

CODE OF HYGIENIC PRACTICE FOR POWDERED FORMULAE FOR INFANTS AND YOUNG CHILDREN

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INTRODUCTION

It is recognized internationally that breast milk is the best source of nutrition for infants. However, there are instances where it may be insufficient or not available and thus, may need to be supplemented or replaced. In those instances, one of the dietary options is the use of powdered formulae (PF).

For the purposes of this document, “powdered formulae” include the following:

- Infant formulae and formulae for special medical purposes intended for infants, which serve as the sole source of nutrition¹;
- Follow-up formulae which are used in combination with other foods as part of the weaning diet of older infants and young children²;
- Powdered formulae for special medical purposes for infants and young children, intended to partially replace or supplement breast milk, infant formulae or follow-up formulae³;
- Human milk fortifiers used to supplement breast milk.

These products are to be distinguished from ready-to-feed liquid formulae that have been commercially sterilized.

As dehydrated products, it is not possible using current technology to produce powdered formulae that are devoid of low levels of microorganisms, i.e., the products cannot be sterilized. Thus, their microbiological safety requires strict adherence to good hygienic practices during both manufacture and use.

Two FAO/WHO meetings of experts on the microbiological safety of powdered infant formula^{4,5} considered cases of illnesses in infants associated with PF consumption either epidemiologically or microbiologically. They identified three categories of microorganisms based on the strength of evidence of a causal association between their presence in PF and illness in infants: A) microorganisms with a clear evidence of causality, namely, *Salmonella enterica*⁶ and *Enterobacter sakazakii*⁷; B) microorganisms for which the causality is plausible but not yet demonstrated, i.e., they are well-established causes of illness in infants and have been found in PF, but contaminated formula has not been convincingly shown, either epidemiologically or microbiologically, to be the vehicle and source of infection, e.g., other Enterobacteriaceae; and C) microorganisms for which causality is less plausible or not yet demonstrated, including microorganisms,

¹ Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants (CODEX STAN 72-108).

² Standard for Follow-up Formula (CODEX STAN 156-1987).

³ Covered in the scope of the Standard for Labelling of and Claims for Foods for Special Medical Purposes (CODEX STAN 180-1991).

⁴ FAO/WHO. 2004. *Enterobacter sakazakii* and other microorganisms in powdered infant formula: meeting report, Microbiological Risk Assessment Series 6.

⁵ FAO/WHO. 2006. *Enterobacter sakazakii* and *Salmonella* in powdered infant formula: meeting report, Microbiological Risk Assessment Series 10.

⁶ *Salmonella enterica* subsp. *enterica* includes the various *Salmonella* serotypes associated with foodborne illness such as *S. enterica* subsp. *enterica* serotype Typhimurium, which is commonly referred to as *Salmonella* Typhimurium. The genus name *Salmonella* will be used in the text to refer to the pathogenic serotypes of *S. enterica* subspecies *enterica*.

⁷ The reclassification of *Enterobacter sakazakii* into a new genus, *Cronobacter* has been proposed based on a manuscript by Iversen *et al.*, International Journal of Systematic and Evolutionary Biology (2008), 58. The 31st Session of the Codex Alimentarius Commission (2008) while adopting the Code had agreed to change *Enterobacter sakazakii* into *Enterobacter sakazakii*(*Cronobacter* species) throughout the text.

which despite causing illness in infants, have not been identified in PF, or microorganisms which have been identified in PF but have not been implicated as causing such illness in infants, including *Bacillus cereus*, *Clostridium botulinum*, *C. difficile*, *C. perfringens*, *Listeria monocytogenes* and *Staphylococcus aureus*.

Salmonella is a well-known long-standing foodborne human pathogen. The incidence of salmonellosis among infants, originating from various sources, was reported to be more than eight times greater than the incidence across all ages in the United States of America (CDC, 2004). Infants are also more likely to experience severe illness or death from salmonellosis, and infants with immunocompromising conditions are particularly vulnerable. It is unclear whether the increased incidence of salmonellosis among infants results from greater susceptibility, or whether infants are more likely than persons in other age groups to seek medical care or have stool cultures performed for symptoms of salmonellosis.

At least 6 reported outbreaks of salmonellosis involving approximately 287 infants have been associated with PF between 1985 and 2005. Most of these outbreaks involved unusual *Salmonella* serotypes, which likely aided in recognition of those outbreaks. It is recognized that outbreaks and sporadic cases of salmonellosis due to powdered infant formula are likely to be under-reported⁵.

Enterobacter sakazakii(*Cronobacter* species) has recently emerged as a pathogen of infants. The FAO/WHO expert meetings have identified all infants (<12 months of age) as the population at particular risk for *E. sakazakii* (*Cronobacter* species) infections. Among this group, those at greatest risk are neonates (<28 days), particularly pre-term, low-birthweight (<2500 g), and immunocompromised infants, and those less than 2 months of age^{4,5}. Infants of HIV-positive mothers are also at risk, because they may specifically require infant formula and may be more susceptible to infection^{5,8}.

Infections from *E. sakazakii*(*Cronobacter* species) have been documented as both sporadic cases and outbreaks. While the incidence of these *E. sakazakii*(*Cronobacter* species) infections in infants appears to be low, the consequences can be severe. The primary manifestations of *E. sakazakii*(*Cronobacter* species) infection in infants, i.e., meningitis and bacteraemia, tend to vary with age. *E. sakazakii*(*Cronobacter* species) meningitis tends to develop in infants during the neonatal period, while *E. sakazakii*(*Cronobacter* species) bacteraemia tends to develop in premature infants outside of the neonatal period with most cases occurring in infants less than 2 months of age. However, infants with immunocompromising conditions have developed bacteraemia as late as 10 months of age and previously healthy infants have also developed invasive disease outside the neonatal period. Infections have occurred in both hospital and outpatient settings. It was noted that as older infants generally live at home in the community, infections in such infants may be more likely to be under-reported.

Reported fatality rates of *E. sakazakii*(*Cronobacter* species) infections in infants vary considerably with rates as high as 50 percent reported in at least one outbreak. In addition, a portion of surviving infants has permanent disabilities such as retardation and other neurological conditions. Although all known outbreaks have involved infants, sporadic cases have been reported in children and adults, however these have not been linked to PF.⁴

While PF was established as the source of *E. sakazakii*(*Cronobacter* species) in some of the cases, in many others it was neither epidemiologically nor microbiologically implicated as the source of infection. However, in such cases, no other source of infection has been epidemiologically or microbiologically implicated. *E. sakazakii*(*Cronobacter* species) is widely found in the environment, so infants, children and adults may be exposed to this organism from a range of sources.

Outbreaks of *E. sakazakii*(*Cronobacter* species) infections have led to the link with PF, especially in the context of neonatal intensive care setting. *E. sakazakii* (*Cronobacter* species) is known to be present at low

⁸ WHO, HIV and infant feeding: framework for priority action. Geneva: World Health Organization, 2003. HIV and Infant Feeding: New Evidence and Programmatic Experience (Report of the Technical Consultation, Geneva, Switzerland, 25-27 October 2006, held on behalf of the interagency task team (IATT) on preventing HIV infection in pregnant women, mothers and their infants (2007).

concentration in a proportion of PF. While the microorganism has been detected in other types of food and environmental settings, only PF has been linked to outbreaks of disease.

For infants at greatest risk, e.g. neonatal intensive care settings, commercially sterile liquid infant formula should be used if available unless the attending physician recommends otherwise. If a non-commercially sterile feeding option is chosen, an effective point-of-use decontamination procedure should be used.

There are four routes by which *E. sakazakii*(*Cronobacter* species) and *Salmonella* can enter PF: 1) through the ingredients added in dry mixing operations during the manufacturing of PF, 2) through contamination of the formula from the processing environment in the steps during or following the drying, 3) through contamination of the PF after the package is opened, and 4) through contamination during or after reconstitution by the caregiver prior to feeding. *E. sakazakii*(*Cronobacter* species) may be found in many environments such as food factories, hospitals, institutions, day-care facilities and homes. In manufacturing, the organism may gain access to the processing line and product, since current technology cannot completely eliminate this organism from the manufacturing environment.

Prevention efforts must be multi-faceted, directed at manufacturers, health-care providers, day care centres as well as infant caregivers in home settings, and take into consideration the risk to infants both within and beyond the neonatal period.

Product labelling, consumer education programs and staff training at hospitals should be updated as appropriate to provide adequate information to caregivers on the safe use of the product and to provide caution regarding the health hazards of inappropriate preparation and handling of PF.

