



GUIDELINES CONCERNING NOTIFICATION AND  
TESTING OF INFANT FORMULAS

INTRODUCTION

The purpose of the Infant Formula Act of 1980 (Act) is to ensure the safety and nutrition of infant formulas – including minimum, and in some cases, maximum levels of specified nutrients. To accomplish this purpose, the Act authorizes the Food and Drug Administration (FDA) to promulgate appropriate regulations. These guidelines address three related requirements:

- (1) Requirements for manufacturer notification of FDA, before the first processing of an infant formula (discussed in Section I below) or
- (2) Requirements for manufacturer notification of FDA, after a change in formulation or processing (discussed in Section II), and
- (3) Manufacturer testing requirements based on regulations with regard to major and minor changes (discussed in Section III).

I. NOTIFICATION OF FDA 90 DAYS PRIOR TO FIRST PROCESSING  
[412 (b) (2)]

A manufacturer must notify FDA 90 days before the first processing of any infant formula, for commercial or charitable distribution for human consumption, that differs fundamentally in processing or in composition from any previous formulation produced by the manufacturer.

Examples of infant formulas deemed to differ fundamentally in processing or in composition include:

- a. The manufacture of a new infant formula.
- b. Any infant formula manufacturer entering the U.S. market.
- c. Any infant formula powder processed and introduced for commercial or charitable distribution by a manufacturer who previously only produced liquids (or vice versa).
- d. Any infant formula having a significant revision, addition, or substitution of a macronutrient (i.e., protein, fat, or carbohydrate), for which the manufacturer has not had previous experience.

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- e. Any infant formula manufactured on a new processing line or in a new plant.

\*These guidelines relate to interpreting paragraphs 412 (b) (2) and (3) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 106.30 (c).

- f. Any infant formula manufactured containing a new constituent not listed in 412 (g) of the FD&C Act and added for its potential nutrient contribution, such as taurine or L-carnitine.
- g. Any manufacturer that processes infant formula on new equipment that utilized a new technology or principle (e.g., a change from terminal sterilization to aseptic processing).
- h. A fundamental change in the type of packaging used (e.g., changing from metal cans to plastic pouches).

## II. NOTIFICATION OF FDA BEFORE FIRST PROCESSING FOR COMMERCIAL OR CHARITABLE DISTRIBUTION (Reformulation and Processing Changes)[412 (b) (3)]

Reformulation changes relate to changes made in the composition of the product. Processing changes can refer to changes either in specified operating parameters, steps in the manufacturing process, or changes in physical equipment. Like for like replacements of individual components or repairs to physical equipment are not considered changes.

21 CFR 106.30 (c) requires all infant formula manufacturers to have change control procedures in place to evaluate all reformulation and processing changes that could affect nutrient quality of the product. These procedures include reviews by appropriate, qualified, technical personnel including those with expertise in the areas affected by the change.

Reportable reformulation and process changes include:

1. Any change that results in changes in quantitative nutrient declaration on the label for nutrients required under section 412 (g) of the Act or trace nutrients voluntarily added consistent with 21 CFR 107.10 (b) (5).

Examples: a. Reducing vitamin K in an oil soluble vitamin premix resulting in a label change.

b. Reducing the level of zinc fortification resulting in a label change.

2. Any reformulation resulting in a nutrient level which is within 10% of the nutrient levels (either minimum or maximum) required by section 412 (g) of the FD&C Act and is at least 10% closer to the required level. Notification is not necessary

for simple adjustments in the level of an ingredient to accommodate inconsistencies in processing.

3. Any change in the identity of the ingredients providing nutrients required under section 412 (g) of the Act or trace nutrients added voluntarily consistent with 21 CFR 107.10 (b) (5).

Examples:

- a. Replacing vitamin D<sub>2</sub> with vitamin D<sub>3</sub>.
- b. Replacing vitamin A acetate with vitamin A palmitate.
- c. Replacing calcium carbonate with tricalcium phosphate.

