nonnutritive sweetener(s) is added, the statement shall indicate the presence of both types of sweetener, e.g., ''Sweetened with nutritive sweetener(s) and nonnutritive sweetener(s).''

(c) *''Low calorie'' foods.* A food purporting to be ''low calorie'' must comply with the criteria set forth for such foods in §101.60(b)(2) and (b)(3) of this chapter.

(d) *''Reduced calorie'' foods and other comparative calorie claims.* A food purporting to be ''reduced calorie'' or otherwise containing fewer calories than a reference food must comply with the criteria set forth for such food in §101.60(b)(4) and (b)(5) of this chapter.

(e) *Label terms suggesting usefulness as low calorie or reduced calorie foods.* (1) Except as provided in paragraphs (e)(2) and (e)(3) of this section, and in §101.13(q)(2) of this chapter for soft drinks, a food may be labeled with terms such as ''diet,'' ''dietetic,'' ''artificially sweetened,'' or ''sweetened with nonnutritive sweetener'' only if the claim is not false and misleading, and the food is labeled ''low calorie'' or ''reduced calorie'' or bears another comparative calorie claim in compliance with part 101 of this chapter and this section.

(2) Paragraph (e)(1) of this section shall not apply to any use of such terms that is specifically authorized by regulation governing a particular food, or, unless otherwise restricted by regulation, to any use of the term ''diet'' that clearly shows that the food is offered solely for a dietary use other than regulating body weight, e.g., ''for low-sodium diets.''

(3) Paragraph (e)(1) of this section shall not apply to any use of such terms on a formulated meal replacement or other food that is represented to be of special dietary use as a whole meal, pending the issuance of a regulation governing the use of such terms on foods.

(f) *''Sugar free,'' and ''no added sugar.''* Criteria for the use of the terms ''sugar free'' and ''no added sugar'' are provided for in §101.60(c) of this chapter.

[58 FR 2430, Jan. 6, 1993]

Subpart C [Reserved]

Subpart D—Standards of Identity [Reserved]

PART 106—INFANT FORMULA REQUIREMENTS PERTAINING TO CURRENT GOOD MANUFACTURING PRACTICE, QUALITY CONTROL PROCEDURES, QUALITY FACTORS, RECORDS AND REPORTS, AND NOTIFICATIONS

Subpart A—General Provisions

Sec.

Subpart B—Current Good Manufacturing Practice

Subpart C—Quality Control Procedures

Subpart D—Conduct of Audits

Subpart E—Quality Factors for Infant Formulas

AUTHORITY: 21 U.S.C. 321, 342, 350a, 371.

SOURCE: 79 FR 8059, Feb. 10, 2014, unless otherwise noted.

EDITORIAL NOTE: Nomenclature changes to part 106 appear at 81 FR 49895, July 29, 2016.

Subpart A—General Provisions

§ 106.1 Status and applicability of the regulations in part 106.

(a) The criteria set forth in subparts B, C, and D of this part prescribe the steps that manufacturers shall take under section 412(b)(2) and (b)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(b)(2) and (b)(3)) in processing infant formula. If the processing of the formula does not comply with any regulation in subparts B, C, or D of this part, the formula will be deemed to be adulterated under section 412(a)(3) of the Federal Food, Drug, and Cosmetic Act.

(b) The criteria set forth in subpart E of this part prescribe the requirements for quality factors that infant formula shall meet under section 412(b)(1) of the Federal Food, Drug, and Cosmetic Act. If the formula fails to comply with any regulation in subpart E of this part, it will be deemed to be adulterated under section 412(a)(2) of the Federal Food, Drug, and Cosmetic Act.