SECTION I. – OBJECTIVES

The objective of this Code is to provide practical guidance and recommendations to governments, industry, health care professionals/caregivers of infants and young children, as appropriate, on the hygienic manufacture of PF and on the subsequent hygienic preparation, handling and use of reconstituted formulae. The Code supplements the *Recommended International Code of Practice - General Principles of Food Hygiene* (CXC 1-1969) and the *Code of Hygienic Practice for Milk and Milk Products* (CXC 57-2004), with an emphasis on the control of microbiological hazards, in particular *Salmonella* and *E. sakazakii* (*Cronobacter* species). The Code identifies relevant control measures at the various steps in the food chain that can be employed to reduce the risks for infants and young children that are associated with the consumption of PF.

SECTION II. – SCOPE, USE AND DEFINITIONS

2.1 SCOPE

This Code covers the production, preparation and use of products available in powdered form, referred to as Powdered Formulae (PF) for the purpose of this document, and specifically manufactured to be used for infants and young children either as a breast milk substitute, to supplement infant formula or fortify human milk or in combination with other foods as part of the weaning diet for older infants and young children. Products included are infant formulae, follow-up formulae, formulae for special medical purposes intended for infants and which serve as the sole source of nutrition, human milk fortifiers and powdered formulae for special medical purposes for infants and young children intended to partially replace or supplement breast milk, infant formulae or follow-up formulae.

The nutritional specifications of these products are beyond the scope of this document. Products should meet the nutritional specifications of the applicable Codex standards^{1,2}.

2.1.2 ROLES OF GOVERNMENTS, INDUSTRY, AND CONSUMERS⁹

Intended users of the document include national governments, manufacturers, health care professionals and professional caregivers to infants and young children.

Although the primary responsibility lies with the manufacturer for ensuring that PF manufactured are safe and suitable for their intended use, there is a continuum of effective control measures that need to be performed by other parties, including manufacturers of ingredients and packaging materials and caregivers of infants and young children, to minimize the risk and to assure the suitability of PF.

The interrelationship and impact of one segment of the food chain on another segment is important to ensure that potential gaps in the food chain are addressed through communication and interaction between the suppliers of ingredients, the manufacturer, the distributor and the caregivers. It is principally the responsibility of the manufacturer to conduct the hazard analysis within the context of developing a control system based on HACCP or other equivalent systems and thus to identify and control hazards associated with the incoming ingredients; however, the caregivers should also have an understanding of the hazards associated with PF, so as to assist in minimizing risks associated with the hazards involved.

To achieve an effective continuum for the purpose of reducing risk, the various parties should pay particular attention to the following responsibilities:

- Producers and manufacturers of raw materials should ensure that good agricultural, hygienic and animal husbandry practices are employed at the farm level. These practices should be adapted, as appropriate, to any specific safety-related needs specified and communicated by the manufacturer.
- Manufacturers of ingredients and packaging materials should utilize good manufacturing and good hygienic practices and have HACCP systems implemented. Any needs for additional measures communicated by the PF manufacturer, and that are needed to control hazards in PF should be implemented.
- Manufacturers of PF should utilize good manufacturing and good hygienic practices, especially those presented in this Code. Any needs for additional measures with regard to controlling hazards earlier in the food chain should be effectively communicated to suppliers to enable them to adapt their operations to meet these measures. Likewise, the manufacturer may have to implement controls or adapt their manufacturing processes based on the ability of the ingredients supplier to minimize or prevent hazards associated with the ingredients. Such additional needs should be supported by an adequate hazard analysis and should, where appropriate, take into consideration technological limitations during processing.
- Manufacturers should provide accurate and understandable information to enable the subsequent person(s) in the food chain, including the final user/caregiver, to use the product appropriately. This includes the additional measures to control hazards in the formulae during and after reconstitution.
- Distributors, transporters and retailers should assure that PF under their control are handled and stored properly and according to the manufacturers' instructions.
- Hospitals and institutions should establish hygienically designed rooms designated for preparation of formulae and good hygienic practices (e.g. HACCP, labelling of prepared food, hygiene and cleaning instructions, temperature control, first in first out, etc.), and should provide effective training to their caregivers of infants.

⁹ In this context, the term "consumers" also includes caregivers of infants and children.

- Health care professionals and professional caregivers should provide effective hygienic training to consumers (parents and other caregivers) to ensure that PF are prepared, handled and stored properly¹⁰ and according to the manufacturers' instructions.
- Caregivers of infants should ensure that PF are prepared handled and stored properly¹⁰ and according to the manufacturer's instructions.
- To ensure effective implementation of this Code, competent authorities should have in place legislative framework (e.g. acts, regulations, guidelines and requirements), an adequate infrastructure and properly trained inspectors and personnel. For food import and export control systems, reference should be made to the *Guidelines for the Design, Operation, Assessment and Accreditation of Food Import and Export Inspection and Certification Systems* (CXG 26-1997) and related Codex texts. Control programs should focus on auditing relevant documentation that shows that each participant along the chain has met their individual responsibilities to ensure that the end products meet established food safety objectives and/or related objectives and criteria. Furthermore, adequate consumer guidance and consumer education programs should be provided.

It is important that clear communications and interactions exist between all parties to help assure that best practices are employed, that problems are identified and resolved in an expeditious manner, and that the integrity of the entire food chain is maintained.

2.2 USE

This document follows the format of the *Codex Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). The provisions in this document are supplemental to and should be used in conjunction with the *General Principles of Food Hygiene* (CXC 1-1969), including its Annex on *Hazard Analysis and Critical Control (HACCP) System and Guidelines for its Application*, and the *Code of Hygienic Practice for Milk and Milk Products* (CXC 57-2004).

Where applicable, this document should be used in combination with the International Code of Marketing of Breast Milk Substitutes, relevant WHA resolutions and the WHO Global Strategy for Infant and Young Child Feeding.

2.3 DEFINITIONS

Infant – a person not more than 12 months of age¹.

Young Children – persons from the age of more than 12 months up to the age of three years (36 months)².

Human milk fortifier – (also referred to as *Human milk complement* or *breast milk fortifier* in some countries) product that may be added to human milk to provide additional nutrients for feeding low-birth weight and premature infants.

Powdered formulae – for the purpose of this Code of Practice includes all types of powdered formulae for infants and young children, including: powdered infant formulae, follow-up formulae, formulae for special medical purposes intended for infants as sole source of nutrition, human milk fortifiers, and formulae for special medical purposes for infants and young children, intended to partially replace or supplement breast milk, infant formulae or follow-up formulae.

Infant formula - means a breast milk substitute specially manufactured to satisfy, by itself, the nutritional requirements of infants during the first months of life up to the introduction of appropriate complementary feeding¹.

¹⁰ FAO/WHO. 2007. Safe preparation, storage and handling of powdered infant formula: guidelines.

Follow-up formula – means a food intended for use as a liquid part of the weaning diet for the infant from the 6th month on and for young children².

Formula for special medical purposes intended for infants (sole source of nutrition) - means a substitute for human milk or infant formula that complies with Section 2, Description, of the Codex Standard for the Labelling of and Claims for Foods for Special Medical Purposes (CODEX STAN 180-1991) and is specially manufactured to satisfy, by itself, the special nutritional requirements of infants with specific disorders, diseases or medical conditions during the first months of life up to the introduction of appropriate complementary feeding¹.

Formula for special medical purposes for infants and young children (not sole source of nutrition) - means a formula that complies with Section 2, Description, of the Codex Standard for the Labelling of and Claims for Foods for Special Medical Purposes (CODEX STAN 180-1991) and is specially manufactured to satisfy, in combination with breast milk or infant formula or follow-up formula, the special nutritional requirements of infants and young children with specific disorders, diseases or medical conditions.

Wet-mix process – manufacturing process by which all constituents of the infant formulae are handled in a liquid phase, and may involve homogenization, heat-treatment, concentration by evaporation, and then dried.

Dry-mix process – manufacturing process by which all constituents of the infant formulae are processed dry and blended to obtain the desired final formula.

Combined process – manufacturing process by which some of the constituents of the infant formulae are wet processed and dried and other ingredients are added in a dry form after the heat treatment.

SECTION III – PRIMARY PRODUCTION

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

SECTION IV – ESTABLISHMENT: DESIGN AND FACILITIES

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Facilities and equipment should be designed, constructed and laid out to prevent entry of *Salmonella* and *E. sakazakii* (*Cronobacter* species) into high hygiene areas and to minimize their establishment or growth in harbourage sites. It is well known that:

- The entry of *Salmonella* and *E. sakazakii* (*Cronobacter* species) in high hygiene areas of establishments manufacturing PF is favoured by an inadequate separation of wet and dry areas and/or by poor control over the movement of employees, equipment and goods.
- The establishment of *Salmonella* and *E. sakazakii* (*Cronobacter* species) in harbourage sites is favoured by conditions such as the presence of water and the occurrence of sites or structures which allow collection of process material and prevent the rapid elimination of the organisms through appropriate cleaning procedures.
- The increase of *E. sakazakii* (*Cronobacter* species), usually already part of the normal microbial flora of such high hygiene areas, is favoured by the presence of water, even in minute quantities as can be found, for example, in condensation spots.
- The application of wet cleaning procedures has been linked to the occurrence and spread of *Salmonella* and particularly *E. sakazakii* (*Cronobacter* species).