4. Any design change in the formulation or processing of an infant formula which the manufacturer determines calls for non-routine nutrient testing which is conducted prior to release, for the purpose of determining whether a possible change has occurred in the levels of nutrients in meeting requirements of section 412 (g) of the Act. Non-routine nutrient testing is any testing that is not done on a batch-by-batch basis to comply with 21 CFR 106. The following are examples of changes, when a manufacturer determines that the particular change can reasonably be expected to have an adverse effect on nutrient level or nutrient availability.

Examples:

- a. Changes in processing equipment (e.g., spray dryer which uses direct heat vs. indirect heat; change in food surface contact material, copper for stainless steel; replacing a heat exchanger with a steam injector – vapor tank system).
- b. Changes in time-temperature conditions of preheating, handling, mixing, or sterilization of in process product.
- c. Changes in the order of addition of the ingredients.

### III. TESTING OF INFANT FORMULAS WHICH HAVE UNDERGONE CHANGES IN FORMULATION OR PROCESSING [21cfr 106 (c)]

FDA has promulgated Quality Control Procedure regulations (21 CFR 106) under the authority provided by the Infant Formula Act. Section 106.30 (c) establishes testing requirements for infant formulas which undergo changes in ingredients or processing conditions that could affect the level of nutrients. FDA establishes two categories of formulation and processing changes, as described below: [(1) major changes (21 CFR 106.30 (c) (2)) and (2) minor changes (21 CFR 106.30 (c) (1))].

1. The changes described in this section would require testing associated with a “major” change as identified in 21 CFR 106.30 (c) (2). \*

A major change can be either in the formulation or processing of an infant formula. A major change is defined as a change where manufacturer's experience or theory would predict possible significant adverse impact on levels of nutrients or availability of nutrients in meeting requirements of section 412 (g) of the Act. Examples of major changes include:

- a. The manufacture of an infant formula in a new plant.
- b. The utilization of a complete, new production line.
- c. The addition of a new macronutrient (i.e., protein, fat, or carbohydrate).
- d. The employment of significant new technology (e.g., the change from terminal sterilization to aseptic processing).
- e. A substantial quantitative change in the protein, fat, or carbohydrate.
- f. The addition of new constituents added for their potential nutrient contribution (e.g., taurine and L-carnitine).
- g. A fundamental change in the type of packaging used (e.g., changing from metal cans to plastic pouches).

FDA has not promulgated specific requirements for the clinical testing of new and reformulated infant formulas. However, FDA has recognized that pre-market clinical evaluation in humans may be appropriate whenever certain changes affecting the nutritional profile of an infant formula are made, particularly in the case of new or reformulated products. FDA has also recognized that the degree and complexity of clinical testing needed will vary according to the extent of the changes in the formula. Until guidelines are developed, it is therefore understood that the scope of the clinical testing necessary for new and reformulated infant formulas will be decided by the manufacturer on a case-by-case basis and that the chemical testing alone for major reformulations may not be sufficient to determine adequacy of the product.

\*IFC members would notify FDA of all "major" changes.

2. The changes described in this section would require testing associated with a "minor" change as identified in 21 CFR 106.30 (c) (1).

A minor change can be either in the formulation or processing of an infant formula. A minor change is defined as a minor reduction in nutrient levels subject to minimum limits, or a minor increase in levels of nutrients that are subject to maximum limits established under section 412 (g) of that Act or any

other change where experience or theory would not predict a possible significant adverse impact on nutrient levels or nutrient availability.

Examples of minor changes include:

- a. Minor reduction of iron level
- b. Replacing certain nutrient forms with another form.
- c. Adjustments in the quantity of a nutrient in a premix or individually added nutrient that results in a specification change for that nutrient in the finished product.
- d. Changes in time-temperature conditions of preheating during handling of bulk product that cannot reasonably be expected to cause an adverse impact on nutrient levels or nutrient availability.
- e. Changes in oxygen content of a packaged product that might have a minimal effect on the level of nutrients.

Reference for above Guidelines

FDA Letter, August 2, 1986. Guidelines are issued to 21 CFR 10.90(b).