(c) The criteria set forth in subpart F of this part prescribe records requirements for quality factors under section 412(b)(1) of the Federal Food, Drug, and Cosmetic Act and for good manufacturing practices and quality control procedures, including distribution and audit records, under section 412(b)(2). If an infant formula manufacturer fails to comply with the quality factor record requirements in subpart F of this part with respect to an infant formula, the formula will be deemed to be adulterated under section 412(a)(2) of the Federal Food, Drug, and Cosmetic Act. If an infant formula manufacturer fails to comply with the good manufacturing practices or quality control procedures record requirements in subpart F of this part with respect to an infant formula, the infant formula will be deemed to be adulterated under section 412(a)(3) of the Federal Food, Drug, and Cosmetic Act. The criteria set forth in subpart F of this part also implement record retention requirements under section 412(b)(4) of the Federal Food, Drug, and Cosmetic Act. Failure to comply with any regulation in subpart F of this part is a violation of section 301(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(e)).

(d) The criteria set forth in subpart G of this part describe, in part, certain good manufacturing practices, quality control procedures, and quality factor records requirements under section 412(b)(1) and (b)(2) of the Federal Food, Drug and Cosmetic Act. If an infant formula manufacturer fails to comply with such records requirements with respect to an infant formula, the infant formula will be deemed to be adulterated under section 412(a)(2) or (a)(3) of the Federal Food, Drug, and Cosmetic Act, as applicable. The criteria set forth in subpart G of this part also describe the circumstances in which an infant formula manufacturer is required to register with, submit to, or notify the Food and Drug Administration, and the content of a registration, submission, or notification, under section 412(c), (d), and (e) of the Federal Food, Drug, and Cosmetic Act. Failure to comply with any regulation in subpart G of this part is a violation of section 301(s) of the Federal Food, Drug, and Cosmetic Act.

§ 106.3 Definitions.

The definitions in this section and the definitions contained in section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321) shall apply to infant formula requirements in 21 CFR parts 106 and 107 of this chapter.

Eligible infant formula means an infant formula that could be lawfully distributed in the United States on December 8, 2014.

Final product stage means the point in the manufacturing process, before distribution of an infant formula, at which the infant formula is homogeneous and is not subject to further degradation due to processing.

Indicator nutrient means a nutrient whose concentration is measured during the manufacture of an infant formula to confirm complete addition and uniform distribution of a premix or other substance of which the indicator nutrient is a part.

Infant means a person not more than 12 months of age.

Infant formula means a food which purports to be or is represented for special dietary use solely as a food for infants by reason of its simulation of human milk or its suitability as a complete or partial substitute for human milk.

In-process production aggregate means a combination of ingredients at any point in the manufacturing process before packaging.

Major change in an infant formula means any new formulation, or any change of ingredients or processes where experience or theory would predict a possible significant adverse impact on levels of nutrients or bioavailability of nutrients, or any change that causes an infant formula to differ 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:

(1) Any infant formula produced by a manufacturer who is entering the U.S. market;

(2) Any infant formula powder processed and distributed by a manufacturer who previously only produced liquids (or vice versa);

(3) Any infant formula having a significant revision, addition, or substitution of a macronutrient (i.e., protein, fat, or carbohydrate), with which the manufacturer has not had previous experience;

(4) Any infant formula manufactured on a new processing line or in a new plant;

(5) Any infant formula manufactured containing a new constituent not listed in section 412(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(i)), such as taurine or L-carnitine;

(6) Any infant formula processed by a manufacturer on new equipment that utilizes a new technology or principle (e.g., from terminal sterilization to aseptic processing); or

(7) An infant formula for which there has been a fundamental change in the type of packaging used (e.g., changing from metal cans to plastic pouches).

Manufacturer means a person who prepares, reconstitutes, or otherwise changes the physical or chemical characteristics of an infant formula or packages or labels the product in a container for distribution. The term ''manufacturer'' does not include a person who prepares, reconstitutes, or mixes infant formula exclusively for an infant under his/her direct care or the direct care of the institution employing such person.

Microorganisms means yeasts, molds, bacteria, and viruses and includes, but is not limited to, species having public health significance.