4.1 LOCATION

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

4.1.1 Establishments

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

4.1.2 Equipment

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Equipment should be designed, placed, installed and maintained in a manner that facilitates effective cleaning and disinfection, thus avoiding the occurrence of sites where accumulation of residues can take place. If water is available, such residues may lead to microbial growth, thus increasing the risk of contamination.

4.2 PREMISES AND ROOMS

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

4.2.1 Design and layout

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Dry processing areas where operations from the drying step up to the filling and hermetic closure of containers are performed, should be maintained as high hygiene areas. The internal design and layout of establishments manufacturing PF need to be such so as to ensure the strict physical separation of wet processing areas from the dry processing areas where post-process contamination from the environment could occur.

To be effective, the physical separation, known as zoning, needs to be complemented by appropriate measures such as maintaining a positive air pressure to prevent the entry of unfiltered air into high hygiene areas.

The access to high hygiene areas needs to be restricted and controlled through measures designed to avoid or minimize the entry of pathogens. This is generally achieved through appropriately designed interfaces such as locks for the personnel (e.g., to allow for putting on protective outer clothing and footwear covers), for incoming materials (e.g., ingredients used in dry-mixing operations or packaging material), for equipment requiring transportation out of the high hygiene areas and back in again (e.g. for maintenance and/or wet cleaning). Filtration systems for the air used in the building or for the transport of ingredients or product are also part of this zoning principle and need to be designed and installed accordingly.

Condensation should be prevented in high hygiene areas.

4.2.2 Internal structures and fittings

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Structures within establishments manufacturing PF should be soundly built of durable materials and easy to maintain, clean and, where appropriate, easy to disinfect. The requirements need to be adapted to the conditions encountered in the different areas (wet and dry) of the establishment as outlined in Section 4.2.1. Particular attention is required in the dry high hygiene areas to avoid the creation of inaccessible hollow sites favouring the accumulation of dust and product residues which may, in the presence of water, lead to the formation of a harbourage site.

Due to the ability of *Salmonella* and *E. sakazakii* (*Cronobacter* species) to survive in dry environments for prolonged periods of time, care should be taken when construction activities are planned, e.g. modifications of layout requiring displacing pieces of equipment. Such activities may dislodge *Salmonella* or *E. sakazakii* (*Cronobacter* species) from harbourage sites that were previously hidden, and contribute to the spread of the organisms throughout the plant. It is therefore important to isolate these construction areas and to reinforce cleaning procedures as well as environmental monitoring as described in Annex III.

4.2.3 Temporary/mobile premises and vending machines

Not applicable for the products considered in this Code.

4.3 EQUIPMENT

4.3.1 General

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Due to the ability of *Salmonella* and *E. sakazakii* (*Cronobacter* species) to persist in harbourage sites for prolonged periods of time, processing equipment should be designed, constructed and maintained to avoid, for example, cracks, crevices, rough welds, hollow tubes and structures, close fittings, metal-to-metal or metal-to-plastic surfaces, interfaces between floors and equipment, inadequately installed and maintained insulations, worn seals or other sites that cannot be reached during cleaning.

While these elements need to be addressed correctly in the whole establishment, particular attention is required in high hygiene areas where contamination should be prevented.

In the case of equipment located in the high hygiene area, particular attention is required to ensure that equipment can be cleaned using dry-cleaning techniques. It is also important to avoid any conditions which may lead to the occurrence of condensation, including on the internal surfaces of equipment.

4.3.2 Food control and monitoring equipment

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

4.3.3 Containers for waste and inedible substances

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

4.4 FACILITIES

4.4.1 Water supply

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

In order to maintain high-hygiene areas as dry as possible, the availability and presence of water and corresponding distribution systems should be limited to the extent possible in these areas.

4.4.2 Drainage and waste disposal

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

In order to maintain high hygiene areas as dry as possible, the use of dry drains is recommended as it would prevent the presence of water residues which could lead to growth and spread of microorganisms including relevant pathogens and process hygiene indicators.

In wet areas, the use of appropriately designed hygienic drains is recommended.

4.4.3 Cleaning

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

In order to maintain high hygiene areas completely dry or as dry as possible, the application of appropriate dry-cleaning procedures is recommended. Such cleaning techniques are applicable to premises as well as to equipment.

If not feasible, controlled wet cleaning may be used as long as prompt and thorough drying of the equipment and environment is ensured.

Where wet cleaning procedures are applied, appropriate management options should be implemented such as operating procedures that would ensure a well-controlled cleaning and the rapid elimination of any water residues immediately thereafter.

4.4.4 Personnel hygiene facilities and toilets

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

4.4.5 Temperature control

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

4.4.6 Air quality and ventilation

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

It is important to install air handling and ventilation units in such a way as to ensure the integrity of the zoning principles. It is important to install and maintain air handling units so that they do not become a source of contamination. For example, appropriate design and installation of the filters should avoid any bypass of unfiltered air, and accumulation of condensates should be avoided through an appropriate design of the drainage.

Air filters should be tightly fitted and properly sealed with gaskets to prevent the entrance of unfiltered air. Outside air intakes should be located away from the exhausts of the drier, boiler and other environmental contaminants. Filters should be replaced or cleaned and disinfected regularly in a manner that does not contaminate the processing environment.

4.4.7 Lighting

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

4.4.8 Storage

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

SECTION V – CONTROL OF OPERATION

5.1 CONTROL OF FOOD HAZARDS

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition, the procedure described in Section 5.1 of the *Code of Hygienic Practice for Milk and Milk Products* (CXC 57-2004) also applies to PF.

Although chemical, microbiological and physical hazards may be associated with PF, this Code of Practice focuses on the microbiological hazards, and specifically on *Salmonella* and *E. sakazakii* (*Cronobacter* species). A combination of control measures should effectively control the identified microbial hazards in PF.

When milk and milk products are used in the manufacturing process, these should meet the requirements of the *Code of Hygienic Practice for Milk and Milk Products* (CXC 57-2004).

5.2 KEY ASPECTS OF HYGIENE CONTROL SYSTEMS

5.2.1 Time and temperature control

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Time/temperature recording devices for any time/temperature control point (heating or chilling) should be checked at regular intervals and tested for accuracy against a calibrated probe. In manufacturing operations where heat treatments are critical control points (CCPs) for the reduction or elimination of a pathogen, appropriate records of the processing time and temperature should be maintained.

5.2.2 Specific process steps

PF is generally manufactured using a wet-mix, dry-mix or combined process.

For all types of processes used, steps should be taken to avoid contamination of the product during dry product handling, following the thermal processing steps that would ensure elimination of *Salmonella* and *E. sakazakii* (*Cronobacter* species).

Steps that contribute to good manufacturing practices include:

5.2.2.1 Thermal processing

For wet-mix process:

The heat treatment is a key step in ensuring the safety of PF and is therefore considered a CCP.

Heat treatments intended as microbiocidal processes¹¹ should, at a minimum, be sufficient to achieve pasteurization, which is based on the reduction of vegetative pathogens to a level where they do not constitute a significant hazard to health. The time/temperature combinations used to achieve pasteurization should take into consideration the properties of the product, e.g., fat content, dry matter, total solids, etc., which may have an impact on the heat resistance of the target organisms. These heat-treatments are considered as CCPs and therefore procedures must be in place to detect deviations, such as temperature drops and insufficient treatment times, and to take appropriate corrective measures such as the redirection of the product to waste or reprocessing¹².

5.2.2.2 Intermediate storage

For wet-mix process:

Raw materials as well as intermediate products can support microbial growth and have therefore to be maintained at temperatures that would prevent such growth from occurring, taking as well the storage time into consideration. While storage under refrigeration is usually applied, storage at high temperatures that do not allow growth may be a suitable alternative.

Intermediate storage of liquids may occur at different steps of the process:

- (i) Liquid raw materials such as raw milk;
- (ii) Intermediate products before the heat processing step;

Uncontrolled microbial growth at these steps may impact the effectiveness of the heat processing. In case of point (i) above, refer to the *Code of Hygienic Practice for Milk and Milk Products* (CXC 57-2004).

- (iii) Intermediate products after the heat processing step and before the drying step.

Microbial growth at this step may lead to non-compliant products as the drying is not considered a controlled killing step.

5.2.2.3 Steps from the Heat Process to the Drying

Control of the contamination of the heat-processed intermediate products is based on the application of high hygiene concepts to all elements of the processing line up to the spray nozzle, i.e., enclosed systems. Such elements may range from simple pipes to more complex combinations of pipes with other pieces of equipment (e.g., storage tanks).

