risks"*.

This email was acknowledged by NZFSA at the end of March 2004, and as a response, in early April 2004 the NZFSA provided some suggestions as to who in the milk industry was dealing with the issue. At that stage the NZFSA was not actively pursuing the issue, although they then commenced work and produced a draft technical report (Appendix H) and sought comment via email from the Ministry of Health in early June 2004, a month or so before the death of the Waikato baby. However the Ministry of Health contact to whom the email was sent was on leave and no Ministry of Health action was taken on these draft reports until the notification of the death of the baby in Waikato hospital in early August 2004.

In early August 2004 the Ministry of Health was contacted about the recent death of an infant at Waikato hospital. There followed discussion with staff from the Public Health Directorate and NZFSA, and a meeting was held at NZFSA on the 6th of August 2004.

By the end of the same day the Ministry of Health had emailed the information about *E.sakazakii* to all paediatricians and contacted all tertiary NICUs to identify whether any still used powdered formula. It was discovered that only Wellington still used powdered formula, considering that the risk to infants was adequately dealt with through good milk-room practice and short hang times. Wellington NICU was advised to change to a liquid Ready-to-feed (RTF) formula as soon as practicable.

On Monday the 10th August 2004 all District Health Board (DHB) Chief Executives were sent a letter advising them of the incident and that the Ministry of Health recommended prepared liquid formula be used in NICUs where possible.

On the 13th of August 2004 all Level 3 and 2+ Neonatal units (who look after the sickest babies) were contacted to ensure that they had received the email advice and to check their protocols for infant formula. They were provided with copies of the press release and parent and health professional information for their information prior to their release.

The Ministry of Health and NZFSA then worked together to put together a press release and information to parents and health practitioners, which were released on the 25th August 2004.

In December 2004 the Ministry of Health conducted a telephone survey of all DHBs to identify compliance with Ministry of Health advice about the use of RTF formula and hang time. By February 2005 it was confirmed that all DHBs were fully compliant.

New Zealand Food Safety Authority actions

In May 2001 the New Zealand Government agreed to integrate the responsibilities of food safety previously shared between the Ministry of Agriculture and Forestry and the Ministry of Health. This recognised the requirement for the NZFSA and the Ministry of Health's Public Health Directorate to collaborate on food issues. The New Zealand Food Safety Authority was subsequently established in July 2002.

NZFSA was informed of the FAO/WHO workshop recommendations by the Ministry of Health in February 2004, and subsequently convened their Dairy Consultative Committee to produce a report on *E.sakazakii* (Noted above Appendix H). This was provided to the Ministry of Health by email for comment in June 2004, but the relevant people in the Ministry of Health did not note the email and no action was taken.

NZFSA was also required to mitigate the risk to the New Zealand milk industry due to overseas countries attempting to use the presence of *E.sakazakii* as a reason for imposing import restrictions on New Zealand milk powder. The organisation considered that the health risks to infants in NICUs was a matter better managed by the Ministry of Health, and they therefore they chose to place the emphasis of their policy on the risk to healthy people from exposure to *E.sakazakii* presence in a range of foodstuffs. As the Ministry of Health was not part of this decision this meant that the risk to premature and sick infants, which was in fact the major health risk posed by this organism was not fully addressed by either of the two organisations.

Report on the appropriateness and timeliness of actions of Government agencies

It is our view that:

Given the information available at the time, the Ministry of Health and the NZFSA acted reasonably in relation to the risks posed by *E.sakazakii*.

- a) The initial response to the issue of *E.sakazakii* following the USFDA recommendations in 2002 was reasonable, in the context of the rareness of the condition and the fact that no known infections had occurred in New Zealand. The issue was at least partially portrayed as relating to one specific brand of product, which was not available in New Zealand.
- b) Although the health sector in New Zealand generally relies more on WHO advice than that emanating from the USFDA, the Ministry of Health could have, at this stage, facilitated the dissemination of the USFDA recommendations to hospitals with Neonatal intensive care units. Further, although it was reasonable in the context not to make the adoption of RTF feeds mandatory, a recommendation to review milk room practices and hang time could have been made.
- c) The Ministry of Health and the NZFSA acted reasonably when informed of the WHO/FAO report in January 2004. Given the rareness of the infection and the ongoing discussion among overseas regulatory agencies, the issue was given an appropriate priority and was being addressed through interagency collaboration, but unfortunately the process was not completed prior to the infant's death.
- d) The Ministry of Health reacted appropriately to the death of the infant at Waikato Hospital, and information was provided to the sector and to the public in a timely and professional fashion.
- e) The Ministry of Health reacted appropriately to the death of the infant at Waikato Hospital, and information was provided to the sector and to the public in a timely and professional fashion.

Recommendations of this review

1. That the Ministry of Health and NZFSA review their MOU in order to clarify the roles and responsibilities of each organisation with respect to food borne infectious diseases, and disseminate the MOU throughout relevant areas of each organisation.
2. That a formal letter should follow all email correspondence between the NZFSA and Ministry of Health when joint review of a food safety topic is necessary. This should be copied to the Deputy Director General – Public Health. Audit trails for incoming correspondence should be reviewed.
3. That the Ministry of Health identify a process through which relevant WHO/FAO, USFDA, CDC and other international health authority decisions and recommendations relating to clinical safety are identified, and passed on to the relevant Directorates. The process should ensure that “new risks’ are on the standing agenda of key committees with clear reporting arrangements to the highest level of the food safety governance framework.
4. That all relevant current Ministry of Health health information and health promotion material relating to infant feeding is reviewed by the end of May 2005 to ensure that it is consistent with the current recommendations.
5. That the current recommendations made by the Ministry of Health and the NZFSA regarding this organism be reviewed in light of emerging information, at latest by October 2005 and going forward on a regular basis as international developments emerge over time.
6. That in order to monitor adequacy of the implementation of the advice to NICUs, and to support health international agencies, infections with *E.sakazakii* be made a notifiable disease under the Health (Infectious and Notifiable Diseases) Regulations 1966. A retrospective review of notifications should be performed, and any isolates properly typed to permit proper identification of the source of outbreaks.

APPENDICES

- Appendix A http://www.codexalimentarius.net/ccfh36/fh04_01e.htm
- Appendix B <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5114a1.htm>
- Appendix C <http://www.cfsan.FDA.gov/~dms/inf-ltr3.html>
- Appendix D http://www.hc-sc.gc.ca/food-aliment/mh-dm/mhe-dme/e_enterobacter_sakazakii.html
- Appendix E <http://www.who.int/foodsafety/micro/meetings/feb2004/en/print.html>
- Appendix F <http://www.jpqn.org/pt/re/jpqn/abstract.00005176-200410000-00002.htm;jsessionid=CZhDLOwy7D2hQNbumnzpUK3f4hgQ8qCimEcap3ScpjWPb11Q151H!2131737664!-949856031!9001!-1>
- Appendix G <http://www.foodsafetycentre.com.au/fsh/fshbull36a.htm>
- Appendix H <http://www.nzfsa.govt.nz/dairy/publications/information-papers/enterobacter-sakazakii/>
- Appendix I http://www.who.int/foodsafety/fs_management/en/No_01_Esakazakii_Jan05_en.pdf
- Appendix J http://www.codexalimentarius.net/ccfh36/fh04_01e.htm