





**INTERNATIONAL FORMULA COUNCIL**

*Formerly the Enteral Nutrition Council and Infant Formula Council*

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**ATTACHMENT D**

Via E-mail and Federal Express

June 27, 2003

Dr. Christine Taylor, HFS-800  
Food and Drug Administration  
CFSAN, CPK1/4C096  
5100 Paint Branch Parkway  
College Park, MD 20740-3835

Dear Dr. Taylor:

In March 2003, FDA charged its Food Advisory Committee, Subcommittee on Contaminants and Natural Toxicants, to address intervention strategies that can be used in infant formula manufacturing processes and plants to reduce the risk of *Enterobacter sakazakii* (*E. sakazakii*). The Subcommittee made the following recommendation: "Intervention strategies, which reduce bacterial presence in powdered infant formula, should be used in manufacturing processes and plants. These include, but are not limited to, prerequisite programs to assure the microbial quality of raw materials, hygienic design and maintenance of equipment, hygienic zoning in plant design, and continuous use and improvement of HACCP programs and their verification."

We earlier advised you that we would be providing information we believe will be of assistance regarding issues related to *E. sakazakii* and powdered infant formula. On this note, attached for your review, is a document developed by the infant formula industry\* addressing *E. sakazakii* with respect to good manufacturing practices entitled "Proposed Discussion Points on Powdered Infant Formula Good Manufacturing Practices." The industry brings forth for discussion those Prerequisite Programs (PrPs) and procedures for powdered infant formula where significant enhancement may have been achieved since the 1996 Proposed Rule: Current Good Manufacturing Practices, Quality Control Procedures, Quality Factors, Notification Requirements, and Record and Reports, for the Production of Infant Formula (i.e. 21 CFR Parts 106 and 107). We look forward to discussing this document with you when we meet.

For your further information, the industry is currently working on two additional documents addressing *E. sakazakii* with respect to microbiological testing and sampling of powdered infant formula, and special products. We believe this information will be of further assistance to you and we will be pleased to provide it as soon as it is available.

Sincerely,

*Robert C. Gelardi*

Robert C. Gelardi  
President

*Mardi K. Mountford*

Mardi K. Mountford  
Executive Director

\* Note: United States infant formula manufacturers are Bristol-Myers Squibb, Mead Johnson Nutritionals; Nestlé USA, Nutrition Division; Abbott Laboratories, Ross Products Division; Solus Products; and Wyeth Nutrition.

cc:	Dr. Sue Anderson	(w/attachment)
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	Dr. Don Zink	" "
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**Proposed Discussion Points on Powdered Infant  
Formula Good Manufacturing Practices**

Introduction

It is clear from the 1996 Proposed Rule: Current Good Manufacturing Practice, Quality Control Procedures, Quality Factors, Notification Requirements, and Records and Reports, for the Production of **Infant Formula**, (i.e. 21 CFR Parts 106 and 107) – as well as from industry comments on that Proposed Rule – that there is a general awareness of the need for control procedures (i.e. HACCP and Prerequisite Programs) to prevent adulteration of in-process and finished products with biological, chemical or physical hazards in addition to formulation/nutrition related hazards. It is also generally understood that, since powdered infant formula is a food, the basic GMPs required for food manufacture represent a minimum threshold requirement.

The proposed control procedures brought forward here for further discussion with the FDA will focus on those Prerequisite Programs (PrPs) and procedures relevant to powdered infant formula where significant enhancement may have been achieved since 1996, or areas where procedures still need to be developed to adequately provide:

- Controls to prevent adulteration caused by workers (Sec. 106.10 a-c).
- Controls to prevent adulteration caused by facilities (Sec.106.20 a-i).
- Controls to prevent adulteration caused by use of equipment or utensils that are of inappropriate design, installation, etc. (Sec. 106.30 a, f).
- Controls to prevent adulteration caused by ingredients, containers, and closures (Sec. 106.40 d).

Prerequisite Programs and procedures relative to "controls to prevent adulteration by microorganisms (i.e. finished product monitoring)" will be addressed by a separate industry proposal.