For wet-mix process:

A drying process is used to convert the liquid mixture into a dry powder. For example, a spray dryer could be used, in which the liquid is heated and pumped under high pressure to spray nozzles or an atomizer mounted in a large drying chamber. This is usually not considered as a microbiocidal step. The drying step needs to be done under strict hygienic conditions to avoid microbial contamination of the final product.

5.2.2.4 Cooling

¹¹ Pasteurization and other heat treatments of milk that have at least an equivalent efficiency are applied at such intensities (sufficient time/temperature combinations) that they practically eliminate specific pathogens. They have therefore been traditionally used as key microbiocidal control measures in the manufacture of milk products (Annex II, *Code of Hygienic Practice for Milk and Milk Products*, CXC 57-2004).

¹² Section 4.1.1.1. FAO/WHO. 2006. *Enterobacter sakazakii* and *Salmonella* in Powdered Infant Formula; Meeting Report. Microbiological Risk Assessment Series 10.

For wet-mix process:

During the drying process, the powder is cooled after the drying chamber. For example, it could pass from the drying chamber to a fluidized cooling bed. The air in contact with the product should be appropriately filtered to prevent microbial contamination of the powder.

5.2.2.5 Blending**For dry-mix and combined processes:**

Blending should be done under strict hygienic conditions to avoid contamination of the final product. Refer to Section 5.3 of the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969), Incoming Material Requirements.

5.2.2.6 Storage

Finished products should be stored under strict hygienic conditions to avoid contamination of the product. Refer to Section 4.4.8 of the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969), Storage.

5.2.2.7 Filling and Primary Packaging¹³

Refer to Section 5.4 of the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969), Packaging. In addition, the following principles should be applied to the manufacture of PF:

- Access to the packaging room should be limited to essential personnel only (*Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969), Section 5.2.4). Access to the packaging area should be through ante rooms where personnel can wash their hands and change their outer garments, hair covering and footwear or footwear covers.
- The packaging area should be supplied with suitably filtered air to prevent airborne contamination of product or packaging. Ideally, the packaging area should be maintained under positive air pressure to prevent the infiltration of contaminated air from the outside or surrounding areas of the manufacturing facility (*Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969), Section 4.4.6).
- Packaging materials (including cans and flexible packaging) should be protected from contamination during shipment, storage and use. Packaging should be inspected immediately prior to use to ensure that it is not contaminated or damaged. Container cleanliness can be ensured by processes such as the use of can inverters, air jets and anti-static electricity devices.

5.2.3 Microbiological and other specifications

Refer to the *Principles for the Establishment and Applications of Microbiological Criteria* (CXG 21-1997) and to Annexes I & II. In addition:

Manufacturers are responsible for ensuring the compliance of finished products. In view of the limitations of end-product testing, compliance should be ensured through the design of an appropriate food safety control system and verification of the effectiveness of control measures through appropriate auditing methods, including review of monitoring records and of deviations and confirmation that CCPs are kept under control and GHPs are adhered to.

¹³ Primary packaging is packaging that comes in direct contact with the product.

These activities can be supplemented, as necessary, by appropriately documented microbiological sampling and analysis plans. The microbiological testing should include, as appropriate, analysis of samples taken from raw materials, production line, ingredients and finished products. Verification and monitoring procedures using environmental testing for PF are described in Annex III. Environmental samples should be taken from those areas most likely to lead to contamination of the product.

When monitoring of control measures and surveillance or verification results demonstrates deviations, appropriate corrective action should be taken and the finished product should not be released until adequate investigation has shown that it complies with appropriate specifications.

5.2.4 Microbiological cross-contamination

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Contamination of the product with *Salmonella* and/or *E. sakazakii*(*Cronobacter* species) may occur after drying and during the subsequent processing steps such as conveying, tipping, mixing, and blending with additional ingredients, up to the point of filling/packaging. Contamination is usually related to the following three factors, the first two of which are linked:

- (1) the presence of these microorganisms in the processing environment, i.e., external parts of equipment and surroundings of the processing lines, presenting the possibility that they may get into the processing lines;
- (2) the presence of these microorganisms, originating from the processing environment (item 1 above), on internal surfaces of equipment that is in direct contact with the product; and,
- (3) the presence of these microorganisms in ingredients added and mixed into the dry base powder after the heat-processing step¹².

Raw or unprocessed foods should be physically separated from processed/ready-to-use foods. Where possible, packaged dry-mix ingredients should be packaged with strippable bags (bags from which the outer layer can be stripped) to prevent contamination at ingredient dumping stations. Packaging material entering restricted area should be clean.

Pathogens such as *Salmonella* and *E. sakazakii*(*Cronobacter* species) can, to varying degrees, contaminate and become established in PF manufacturing plants. Harbourage sites can serve as a source of product contamination unless these areas are identified, cleaned and disinfected to eliminate pathogens. Manufacturers should implement an ongoing microbiological monitoring program for the drying, blending and packaging areas of the plant and for food contact surfaces/equipment (Annex III). When pathogens or indicator microorganisms are detected in the plant environment, appropriate measures should be taken to investigate the source of contamination and to eliminate or control the microorganism(s) in the environment.

Increases in the levels or frequency of detection of *E. sakazakii*(*Cronobacter* species) or more generally levels of Enterobacteriaceae in processing environments can be either due to a massive and sudden entry of microorganisms due to poorly planned construction or maintenance activities, or more commonly due to conditions which allow the proliferation of the low number of microorganisms already present in the environment¹⁴.

Growth is only possible in the presence of water, therefore the environment has to be kept as dry as possible. Dry conditions should be maintained in the processing environment, including drying, blending and packaging areas. The presence of water in the processing environment can be as a result of wet cleaning of environments or equipment without appropriate immediate drying, the formation of condensation spots,

¹⁴ Section 4.1.2. FAO/WHO. 2006. *Enterobacter sakazakii* and *Salmonella* in Powdered Infant Formula; Meeting Report. Microbiological Risk Assessment Series 10.

leaking water valves, backed up floor drains, etc., or occasionally as a result of water infiltration following heavy rains or the use of water showers in the case of fire emergencies.

5.2.5 Physical and chemical contamination

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

5.3 INCOMING MATERIAL REQUIREMENTS

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

For dry-mix and combined processes:

Since a dry-mix process and combined processes incorporate ingredients that may not include a microbiocidal heat treatment by the formulae manufacturer, the microbiological safety of these ingredients is dependent on the treatments performed by the ingredient manufacturers and the assurance that the integrity of the packaging has been maintained during shipment and storage.

Manufacturers should take steps to ensure that the microbiological quality of the dry-mix ingredients meets the requirements for the finished products. They should take into consideration the procedures and safeguards employed by their ingredient suppliers and should have in place a verification procedure that can verify their suppliers' performance. This can be achieved through such measures as carefully selecting suppliers, performing audits to assess the suppliers' processes, controlling and monitoring procedures, and periodic evaluations of incoming ingredients.

5.4 PACKAGING

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

5.5 WATER

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

5.6 MANAGEMENT AND SUPERVISION

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

5.7 DOCUMENTATION AND RECORDS

Appropriate records of processing, production and distribution should be kept and retained for a period that exceeds the shelf-life of the product. Documentation can enhance the credibility and effectiveness of the food safety control system.

Manufacturers should establish documentation and records concerning all procedures and applications related to the HACCP plan or other food safety control systems in addition to documentation and records pertaining to good hygienic practices. In particular, the manufacturer should keep records detailing all incoming material (e.g., dry ingredients, liquid milk); the monitoring of CCPs (e.g., records outlining effective thermal processing with actual processing temperatures); the verification of the HACCP plan; the cleaning practices and sanitation processes; and the application of procedures to verify that microbiological specifications for finished products and environmental sampling and testing are met. Documentation should be sufficient to facilitate product traceability in the event that a recall may prove necessary.

5.8 RECALL PROCEDURES

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

As PF is regularly traded internationally, the Principles and Guidelines for the Exchange of Information in Food Safety Emergency Situations (CXG 19-1995), the Principles and Guidelines for the Exchange of Information between Countries on Rejection of Imported Food (CXG 25-1997), Principles for Traceability/Product Tracing as a Tool Within a Food Inspection and Certification System (CXG 60-2006) and International Health Regulation (WHA, 2005) should be used in the event of a product recall.

SECTION VI. – ESTABLISHMENT: MAINTENANCE AND SANITATION

6.1 MAINTENANCE AND CLEANING

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

6.1.2 CLEANING PROCEDURES AND METHODS

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Wet cleaning should be minimized and limited to parts of equipment that can be taken out to a dedicated room or where adequate drying parameters can be applied immediately after wet cleaning. Implementation of dry cleaning procedures for the processing lines, equipment and the processing environment is considered to be the most effective method of avoiding multiplication of microorganisms¹⁵.