New infant formula means:

(1) An infant formula manufactured by a person that has not previously manufactured an infant formula, and

(2) An infant formula manufactured by a person that has previously manufactured infant formula and in which there is a major change in processing or formulation from a current or any previous formulation produced by such manufacturer, or which has not previously been the subject of a submission under section 412(c) of the Federal Food, Drug, and Cosmetic Act for the U.S. market.

Nutrient means any vitamin, mineral, or other substance or ingredient that is required in accordance with the ''Nutrients'' table set out in section 412(i)(1) of the Federal Food, Drug, and Cosmetic Act or by regulations issued under section 412(i)(2) or that is identified as essential for infants by the Food and Nutrition Board of the Institute of Medicine through its development of a Dietary Reference Intake, or that has

been identified as essential for infants by the Food and Drug Administration through a FEDERAL REGISTER publication.

Nutrient premix means a combination of ingredients containing two or more nutrients received from a supplier or prepared by an infant formula manufacturer.

Production aggregate means a quantity of product, or, in the case of an infant formula produced by continuous process, a specific identified amount produced in a unit of time, that is intended to have uniform composition, character, and quality, within specified limits, and is produced according to a master manufacturing order.

Production unit means a specific quantity of an infant formula produced during a single cycle of manufacture that has uniform composition, character, and quality, within specified limits.

Production unit number or production aggregate number means any distinctive combination of letters, numbers, symbols, or any combination of them, from which the complete history of the manufacture, processing, packing, holding, and distribution of a production aggregate or a production unit of infant formula can be determined.

Quality factors means those factors necessary to demonstrate the safety of the infant formula and the bioavailability of its nutrients, as prepared for market and when fed as the sole source of nutrition, to ensure the healthy growth of infants.

Representative sample means a sample that consists of a number of units that are drawn based on rational criteria, such as random sampling, and intended to ensure that the sample accurately portrays the material being sampled.

Shall is used to state mandatory requirements.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33070, June 10, 2014]

Subpart B—Current Good Manufacturing Practice

§ 106.5 Current good manufacturing practice.

(a) The regulations set forth in this subpart define the minimum current good manufacturing practices that are to be used in, and the facilities or controls that are to be used for, the manufacture, processing, packing, or holding of an infant formula. Compliance with these provisions is necessary to ensure that such infant formula provides the nutrients required under §107.100 of this chapter and is manufactured in a manner designed to prevent its adulteration. A liquid infant formula that is a thermally processed low-acid food packaged in a hermetically sealed container is also subject to the regulations in part 113 of this chapter, and an infant formula that is an acidified food, as defined in §114.3(b) of this chapter, is also subject to the regulations in part 114 of this chapter.

(b) The failure to comply with any regulation in this subpart in the manufacture, processing, packing, or holding of an infant formula shall render such infant formula adulterated under section 412(a)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(a)(3)); the failure to comply with any regulation in part 113 of this chapter in the manufacture, processing, packing, or holding of a liquid infant formula shall render such infant formula adulterated under section 412(a)(3); and the failure to comply with any regulation in part 114 of this chapter in the manufacture, processing, packing, or holding of an infant formula that is an acidified food shall render such infant formula adulterated under section 412(a)(3).

§ 106.6 Production and in-process control system.

(a) A manufacturer shall conform to the requirements of this subpart by implementing a system of production and in-process controls. This production and in-process control system shall cover all stages of processing, from the receipt and acceptance of the raw materials, ingredients, and components through the storage and distribution of the finished product and shall be designed to ensure that all the requirements of this subpart are met.

(b) The production and in-process control system shall be set out in a written plan or set of procedures that is designed to ensure that an infant formula is manufactured in a manner

that will prevent adulteration of the infant formula.