**Discussion Points**

**1. Controls to prevent adulteration caused by workers (Sec. 106.10 a-c)**

Beyond the norm for industry Personnel GMPs, the following enhanced practices or components of PrPs may provide an extra measure of protection against recontamination by biological, chemical, and physical hazards of in-process and finished product materials:

- Dedication of outer garments including footwear for use in High Hygiene areas. *High Hygiene areas will be defined as those areas where infant powder is exposed to the environment in its final form as it is processed, conveyed, stored, or filled into primary packaging.* The effectiveness of this practice can be further enhanced by the use of specially designed anterooms/airlock where outer garments and footwear can be changed while moving from one hygiene level zone to another. Facilities for hand disinfection may also be provided. (See Hygienic Zoning below.)
- Inclusion of strict hygienic procedures, for outer garments, tools, and utensils which may come in contact with the food contact surfaces, in personnel practices particularly for maintenance and line workers required to make line interventions due to process stoppage for any number of reasons.
- Enhancement of practices for all contractors' performing work within the factory, equivalent to those required for factory personnel.

## **2. Controls to prevent adulteration caused by facilities (Sec.106.20 a-i).**

Beyond the norm for industry Facility GMPs, the following enhanced practices or components of PrPs may provide an extra measure of protection against recontamination by microbiological hazards of in-process and finished product materials:

- Physical segregation of different unit operations or activities including the use of physical barriers (i.e. Hygienic Zoning) in regards to hygiene levels (i.e. High, Medium, and Base GMP for example).
  - High Level areas are where processed products are exposed and vulnerable to process environmental influences for recontamination. Enhanced microbial environmental control practices with verification required. Dry cleaning practices are also normally required for such designated areas.
  - Medium Level areas are where experience should demonstrate that sensitivity of the product stream is reduced from that described for High Hygiene zones. Typically, process line may be enclosed and risk of recontamination is lower. Microbial environmental control practices with verification are still required. Dry and wet cleaning or controlled wet cleaning practices may be employed.
  - Base GMP Level areas would represent general facility area such as warehousing, maintenance, personnel traffic areas and do not require the same level of control or verification as the High and Medium Level zoned areas.
- Physical separation including, but not limited to, hygienic engineering design to accomplish segregation of:
  - Wet and dry manufacturing processes.
  - Wet and dry cleaning and Sanitary Standard Operating Procedures (SSOPs).
  - Raw materials handling and finished goods handling activities.
  - Processing, packaging and general warehousing areas.
  - Filtered ambient air and non-filtered air process environments.
- Zoning to provide control over personnel, equipment, and materials traffic as well as circulation of ambient air (i.e. treated/filtered versus non-treated/filtered) and makeup air for treated/filtered process air. Details of the manufacturing line layout and equipment installation must complement the concept of zoning.
- Use and management of water within the manufacturing process and environment to provide for strict control and minimization wherever possible to reduce the risk of microbial proliferation. This control should be addressed in PrPs related to SSOPs and facility hygienic design.

## **3. Controls to prevent adulteration caused by use of equipment or utensils that are of inappropriate design, installation, etc. (Sec. 106.30 a, f)**

Beyond the norm for industry Equipment GMPs, the following enhanced practices or components of PrPs may provide an extra measure of protection against recontamination by microbiological hazards of in-process and finished product materials:

- Hygienic design for all processing equipment, tools, utensils, etc. to assure cleanability and the elimination of hollow body components that may provide micro-niches for microbial proliferation.
- Hygienic design of processing equipment to eliminate water to the extent possible from the process (e.g., steam condensate, condensate from coolers, spray dryer exhaust water scrubbers). Dehumidification of cooling and transport air will also contribute to the elimination of moisture.
- Hygienic design of processing equipment to assure use of process water/agglomerator rewet water of highest microbiological and chemical quality.

- Design of processes to minimize the addition of ingredients to the process stream post-heat treatment to avoid post-process contamination. Assure appropriate PrPs for any ingredients that are added after heat treatment.
- Explore the design of possible manufacturing operations to provide dedicated equipment for products where allergens may be of concern. Allow for longer and drier process runs and further reduction of the need for wet cleanup.
- Continue use of improved cleaning SSOPs and equipment to assure adequate cleaning and appropriate control of residual moisture. Work with vendors should continue in order to develop equipment with improved sanitary design and enhanced efficacy of cleaning/sanitizing tools, chemicals, and practices.

#### **4. Controls to prevent adulteration caused by ingredients, containers, and closures (Sec. 106.40 d)**

Beyond the norm for industry Ingredient, Packaging, and Closure GMPs, the following enhanced practices or components of PrPs may provide an extra measure of protection against recontamination by microbiological hazards of in-process and finished product materials:

- Implementation and maintenance of a strict ingredient supplier quality assurance program for all raw materials suppliers deemed sensitive or critical (particularly for dry mix operations). The industry as a whole may benefit from a collaboration in this area due to the limited number of qualified suppliers for common ingredients such as milk derivatives (e.g. whey and casein powders) and soy derivatives (e.g. isolated soy proteins, soy protein concentrates) to name a few.