6.2 CLEANING PROGRAMMES

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

6.3 PEST CONTROL SYSTEMS

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

6.4 WASTE MANAGEMENT

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

6.5 MONITORING EFFECTIVENESS

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Manufacturers of PF should establish effective supervisory procedures to ensure that critical procedures such as manual cleaning, cleaning-in-place (CIP) systems operation, and equipment maintenance are conducted according to established protocols and standards. In particular, it is important to ensure that cleaning and disinfection solutions are appropriate for their intended use and are of the proper concentration, that

¹⁵ Recommendations. FAO/WHO. 2006. *Enterobacter sakazakii* and *Salmonella* in Powdered Infant Formula; Meeting Report. Microbiological Risk Assessment Series 10.

temperature and flow rate requirements are met for CIP systems and that equipment is properly rinsed when required.

A critical activity to minimize the risk associated with PF is the implementation of environmental management programs (environmental samples, product contact surfaces, finished products) based on Enterobacteriaceae as indicators for process hygiene, and *Salmonella* and *E. sakazakii* (*Cronobacter* species) in relevant samples to demonstrate control or to detect deviations and assess the effect of corrective actions¹⁶. Guidance on the establishment of an environmental monitoring program for *Salmonella*, *E. sakazakii* (*Cronobacter* species) and other Enterobacteriaceae is given in Annex III.

SECTION VII – ESTABLISHMENT: PERSONAL HYGIENE

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

SECTION VIII – TRANSPORTATION

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

SECTION IX – PRODUCT INFORMATION AND CONSUMER AWARENESS

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

Microbiological hazards are controlled through the appropriate selection and combination of control measures applied during the manufacture of PF in combination with control measures applied during and after reconstitution.

Even when products have been manufactured according to this Code, a certain number of servings may contain pathogenic microorganisms (see Annexes I and II¹⁷). Additional risk may be associated with any contamination of the formula during its preparation, handling and use. Therefore, control measures during reconstitution, handling and feeding of reconstituted formula are necessary.

All health care professionals and caregivers should be informed that, because powdered formulae are not sterile, the use of Good Hygienic Practices during reconstitution, handling, and feeding, including appropriate storage is essential to minimize the risk of foodborne illness.

Clear instructions for the appropriate preparation, handling and use of PF should be communicated to caregivers and health care professionals. Various combination of hygienic measures can achieve significant risk reduction and are addressed in the report of the 2006 FAO/WHO expert meeting on *E. sakazakii* (*Cronobacter* species) and *Salmonella* in powdered infant formula⁵ and can be used according to the risk reduction strategy chosen. For example, one risk reduction strategy includes feeding the formula immediately after reconstitution and rapid cooling to the appropriate feeding temperature. To this effect, (i) the feeding period¹⁸ should be minimized and should not exceed two hours, (ii) leftover formula should be discarded, and (iii) any formula prepared for later use should be refrigerated immediately following reconstitution and used within 24 hours. Various other risk reduction strategies for the preparation, storage and handling are provided in the guidelines of the FAO/WHO on the safe preparation, storage and handling of powdered infant formula (2007)¹⁰.

¹⁶ Section 4.1.4. FAO/WHO. 2006. *Enterobacter sakazakii* and *Salmonella* in Powdered Infant Formula; Meeting Report. Microbiological Risk Assessment Series 10.

¹⁷ Annex II is under elaboration.

¹⁸ Feeding period is defined here as the time after re-warming (or after storage, if no re-warming) until all of the prepared formula has been consumed²¹.

In certain situations, e.g., where there is a high confidence in the microbiological quality of the product and adherence with good hygienic practices in the preparation, handling and use of the formula, or when there are heat-labile components in the formula, alternative risk management strategies are available to the reconstitution temperature of 70°C recommended in the FAO/WHO guidelines. The 2006 report of the FAO/WHO expert meeting⁵ and the associated web-based tool provide a means to consider different risk management options which may be appropriate in certain situations as described above.

Control measures should be communicated to different stakeholders such as parents, caregivers and healthcare professionals through appropriate product labelling (which may include separate written information), written procedures (e.g., in professional institutions) and/or through oral instructions and/or training. These instructions, if adhered to, would help manage the risk associated with the product.

In hospitals and other health care delivery institutions, milk/formula preparation units require special precautions in the preparation, storage, and handling of PF, and guidance can be found in the FAO/WHO guidelines¹⁰.

Recommendations regarding the type of formula to be used, e.g., commercially sterile liquid formula, PF, etc., should be made by health care professionals, as needed.

For infants at greatest risk, when feasible, commercially available sterilized liquid products or other equivalent infant feeding options which have undergone an effective point of use decontamination procedure should be used instead of PF.

9.1 LOT IDENTIFICATION

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

9.2 PRODUCT INFORMATION

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969).

9.3 LABELLING

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

The label should communicate the control measures that the caregiver should follow for the safe preparation, handling and use of PF.

The label should carry clear graphic instructions illustrating the method of preparation.

Guidance should be provided on: i) the use of hygienic practices, e.g., clean hands, preparation surfaces, and clean utensils (nipples, caps, utensils, including sterilization, as necessary); ii) the need to boil water and sterilise utensils, as necessary; iii) the need to cool the formula before feeding if using hot water for reconstitution; and iv) the need to refrigerate product, if formula is not used immediately. The importance of discarding leftovers should be emphasized.

The label should include information to make clear the potential risks of inappropriate preparation, handling and use because powdered formula is not sterile and because failure to follow manufacturers' instructions may cause serious illness. Industry and national governments should be encouraged to cooperate in order to ensure that the intended messages are understood by all potential users. When considering the wording of such information, consideration should also be given to any potential risk of caregivers being inadvertently encouraged to use inappropriate alternatives to powdered infant formulae (e.g., milk powder). The label should also include information that can enable consumers to easily identify products in the event of a recall.

9.4 EDUCATION

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

The development and distribution of educational documents related to the preparation, handling and use of PF to all caregivers should be encouraged. These programs should enable one to i) understand the importance of product information, ii) follow instructions accompanying products, and iii) make informed choices after discussing with professional caregivers, as needed.

Infants and young children who are not breastfed require a suitable breast milk substitute. When PF is used, national governments are encouraged to provide all caregivers with appropriate educational material. The guidelines for the safe preparation, storage and handling of powdered infant formula developed by the FAO/WHO¹⁰ may be used.

All caregivers should be informed of the potential risks associated with the inappropriate preparation, handling and use of PF which may result in serious illness. It should also be noted that other ingredients which are added to formula during/after reconstitution may not be sterile and thus, may also present a potential for contamination.

Stringent hygienic preparation and storage conditions should be emphasized due to the potential for contamination of the product from various sources, e.g., equipment, utensils, the preparation environment, other ingredients/foods. Likewise, the water used to rehydrate PF will greatly impact the safety of the product. Appropriate preparation and handling, according to manufacturer's instructions reduces the risk of illness and, when appropriate, these should be emphasized by national governments. Additionally, experience has indicated that all caregivers need to be periodically reminded that bottled water is not a sterile product unless specifically indicated as such on the product. Information/education about the need to follow good hygiene practices during preparation, handling and storage at home, in hospitals, day care or other settings should be emphasized. It is important to stress the fact that reconstituted formula may allow the growth of microorganisms, and temperature abuse may lead to foodborne illness. Reconstituted powdered formula should be fed immediately when possible or kept refrigerated for no more than 24 hours. Reconstituted PF should be refrigerated promptly in containers and volumes that allow the reconstituted PF to cool rapidly. Thus, it should be kept refrigerated if not used immediately following preparation. Refrigerated storage should not exceed 24 hours following reconstitution. Temperature abuse may lead to foodborne illness. Improper handling and storage of reconstituted PF can promote the growth of pathogens (e.g., *Salmonella*, *E. sakazakii*(*Cronobacter* species), and other microorganisms such as sporeformers) which may be present initially at low levels, or which may have contaminated the product during handling and preparation.

Guidance on microbiological monitoring in powdered formula preparation units in health care settings is provided in Annex III and should be followed as appropriate.

SECTION X – TRAINING

Refer to the *Recommended International Code of Practice – General Principles of Food Hygiene* (CXC 1-1969). In addition:

The FAO/WHO Guidelines for the Safe Preparation, Storage and Handling of Powdered Infant Formula (2007)¹⁰ should be used as a reference for training.

ANNEX I

MICROBIOLOGICAL CRITERIA FOR POWDERED INFANT FORMULA, FORMULA FOR SPECIAL MEDICAL PURPOSES¹⁹ AND HUMAN MILK FORTIFIERS

Microbiological criteria should be established in the context of risk management options and in accordance with the *Principles for the Establishment and Application of Microbiological Criteria for Foods* (CXG 21-97). Two sets of criteria are provided below, one for pathogens and a second for process hygiene indicators.