(c) At any point, step, or stage in the production process where control is necessary to prevent adulteration, a manufacturer shall:

(1) Establish specifications to be met;

(2) Monitor the production and in-process control point, step, or stage;

(3) Establish a corrective action plan for use when a specification established in accordance with paragraph (c)(1) of this section is not met;

(4) Review the results of the monitoring required by paragraph (c)(2) of this section, and review and evaluate the public health significance of any deviation from specifications that have been established in accordance with paragraph (c)(1) of this section. For any specification established in accordance with paragraph (c)(1) of this section that a manufacturer fails to meet, an individual qualified by education, training, or experience shall conduct a documented review and shall make a material disposition decision to reject the affected article, to reprocess or otherwise recondition the affected article, or to approve and release the article for use or distribution; and

(5) Establish recordkeeping procedures, in accordance with §106.100(e)(3), that ensure that compliance with the requirements of this section is documented.

(d) Any article that fails to meet a specification established in accordance with paragraph (c)(1) of this section shall be controlled under a quarantine system designed to prevent its use pending the completion of a documented review and material disposition decision.

§106.10 Controls to prevent adulteration by workers.

(a) A manufacturer shall employ sufficient personnel, qualified by education, training, or experience, to perform all operations, including all required recordkeeping, in the manufacture, processing, packing, and holding of each infant formula and to supervise such operations to ensure that the operations are correctly and fully performed.

(b) Personnel working directly with infant formula, infant formula raw materials, infant formula packaging, or infant formula equipment or utensil contact surfaces shall practice good personal hygiene to protect the infant formula against contamination. Good personal hygiene includes:

(1) Wearing clean outer garments and, as necessary, protective apparel such as head, face, hand, and arm coverings; and

(2) Washing hands thoroughly in a hand washing facility with soap and running water at a suitable temperature before starting work, after each absence from the work station, and at any other time when the hands may become soiled or contaminated.

(c) Any person who reports that he or she has, or appears by medical examination or supervisory observation to have, an illness, open lesion (including boils, sores, or infected wounds), or any other source of microbial contamination that creates a reasonable possibility that the safety of an infant formula may be adversely affected, shall be excluded from direct contact with ingredients, containers, closures, in-process materials, equipment, utensils, and infant formula product until the condition is corrected or determined by competent medical personnel not to jeopardize the safety of the infant formula.

§106.20 Controls to prevent adulteration caused by facilities.

(a) Buildings used in the manufacture, processing, packing, or holding of infant formula shall be maintained in a clean and sanitary condition and shall have space for the separation of incompatible operations, such as the handling of raw materials, the manufacture of the product, and packaging and labeling operations.

(b) Separate areas or another system of separation, such as a computerized inventory control, a written card system, or an automated system of segregation, shall be used for holding raw materials, in-process materials, and final infant formula product at the following times:

(1) Pending release for use in infant formula production or pending release of the final product;

(2) After rejection for use in, or as, infant formula; and

(3) After release for use in infant formula production or after release of the final product.

(c) Lighting shall allow easy identification of raw materials, packaging, labeling, in-process materials, and finished products that have been released for use in infant formula production and shall permit the easy reading of instruments and controls necessary in processing, packaging, and laboratory analysis. Any lighting fixtures directly over or adjacent to exposed raw materials, in-process materials, or bulk (unpackaged) finished product shall be protected to prevent glass from contaminating the product in the event of breakage.

(d) A manufacturer shall provide adequate ventilation or control equipment to minimize odors and vapors (including steam and noxious fumes) in areas where they may contaminate the infant formula; and shall minimize the potential for contamination of raw materials, in-process materials, final product infant formula, packing materials, and infant formula-contact surfaces, through the use of appropriate measures, which may include the use of air filtration.

(e) All rodenticides, insecticides, fungicides, fumigating agents, and cleaning and sanitizing agents shall be stored and used in a manner that protects against contamination of infant formula.

