Jeb Bush
Governor

FLORIDA DEPARTMENT OF HEALTH

John O. Agwunobi, M.D., M.B.A.
Secretary

June 18, 2003

Dockets Management Branch
HFA-- 305
Food and Drug Administration
5630 Fisher's Lane, Room 1061
Rockville, Maryland 20852

RE: Docket No. 95N-0309

Dear Sirs:

This letter is in response to the April 28, 2003 notice that reopens the comment period for the proposed rule published in the Federal Register of July 9, 1996 (61FR 36154), revising infant formula regulations in 21 CFR parts 106 and 107. We are writing to express our support for the Food and Drug Administration (FDA) to establish critical manufacturing standards that will ensure powdered infant formulas are manufactured under strict quality control guidelines, and that new ingredients are thoroughly tested for safety. In addition, we recommend that an enhanced surveillance system for powdered infant formulas be implemented, including post marketing surveillance.

The Florida Department of Health is concerned that both consumers and physicians currently think powdered formulas, which make up 50% of the market, are sterile products. This misunderstanding, and the fact that there have been several documented outbreaks of infants becoming infected with *Enterobacter sakazakii* after consumption of contaminated powdered formula, is of great concern to us. Many of the infected infants have either died, developed meningitis with residual complications, had necrotizing enterocolitis or other serious health problems, as a result of ingesting contaminated formulas. Such outbreaks have been reported for at least two decades. The most recent outbreak occurred in Tennessee and was investigated by a team from the Centers for Disease Control and Prevention (CDC).

We are aware that at least one infant formula manufacturer is proposing to add bacteria to its powdered formula in hopes of providing formula-fed infants the same type of protective bacterial flora that has been documented among breast-fed infants. This addition of bacteria to formula is being referred to as "probiotic manufacturing". It is our understanding that these bacteria are considered "safe" under existing FDA guidelines. Given the problem with incomplete standards for the manufacture of powdered formula, the proposed addition of bacteria to infant formula concerns us because the manufacturer proposing to manufacture and market this formula currently holds the WIC contract in Florida.

Florida has approximately 200,000 live births each year, and approximately half of those births are to women on Medicaid. Our WIC office estimates that it purchases standard infant formulas for approximately 86,000 infants in the state each year. Hence, the development of

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standards requiring appropriate manufacturing processes covering powdered formula would better protect a large number of Florida's infants.

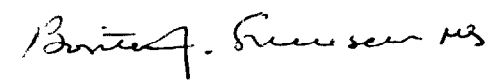
Good manufacturing standards should apply to both of the processes – dry blending and wet mixing-spray drying – that are used to make powdered infant formulas. We understand that approximately 10-12 plants in the United States are involved in the manufacture of powdered formula, but we do not have information regarding how much powdered formula is manufactured outside of the country and imported into the United States. Given the cross contamination of the toxin that resulted in the eosinophilia myalgia outbreaks in the early 1990's, in conjunction with the consumption of tryptophan, it is recommended that protocols be in place to assure the quality of any imported powdered formula. This is a realistic concern because the manufacturer currently proposing to add bacteria to formula is an international company with manufacturing capability outside the United States.

We are aware that the FDA and the CDC issued guidelines in 2002 to physicians and hospitals to reduce the likelihood of outbreaks with *Enterobacter sakazakii* in the settings of neonatal intensive care units. It is our understanding that the new proposed formula with added bacteria would be intended for use by term infants (not immuno-compromised infants), and would presumably be prepared by their mothers or other caregivers. This raises the possibility that additional outbreaks could occur if strict label and preparation instructions are not provided to the general population of mothers. Our assumption is that medical and nursing personnel working in neonatal intensive care units may have a greater knowledge of the risks involved with powdered formula than the general population of mothers who are feeding infants at home. In addition, Florida's infants represent a diverse population of racial and ethnic groups whose primary language may not be English. We believe that much-improved guidance in the form of enhanced labeling on formula should be required.

In addition, enhanced surveillance of powdered formula should be implemented as part of post-marketing surveillance for illnesses from these formulas. The MedWatch program, while a good start, is not sufficient. It is our understanding that some formula surveillance is conducted through the CDC, which maintains a sentinel hospital network of approximately 300 institutions. That effort should be expanded to include specific surveillance for *Enterobacter sakazakii* and should include post-marketing studies of the safety of bacteria that are added to formula. Such bacteria could possibly be pathogenic to infants if powdered formula is cross-contaminated, mixed improperly, stored improperly or kept too long. Surveillance activities through emergency rooms could enhance existing surveillance.

We appreciate the opportunity to comment.

Sincerely,



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