Criteria for pathogenic microorganisms

These are to be applied to the finished product (powder form) after primary packaging or anytime thereafter up to the point when the primary package is opened.

Microorganisms	n	c	m	Class Plan
<i>Enterobacter sakazakii</i> (<i>Cronobacter</i> species)*	30	0	0/10 g	2
<i>Salmonella</i> **	60	0	0/25 g	2

Where n = number of samples that must conform to the criteria: c = the maximum allowable number of defective sample units in a 2-class plan. m = a microbiological limit which, in a 2-class plan, separates good quality from defective quality.

*The mean concentration detected is 1 cfu in 340g (if the assumed standard deviation is 0.8 and probability of detection is 95%) or 1 cfu in 100g (if the assumed standard deviation is 0.5 and probability of detection is 99%)

**The mean concentration detected is 1 cfu in 526g (if the assumed standard deviation is 0.8 and probability of detection is 95%)²⁰.

The methods to be employed for *E. sakazakii*(*Cronobacter* species) and *Salmonella* should be the most recent editions of ISO/TS 22964:2006 and ISO 6579, respectively, or other validated methods that provide equivalent sensitivity, reproducibility, reliability, etc.

The criteria above are applied with the underlying assumption that the history of the lot is unknown, and the criteria are being used on a lot-by-lot basis. In those instances where the history of the product is known (e.g., the product is produced under a fully documented HACCP system), alternate sampling criteria involving between-lot process control testing may be feasible²¹. The typical action to be taken when there is a failure to meet the above criteria would be to (1) prevent the affected lot from being released for human consumption and (2) recall the product if it has been released for human consumption, and (3) determine and correct the root cause of the failure.

¹⁹ This category includes formula for special medical purposes intended for infants as the sole source of nutrition and formula for special medical purposes for infants, intended to partially replace or supplement breast-milk or infant formula.

²⁰ Relating Microbiological Criteria to Food Safety Objectives and Performance Objectives by M. van Schothorst; M. H. Zwietering; Ross; R. L. Buchanan; M. B Cole & International Commission on Microbiological Specifications for Foods, *J. Food Control* (ICMSF), *J. Food Control* 20 (2009) 967–979.

²¹ Section 4.3, FAO/WHO. 2006. *Enterobacter sakazakii* and *Salmonella* in powdered infant formula: meeting report, Microbiological Risk Assessment Series 10.

Criteria for process hygiene

These are to be applied to the finished product (powder form) or at any other previous point that provides the information necessary for the purpose of the verification.

The safe production of these products is dependent on maintaining a high level of hygienic control. The following additional microbiological criteria are intended to be used by the manufacturer as a means of ongoing assessment of their hygiene programs, and not by the competent authority. As such these tests are not intended to be used for assessing the safety of a specific lot of product, but instead are intended to be used for verification of the hygiene programs.

Microorganisms	n	c	m	M	Class Plan
Mesophilic Aerobic Bacteria*	5	2	500/g	5000/g	3
Enterobacteriaceae**	10	2 ²²	0/10 g	Not applicable	2

Where n = number of samples that must conform to the criteria: c = the maximum allowable number of defective sample units in a 2-class plan or marginally acceptable sample units in a 3-class plan: m = a microbiological limit which, in a 2-class plan, separates good quality from defective quality or, in a 3-class plan, separates good quality from marginally acceptable quality: M = a microbiological limit which, in a 3-class plan, separates marginally acceptable quality from defective quality.

* The proposed criteria for mesophilic aerobic bacteria are reflective of Good Manufacturing Practices and do not include microorganisms that may be intentionally added such as probiotics. Mesophilic aerobic counts provide useful indications on the hygienic status of wet processing steps. Increases beyond the recommended limits are indicative of the build-up of bacteria in equipment such as evaporators or contamination due to leaks in plate-heat exchangers (refer to Annex III).

²² This 2 class plan is proposed because a 3 class plan with equivalent performance would not be practical analytically, given the low levels of EB typically occurring when stringent hygiene conditions are maintained.

It may seem that peak contaminations in up to 2 samples are tolerated in this Microbiological criterion (MC). However, it is assumed that the product is sufficiently homogeneous that high level contaminations will fail the MC. It is further assumed that, in practice, under sufficiently strict hygienic operation, the manufacturer will normally not find positives and that if, occasionally, positives are found the manufacturer will take appropriate actions.

Finding 1 or 2 positives should indicate to the manufacturer a trend toward potential loss of process control and appropriate actions would include further microbial evaluation of the implicated end product (i.e. re-evaluation of the EB content; when EB MC fails, evaluation of product safety using the proposed MCs for *Salmonella* and *E. sakazakii* (*Cronobacter species* (*Cronobacter species*)) before its release as well as evaluation of the hygiene programme to confirm it is suitable to maintain ongoing hygiene control or to amend the programme such that is suitable to do so).

Finding 3 or more positives should signal to the manufacturer loss of process control and appropriate actions should be the evaluation of product safety using the proposed MCs for *Salmonella* and *E. sakazakii* (*Cronobacter species*) before release of the implicated product as well as evaluation of the hygiene programme to amend the programme such that it is suitable to maintain high hygiene control on an ongoing basis before production is resumed.

The rationale for using 2 class plans for hygiene indicators in particular situations is explained in ICMSF, 2002. Microorganisms in Foods. Book 7. Microbiological Testing in Food Safety Management. Kluwer Academic/Plenum, NY. ISBN 0-306-47262-7.

** The mean concentration detected is 1 cfu in 16g (if the assumed standard deviation is 0.8 and probability of detection is 95%) or 1 cfu in 10g (if the assumed standard deviation is 0.5 and probability of detection is 99%).

The methods to be employed for Mesophilic Aerobic Bacteria and Enterobacteriaceae should be the most recent editions of ISO [4833:2003](#) and ISO 21528-1/21528-2, respectively, or other validated methods that provide equivalent sensitivity, reproducibility, reliability, etc. The criteria above are intended to be used as a means of achieving ongoing verification of a facility's microbiological hygiene programs. Such indicator tests are most effective when the stringency of the criteria allows deviations to be detected and corrective actions to be taken before limits are exceeded. The typical action to be taken when there is a failure to meet the above criteria would be to determine and correct the root cause of the failure and, as appropriate, review monitoring procedures, environmental surveillance (Annex III), and review prerequisite programs in particular the hygienic conditions from the drying step up to the packaging step (*Enterobacteriaceae*) and the process conditions during wet processing (mesophilic aerobes). Continued failures should be accompanied by increased sampling of the product for *E. sakazakii* (*Cronobacter* species) and *Salmonella* and potential re-validation of the control measures.

While these tests were originally developed for lot-by-lot applications where the history of the lot was unknown, their usefulness is much greater when there is a full understanding of the product and the processes used in its manufacture, in which case this can provide a means of verifying correct implementation of specific hygiene measures. Such indicator tests are particularly amenable to alternative process control sampling plans and statistics.

ANNEX II

MICROBIOLOGICAL CRITERIA FOR POWDERED FOLLOW-UP FORMULAE AND FORMULAE FOR SPECIAL MEDICAL PURPOSES FOR YOUNG CHILDREN

Microbiological criteria should be established in the context of available risk management options and in accordance with the *Principles for the Establishment and Application of Microbiological Criteria for Foods* (CXG 21-97). Two sets of criteria are provided below, one for a pathogen and a second for process hygiene indicators.

Where a Competent Authority assesses that there is scientific evidence of a risk in relation to *E. sakazakii* (*Cronobacter* spp.) from consumption of follow-up formulae in the national population, under current manufacturing conditions and control measures, it may consider strengthening the combination of available control measures, including consideration of an appropriate microbiological criterion.

Criteria for pathogenic microorganisms

Microorganisms	n	c	m	Class Plan
<i>Salmonella</i> *	60	0	0/25 g	2

Where n = number of samples that must conform to the criterion: c = the maximum allowable number of defective sample units in a 2-class plan. m= a microbiological limit which, in a 2-class plan, separates acceptable lots from unacceptable lots.

* The mean concentration detected is 1 cfu in 2034g (if the assumed standard deviation is 0.8 and probability of detection is 95%) or 1 cfu in 577g ((if the assumed standard deviation is 0.5 and probability of detection is 99%)²³.

This criterion is to be applied to the finished product (powder form) after primary packaging or anytime thereafter up to the point when the primary package is opened.

The method to be employed for *Salmonella* should be the most recent edition of ISO 6579 or other validated methods that provide equivalent sensitivity, reproducibility, reliability, etc.

The criterion above is applied with the underlying assumption that the history of the lot is unknown, and the criterion is being used on a lot-by-lot basis. In those instances where the history of the product is known (e.g., the product is produced under a fully documented HACCP system), alternate sampling criteria involving between-lot process control testing may be feasible. The typical action to be taken when there is a failure to meet the above criterion would be to (1) prevent the affected lot from being released for human consumption; (2) recall the product if it has been released for human consumption and (3) determine and correct the root cause of the failure.