(f) Potable water used in the manufacture of infant formula shall meet the standards prescribed in the Environmental Protection Agency's (EPA's) Primary Drinking Water regulations in 40 CFR part 141, except that the water used in infant formula manufacturing shall not be fluoridated or shall be defluoridated to a level as low as possible prior to use.

(1) The water shall be supplied under continuous positive pressure in a plumbing system that is free of defects that could contaminate an infant formula.

(2) A manufacturer shall test representative samples of the potable water drawn at a point in the system at which the water is in the same condition that it will be when it is used in infant formula manufacturing.

(3) A manufacturer shall conduct the tests required by paragraph (f)(2) of this section with sufficient frequency to ensure that the water meets the EPA's Primary Drinking Water Regulations but shall not conduct these tests less frequently than annually for chemical contaminants, every 4 years for radiological contaminants, and weekly for bacteriological contaminants.

(4) A manufacturer shall make and retain records, in accordance with §106.100(f)(1), of the frequency and results of testing of the water used in the production of infant formula.

(g) There shall be no backflow from, or cross-connection between, piping systems that discharge waste water or sewage and piping systems that carry water for infant formula manufacturing.

(h) Only culinary steam shall be used at all direct infant formula product contact points. Culinary steam shall be in compliance with the 3–A Sanitary Standards, No. 60903, which is incorporated by reference at §106.160. Boiler water additives in the steam shall be used in accordance with §173.310 of this chapter.

(i) Each infant formula manufacturing site shall provide its employees with readily accessible toilet facilities and hand washing facilities that include hot and cold water, soap or detergent, single-service towels or air dryers in toilet facilities. These facilities shall be maintained in good repair and in a sanitary condition at all times. These facilities shall provide for proper disposal of the sewage. Doors to the toilet facility shall not open into areas where infant formula, ingredients, containers, or closures are processed, handled, or stored, except where alternate means have been taken to protect against contamination.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33070, June 10, 2014]

§106.30 Controls to prevent adulteration caused by equipment or utensils.

(a) A manufacturer shall ensure that equipment and utensils used in the manufacture, processing, packing, or

holding of an infant formula are of appropriate design and are installed to facilitate their intended function and their cleaning and maintenance.

(b) A manufacturer shall ensure that equipment and utensils used in the manufacture, processing, packing, or holding of an infant formula are constructed so that surfaces that contact ingredients, in-process materials, or infant formula are made of nontoxic materials and are not reactive or absorptive. A manufacturer shall ensure that such equipment and utensils are designed to be easily cleanable and to withstand the environment of their intended use and that all surfaces that contact ingredients, in-process materials, or infant formula are cleaned and sanitized, as necessary, and are maintained to protect infant formula from being contaminated by any source. All sanitizing agents used on such equipment and utensils that are regulated as pesticide chemicals under 21 U.S.C. 346a(a) shall comply with the Environmental Protection Agency's regulations established under such section, and all other such sanitizers shall comply with all applicable Food and Drug Administration laws and regulations.

(c) A manufacturer shall ensure that any substance, such as a lubricant or a coolant, that is required for operation of infant formula manufacturing equipment and which would render the infant formula adulterated if such substance were to come in contact with the formula, does not come in contact with formula ingredients, containers, closures, in-process materials, or with infant formula product during the manufacture of an infant formula.

(d) A manufacturer shall ensure that each instrument used for measuring, regulating, or controlling mixing time and speed, temperature, pressure, moisture, water activity, or other parameter at any point, step, or stage where control is necessary to prevent adulteration of an infant formula during processing is accurate, easily read, properly maintained, and present in sufficient number for its intended use.

(1) The instruments and controls shall be calibrated against a known reference standard at the time of or before first use and thereafter at routine intervals, as specified in writing by the manufacturer of the instrument or control, or as otherwise deemed necessary to ensure the accuracy of the instrument or control. The known reference standard shall be certified for accuracy at the intervals specified in writing by the manufacturer of the instrument or control, or at routine intervals otherwise deemed necessary to ensure the accuracy of the instrument or control. A manufacturer shall make and retain records of the calibration activities in accordance with § 106.100(f)(2).

