

NATIONAL STANDARD METHOD

# **PRESUMPTIVE DIAGNOSIS OF *CRONOBACTER SAKAZAKII* INFECTION IN INFANTS**

**QSOP 58**

Issued by Standards Unit, Department for Evaluations, Standards and Training  
**Centre for Infections**







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## Suggested citation for this document:

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# AMENDMENT PROCEDURE

Controlled document reference	QSOP 58
Controlled document title	Presumptive Diagnosis Of <i>Cronobacter Sakazakii</i> Infection In Infants

Each National Standard Method has an individual record of amendments. The current amendments are listed on this page. The amendment history is available from [standards@hpa.org.uk](mailto:standards@hpa.org.uk).

On issue of revised or new pages each controlled document should be updated by the copyholder in the laboratory.

Amendment Number/ Date	Issue no. Discarded	Insert Issue no.	Page	Section(s) involved	Amendment
1/ 10.03.2010	1	2	All	<b>All</b>	Title of document changed to 'Presumptive diagnosis of <i>Cronobacter sakazakii</i> infection in infants'
			All	<b>All</b>	<i>Enterobacter sakazakii</i> changed to <i>Cronobacter sakazakii</i>
			1	<b>Title Page</b>	SMF logo added
				<b>References</b>	Assessed and updated

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# PRESUMPTIVE DIAGNOSIS OF *CRONOBACTER SAKAZAKII* IN INFANTS

**Types of specimen:** Blood  
CSF  
Stools  
Urine  
Gastric aspirate

## INTRODUCTION

The aim of this document is to provide guidance for communications and action across the Health Protection Agency (HPA), National Health Service (NHS), Department of Health (DH) and Food Standards Agency (FSA) following a presumptive diagnosis of *Cronobacter sakazakii*<sup>2</sup> infection in infants that might be associated with powdered infant formula at a local hospital laboratory. *Salmonella* and *C. sakazakii* are the micro-organisms of greatest concern in infant formulae, formulae for special medical purposes and follow-on formulae. The presence of these pathogens constitutes a considerable risk if conditions after reconstitution permit multiplication<sup>3</sup>.

Contamination of powdered infant formula with *C. sakazakii* and with salmonellae has been the cause of infection in infants, sometimes with serious sequelae or death. Although *C. sakazakii* has caused illness in all age groups of neonates (up to approximately 4-6 weeks of age), pre-term or low birth weight infants and those who are immunocompromised are at greatest risk<sup>3</sup>.

**Note:** It is the purpose of this NSM to provide diagnostic microbiology laboratories with information regarding the organism *Cronobacter sakazakii* and its association with infant formula.

## Taxonomy

*Cronobacter sakazakii* is a member of the family Enterobacteriaceae, genus *Cronobacter*<sup>4</sup> and it is a peritrichous, motile, Gram-negative rod<sup>5</sup>.

*C. sakazakii* was originally designated as a yellow-pigmented variant of *Cronobacter cloacae*. In 1980 *C. sakazakii* was introduced as a new species based on differences between *C. sakazakii* and *C. cloacae* in DNA-DNA hybridisation, biochemical reactions, the production of yellow-pigmented colonies and differences in antibiotic susceptibility<sup>4,5</sup>.

## Clinical features

*Cronobacter sakazakii* is an opportunistic pathogen that can cause life threatening bacterial infections in infants<sup>6</sup>. It has been found to be the causative agent of invasive infection in neonates and has been linked to several outbreaks of neonatal meningitis and necrotising enterocolitis<sup>7</sup>. Very low birth weight, premature or immunosuppressed babies are most at risk of infection<sup>3,8</sup>. Healthy babies are at less risk from this organism<sup>9</sup>. *C. sakazakii* infection has a high mortality rate estimated between 40-80% in vulnerable infants<sup>4,10</sup>. In surviving patients, severe neurological sequelae have occurred, including hydrocephalus, quadriplegia and developmental delay<sup>4</sup>.

## Infant formula outbreaks

Overall since 1958 (when the first case of neonatal meningitis due to *Cronobacter sakazakii* was reported) there have been at least 111 cases and 26 deaths worldwide<sup>11</sup>. Contaminated powdered formula milk has been implicated as the source of the infection in at least five *C. sakazakii* outbreaks in both the United States and Europe<sup>7,9,10,12</sup>. In an outbreak, between October and December 2004, five neonates in France were diagnosed with *C. sakazakii* infection, including two deaths. There were also five cases of digestive tract colonisation. This prompted a voluntary international withdrawal of the implicated powdered baby milk (except in the United States and Canada)<sup>13</sup>.

Powdered infant formula, meeting current standards, is not a sterile product. The EC Regulation on microbiological criteria for foodstuffs<sup>14</sup> however, provides that *C. sakazakii* should be absent from dried infant formula and dried dietary foods for special medical purposes intended for infants below six months of age<sup>14</sup>. *C. sakazakii* does not survive the pasteurisation process of powdered formula milk production. However, this milk may become contaminated following pasteurisation, during the

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addition of micronutrients or during reconstitution<sup>3,15</sup>. The natural environment of *C. sakazakii* is not known though it is suspected to be a widespread micro-organism. *C. sakazakii* has been isolated from a number of environments including hospitals, households, cereal factories and milk powder factories<sup>15</sup>. It has also been found in a variety of food products<sup>16</sup>.

# 1 PRESUMPTIVE DIAGNOSIS OF *CRONOBACTER SAKAZAKII*

A presumptive diagnosis of *C. sakazakii* may be made if appropriate growth characteristics and biochemical reactions are demonstrated at the local laboratory. The following are suggested actions:

## 1.1 LOCAL MICROBIOLOGIST

- Urgently send the isolate to the Laboratory of Healthcare Associated Infections (LHCAI), Centre for Infections, Health Protection Agency for confirmation
- Inform LHCAI that the isolates are on the way to the lab (telephone 020 8327 7241). Out of hours telephone 020 8200 6868 for the duty doctor
- For further advice please contact LHCAI, Cfl (telephone 020 8327 7224)
- Inform HPA Regional Microbiologist of presumptive diagnosis of *C. sakazakii*.
- Suspected contaminated infant milk formula or breast milk should be collected and submitted to an HPA Food, Water & Environmental Laboratory accredited for examination of infant formula and follow-on formula for *Cronobacter sakazakii*. Inform the laboratory Food Examiner in advance of samples being submitted to the laboratory. In the case where a suspect pathogen is isolated, the laboratory will follow guidance outlining the procedure for dealing with presumptive pathogens isolated from ready-to-eat foods. See [QSOP 37 - Procedure for dealing with presumptive pathogens isolated from ready-to-eat foods](#)
- Inform local Health Protection Unit of presumptive diagnosis of *C. sakazakii*

**Note:** All unusual clusters of illness in infants that may be associated with powdered milk formula should be reported in a similar way.

# 2 DEFINITIVE DIAGNOSIS OF *CRONOBACTER SAKAZAKII*

If *C. sakazakii* is confirmed by the reference laboratory then LHCAI will undertake a timely review of all relevant information and decide upon further action and communication. The local microbiologist and HPU will be fully and appropriately involved in this process.

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### 3 ACKNOWLEDGEMENTS AND CONTACTS

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The National Standard Methods are issued by Standards Unit, Department for Evaluations, Standards and Training, Centre for Infections, Health Protection Agency, London.

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