Criteria for process hygiene

These criteria are to be applied to the finished product (powder form) or at any other previous point that provides the information necessary for the purpose of the verification.

²³ International Commission on Microbiological Specifications for Foods, 2002, *Microorganisms in Foods 7: Microbiological Testing in Food Safety Management*, Kluwer Academic/Plenum Publishers NY. ISBN 0-306-47262-7. Relating Microbiological Criteria to Food Safety Objectives and Performance Objectives by M. van Schothorst; M. H. Zwietering; Ross; R. L. Buchanan; M. B Cole & International Commission on Microbiological Specifications for Foods, *J. Food Control* (ICMSF), *J. Food Control* 20 (2009) 967–979.

The safe production of these products is dependent on maintaining a high level of hygienic control. The following additional microbiological criteria are intended to be used by the manufacturer as a means of ongoing assessment of their hygiene programs, and not by the competent authority. As such these tests are not intended to be used for assessing the safety of a specific lot of product, but instead are intended to be used for verification of the hygiene programs.

Microorganisms	n	c	m	M	Class Plan
Mesophilic Aerobic Bacteria*	5	2	500/g	5000/g	3
Enterobacteriaceae**	10	2 ²⁴	0/10 g	Not Applicable	2

Where n = number of samples that must conform to the criterion; c = the maximum allowable number of defective sample units in a 2-class plan; m = a microbiological limit which, in a 2-class plan, separates acceptable lots from unacceptable lots, or in a 3-class plan, separates acceptable lots from marginally acceptable lots; M = a microbiological limit which, in a 3-class plan, separates marginally acceptable lots from unacceptable lots.

* The proposed criteria for mesophilic aerobic bacteria are reflective of Good Manufacturing Practices and do not include microorganisms that may be intentionally added such as probiotics. Mesophilic aerobic bacteria counts provide useful indications on the hygienic status of wet processing steps. Increases beyond the recommended limits are indicative of the build-up of bacteria in equipment such as evaporators or contamination due to leaks in plate-heat exchangers (refer to Annex III).

** The mean concentration detected is 1 cfu in 16g (if the assumed standard deviation is 0.8 and probability of detection is 95%) or 1 cfu in 10g (if the assumed standard deviation is 0.5 and probability of detection is 99%).

²⁴ This 2- class plan is used because a 3- class plan with equivalent performance would not be practical analytically, given the low levels of Enterobacteriaceae (EB) typically occurring when stringent hygiene conditions are maintained.

It may seem that peak contaminations in up to 2 samples are tolerated in this microbiological criterion (MC). However, it is assumed that the product is sufficiently homogeneous that high level contaminations will fail the MC. It is further assumed that, in practice, under sufficiently strict hygienic operation, the manufacturer will normally not find positives and that if, occasionally, positives are found the manufacturer will take appropriate actions.

Finding 1 or 2 positives should indicate to the manufacturer a trend toward potential loss of process control and appropriate actions would include further microbial evaluation of the implicated end product (i.e. re-evaluation of the EB content; when EB MC fails, evaluation of product safety using the proposed MC for *Salmonella* before its release as well as evaluation of the hygiene programme to confirm it is suitable to maintain ongoing hygiene control or to amend the programme such that is suitable to do so).

Finding 3 or more positives should signal to the manufacturer loss of process control and appropriate actions should be the evaluation of product safety using the proposed MC for *Salmonella* before release of the implicated product as well as evaluation of the hygiene programme to amend the programme such that it is suitable to maintain high hygiene control on an ongoing basis before production is resumed.

The rationale for using 2- class plans for hygiene indicators in particular situations is explained in Book 7 of the International Commission on Microbiological Specifications for Foods, 2002. *Microorganisms in Foods 7. Microbiological Testing in Food Safety Management*, Kluwer Academic/Plenum, Publishers NY. ISBN 0-306-47262-7.

The methods to be employed for Mesophilic Aerobic Bacteria and Enterobacteriaceae (EB) should be the most recent editions of ISO [4833](#) and ISO 21528-1/21528-2, respectively, or other validated methods that provide equivalent sensitivity, reproducibility, reliability, etc. The criteria above are intended to assist in verifying a facility's microbiological hygiene programs. Such indicator tests are most effective when the stringency of the criteria allows deviations to be detected and corrective actions to be taken before limits are exceeded. The typical action to be taken when there is a failure to meet the above criteria would be to determine and correct the root cause of the failure and, as appropriate, review monitoring procedures, including environmental monitoring (Annex III), and review prerequisite programs in particular the hygienic conditions from the drying step up to the packaging step (Enterobacteriaceae) and the process conditions during wet processing (mesophilic aerobic bacteria). Continued failures should be accompanied by increased sampling of the product for *Salmonella* and potential re-validation of the control measures.

While these tests were originally developed for lot-by-lot applications where the history of the lot was unknown, their usefulness is much greater when there is a full understanding of the product and the processes used in its manufacture, in which case this can provide a means of verifying correct implementation of specific hygiene measures. Such indicator tests are particularly amenable to alternative process control sampling plans and statistics.

Labelling and Education

Follow-up formulae should only be used for the target population for which they are intended. There should be increased emphasis on the education of caregivers and healthcare professionals as to the appropriate uses of follow-up formulae, in addition to the training and education on the safe preparation, handling and storage (as recommended in Section IX of this Code of Practice) and effective labelling²⁵ with respect to the intended consumer.

²⁵ Guideline for the Validation of Food Safety Control Measures (CXG 69-2008).

ANNEX III

GUIDANCE FOR THE ESTABLISHMENT OF MONITORING PROGRAMS FOR *SALMONELLA*, *ENTEROBACTER SAKAZAKII* (*CRONOBACTER* SPECIES) AND OTHER ENTEROBACTERIACEAE IN HIGH HYGIENE PROCESSING AREAS AND IN POWDERED FORMULA PREPARATION UNITS

1. GUIDANCE FOR THE ESTABLISHMENT OF AN ENVIRONMENTAL MONITORING AND PROCESS CONTROL PROGRAM IN HIGH HYGIENE PROCESSING AREAS

Even under adequate hygienic conditions, low levels of Enterobacteriaceae (EB), including *E. sakazakii* (*Cronobacter* species), may be present in the processing plant environment. This could lead to the sporadic presence of low levels of EB in the finished product due to post-pasteurization contamination from the environment. Tracking the level of EB in the processing plant environment is a useful means of verifying effectiveness of the hygienic procedures applied and also allows undertaking corrective actions in a timely manner. Environmental monitoring of EB provides baseline levels and therefore allows the tracking of changes over time. Although it is recognized that there is no universally demonstrated correlation to date between counts of EB and *E. sakazakii*(*Cronobacter* species)/*Salmonella*, it has been demonstrated at the individual processing plant level that a reduction in the levels of the EB in the environment leading to lower levels of EB (including *E. sakazakii*(*Cronobacter* species) and *Salmonella*) in the finished product.

In view of the limitations of end product testing alone, it is important to have an environmental monitoring program for these products, particularly since contamination has led to several recognized outbreaks.

Such a monitoring program could be used to assess control of the processing plant environment in the high hygiene areas (dry areas) where contamination might take place, and, thus, would be an essential food safety management tool.

The monitoring program should be part of a food safety control system incorporating prerequisite programs such as good hygienic practices and a HACCP program.

In order to design an appropriate monitoring program, it is important to understand the ecology of *Salmonella* and *E. sakazakii*(*Cronobacter* species) as well as the ecology of EB (used as indicators of process hygiene).

- *Salmonella* is rarely found in dry processing areas and monitoring should be designed to assess whether the control measures to prevent entry have been effective. It should also allow one to assess whether, in case of entry, establishment in harbourage sites and spread throughout the area could be prevented or has taken place.
- *E. sakazakii*(*Cronobacter* species) is more frequently found than *Salmonella* in dry processing areas and is found regularly when using appropriate sampling and testing methods. The monitoring program should be designed to assess whether *E. sakazakii*(*Cronobacter* species) is increasing and whether the control measures are effective to prevent the growth of the organism.
- Enterobacteriaceae are widespread and therefore part of the normal flora in dry processing areas. They are found regularly when using appropriate sampling and testing (quantitative) methods. EB have been used for decades as indicators of process hygiene to detect deviations in good hygienic practices.

A number of factors (a – i) should be considered when developing the sampling program to ensure its effectiveness:

(a) Type of product and process/operation

The need for and extent of the sampling program should be defined according to the characteristics of the products and in particular the age and health status of the consumer. While *Salmonella* is considered a pathogen for all categories of products included in this Code, *E. sakazakii*(*Cronobacter* species) may only be relevant for specific products.

Monitoring activities should be focused in areas where contamination is likely to occur, i.e., in the dry processing areas located in the high hygiene zones. Particular attention should be given to interfaces between these areas and external areas of a lower hygiene level as well as areas close to processing line and to equipment where contamination is more likely to occur, e.g., due to the design of equipment, presence of openings such as hatches which may be opened occasionally for inspections. Known or likely harbourage sites should be given priority for monitoring.

Sampling of areas far from the processing line or even external areas is of limited use.

(b) Types of samples

Two types of samples should be included in monitoring programs:

(1) Environmental samples collected from non food contact surface areas such as external parts of equipment, floors surrounding the line, pipeline and platforms. In this case, the risk of contamination will depend on the location and design of the processing line and equipment as well as on the levels determined.

(2) Samples (line samples) collected from food contact surfaces inside the equipment located after the dryer and prior to packaging and which present a higher risk of directly contaminating the product. Examples of such areas are sifter tailings where product lumps will accumulate and which may be indicative of moisture uptake. The presence of indicator microorganisms, *E. sakazakii* (*Cronobacter* species) or *Salmonella* on food contact surfaces represents a very high risk of directly contaminating the product.

(c) Target organisms

While *Salmonella* and *E. sakazakii*(*Cronobacter* species) are the main target organisms, industry has found it advantageous to include EB as indicators of process hygiene. Their levels are good indicators of conditions supporting the potential presence of *Salmonella* and the potential for growth of *Salmonella* and *E. sakazakii*(*Cronobacter* species).

(d) Sampling locations and number of samples

The number of samples will vary with the complexity of the process and processing lines.

Preferential locations for sampling should focus on areas where harbourage or entry leading to contamination is likely to occur. Information on appropriate locations can be found in the published literature and can be based on process experience and expertise, or on historical data gathered through plant surveys. Sampling locations should be reviewed on a regular basis and additional ones may need to be included in the program, depending on special situations such as major maintenance or construction activities or where there is any observed indication of poor hygiene.

Care should be taken not to introduce a bias in the time samples are taken. This includes ensuring that there is adequate sampling of all manufacturing shifts and production periods within these shifts. Additional samples just prior to start-up are good indices of the effectiveness of cleaning operations.

(e) Frequency of sampling

The frequency of environmental sampling for the different parameters should be based primarily on factors outlined under (a). It should be defined based on existing data on the presence of relevant microorganisms in the areas submitted to such a monitoring program. In the absence of such information, sufficient suitable data should be generated to correctly define the appropriate frequency. Such data should be collected over sufficiently long periods of time so as to provide representative and reliable information on the prevalence and occurrence of *Salmonella* over time, and/or *E. sakazakii*(*Cronobacter* species), where appropriate.

The frequency of the environmental monitoring program needs to be adjusted according to the findings and their significance in terms of risk of contamination. In particular, the detection of pathogens and/or increased levels of indicator organisms in the finished product should lead to increased environmental and investigational sampling to identify the contamination sources. The frequency also needs to be increased in situations where an increased risk of contamination can be expected, e.g., in case of maintenance or construction activities or following wet cleaning activities.

(f) Sampling tools and techniques

It is important to choose and adapt the type of sampling tools and techniques to the type of surfaces and sampling locations. For example, scrapings of residues or residues from vacuum cleaners provide useful samples, and humidified sponges (or dry swabs) may be more appropriate for larger surfaces.

(g) Analytical methods

The analytical methods used to analyse environmental samples should be suitable for the detection of the target organisms. Considering the characteristics of environmental samples it is important to demonstrate that the methods are able to detect, with acceptable sensitivity, the target organisms. This should be documented appropriately. Under certain circumstances, it may be possible to composite (pool) certain samples without losing the required sensitivity. However, in the case of positive findings additional testing will be necessary to determine the location of the positive sample. Fingerprinting isolates by one or more of the available genetic techniques (e.g., pulsed-field gel electrophoresis) can potentially provide very useful information about the source(s) of *E. sakazakii*(*Cronobacter* species) and pathway(s) that lead to contamination of PF.

(h) Data management

The monitoring program should include a system to record the data and their evaluation, e.g. performing trend analyses. A continual review of the data is important to revise and adjust monitoring programs. For EB and *E. sakazakii*(*Cronobacter* species), it can also reveal low level, intermittent contamination that may otherwise go unnoticed.

(i) Actions in case of positive results

The purpose of the monitoring program is to find target organisms if present in the environment. Decision criteria and responses based on these monitoring programs should be articulated prior to the establishment of the program. The plan should define the specific action to be taken and the rationale. This could range from no action (no risk of contamination), to intensified cleaning, to source tracing (increased environmental testing), to review of hygienic practices up to holding and testing of product.

Generally manufacturers should expect to find EB and *E. sakazakii*(*Cronobacter* species) in the processing environment. Therefore an appropriate action plan should be designed and established to adequately respond where decision criteria are exceeded. A review of hygiene procedures and controls should be considered. The manufacturer should address each positive result of *Salmonella* and evaluate changes in the trends of *E. sakazakii*(*Cronobacter* species) and EB counts; the type of action will depend upon the likelihood of contaminating the product with *Salmonella* and *E. sakazakii*(*Cronobacter* species).

2. MICROBIOLOGICAL MONITORING IN POWDERED FORMULA PREPARATION UNITS

The extrinsic microbiological contamination of powdered formulae during preparation is a factor which needs to be taken into consideration in the design of preventive measures in health care and child care facilities. Such measures are based, as in the case of the manufacture of the powdered formulae, on the application of Good Hygienic Practices as relevant for any establishment handling foods (*Recommended International Code of Practice – General Principles of Food Hygiene (CXC 1-1969)*) and on the application of HACCP or similar systems to address specific hazards.

Such extrinsic microbiological contamination can occur either from the preparation environment, from preparation surfaces, and/or from utensils used during preparation. It is therefore important to assess and verify that the implemented measures are effective.

Microbiological monitoring of powdered formula storage areas, preparation areas, and surfaces in direct contact with the product (e.g., utensils) represents an essential element of the quality assurance program.

Results from a properly designed monitoring program will assist in identifying potential sources of contamination and in demonstrating the efficacy of cleaning and disinfections procedures.

As for section 1 of this annex, a number of factors should be considered when developing the sampling program to ensure its effectiveness, including the target organisms, types of samples, sampling locations, number of samples, frequency of sampling and tools and techniques, analytical methods, data management and actions to take in case of positive results.

A monitoring program of PF preparation units is best achieved through sampling and testing of environmental samples for relevant microorganisms such as *Salmonella* and *E. sakazakii* (*Cronobacter* species) or hygiene indicators such as EB. It should include swabs from surfaces of preparation areas, sinks, equipment and utensils used as well as residues, for example from vacuum cleaners, collected in the area.

It is important that the sampling be done using appropriate sampling tools and techniques, adapted to the type of surfaces and location, and from relevant sites which may, if contaminated, lead to (extrinsic) contamination of PF.

The analytical methods used should be suitable for the detection of the target organisms. Considering the characteristics of samples, it is important to demonstrate that the methods are able to detect, with acceptable sensitivity, the target organisms. This should be documented appropriately. Under certain circumstances, it may be possible to composite (pool) certain samples without losing the required sensitivity. However, in the case of positive findings additional testing will be necessary to determine the location of the positive sample. Fingerprinting isolates by one or more of the available genetic techniques (e.g., pulsed-field gel electrophoresis) can potentially provide very useful information about the source(s) of *E. sakazakii* (*Cronobacter* species) and pathway(s) that lead to contamination of PF.

It is important as well to document sampling activities and to include a system to record the data and their evaluation, e.g., performing trend analyses, and to use the data to initiate corrective actions where necessary. For this purpose, it is important to define targets to be achieved, e.g., in terms of acceptable levels of hygiene indicators or absence of pathogens. Such targets should be based on historical data or, if not available, on an initial survey that would permit one to define the normal microbiological status of the different sampling points. For EB and *E. sakazakii* (*Cronobacter* species), it can also reveal low level, intermittent contamination that may otherwise go unnoticed.

The purpose of the monitoring program is to find target organisms, if they are present. Generally, it is expected that EB and *E. sakazakii* (*Cronobacter* species) would be present in the preparation room environment. Decision criteria and responses based on the monitoring program should be articulated prior to the establishment of the program. The plan should define the specific action to be taken where decision criteria are exceeded and the rationale for such action. Each positive result for *Salmonella* and *E. sakazakii* (*Cronobacter* species) should be addressed and changes in the trends of EB counts should be evaluated. The

type of action will depend upon the likelihood of contaminating the formulae with *Salmonella* and *E. sakazakii* (*Cronobacter* species). This could range from no action (no risk of contamination), to intensified cleaning, to source tracing, to the review of hygienic practices.

It is also important to review the monitoring program on a regular basis to take into account changes in the set-up, trends, etc.