(2) Instruments and controls that cannot be adjusted to agree with the reference standard shall be repaired or replaced.

(3) If calibration of an instrument shows a failure to meet a specification for a point where control is deemed necessary to prevent adulteration of infant formula product, a written evaluation of all affected product, and of any actions that need to be taken with respect to that product, shall be made, in accordance with § 106.100(f)(2).

(e) The following provisions apply to thermal processing and cold storage of infant formulas:

(1) Equipment and procedures for thermal processing of infant formula packaged in hermetically sealed containers shall conform to the requirements in 21 CFR parts 108 and 113.

(2)(i) Except as provided in paragraph (e)(2)(ii) of this section, a manufacturer shall maintain all areas of cold storage at a temperature of 40 °F (4.4 °C) or below.

(ii) A manufacturer may maintain a cold storage area for an in-process infant formula or for a final infant formula at a temperature not to exceed 45 °F (7.2 °C) for a defined period of time provided that the manufacturer has scientific data and other information to demonstrate that the time and temperature conditions of such storage are sufficient to ensure that there is no significant growth of microorganisms of public health significance during the period of storage of the in-process or final infant formula product.

(3)(i) Cold storage compartments and thermal processing equipment shall be equipped with easily readable, accurate temperature-indicating devices.

(ii) A manufacturer shall ensure that the temperature of each cold storage compartment is maintained by:

(A) Monitoring the temperature of the cold storage compartment on a temperature-indicating device and recording this temperature in a record with such frequency as is necessary to ensure that temperature control is maintained;

(B) Equipping the cold storage compartment with one or more temperature-recording devices that will reflect, on a continuing basis, the true temperature, within the compartment;

(C) Equipping the cold storage compartment with a high temperature alarm that has been validated to function properly and recording the temperature in a record with such frequency as is necessary to ensure that temperature control is maintained; or

(D) Equipping the cold storage compartment with a maximum-indicating thermometer that has been validated to function properly and recording this temperature in a record with such frequency as is necessary to ensure that temperature control is maintained.

(iii) A manufacturer shall, in accordance with §106.100(f)(3), make and retain records of the temperatures recorded in compliance with §106.30(e)(3)(ii).

(4) When a manufacturer uses a temperature-recording device for a cold storage compartment, such device shall not read lower than the reference temperature-indicating device.

(5) A manufacturer shall monitor the temperature in thermal processing equipment at points where temperature control is necessary to prevent adulteration. Such monitoring shall be at such frequency as is required by regulation or is necessary to ensure that temperature control is maintained.

(f) A manufacturer shall ensure that equipment and utensils used in the manufacture of infant formula are cleaned, sanitized, and maintained at regular intervals to prevent adulteration of the infant formula.

(1) An individual qualified by education, training, or experience to conduct such a review shall review all cleaning, sanitizing, and maintenance to ensure that it has been satisfactorily completed.

(2) A manufacturer shall make and retain records on equipment cleaning, sanitizing, and maintenance, in accordance with §106.100(f)(4).

(g) A manufacturer shall ensure that compressed air or other gases that are mechanically introduced into infant formula, that are used to clean any equipment, or that come into contact with any other surface that contacts ingredients, in-process materials, or infant formula product are treated in such a way that their use will not contaminate the infant formula with unlawful or other chemical, physical, or microbiological contaminants. When compressed gases are used at product filling machines to replace air removed from the headspace of containers, a manufacturer shall install, as close as practical to the end of the gas line that feeds gas into the space, a filter capable of retaining particles 0.5 micrometer or smaller.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33071, June 10, 2014]

§106.35 Controls to prevent adulteration due to automatic (mechanical or electronic) equipment.

(a) For the purposes of this section:

(1) ''Hardware'' means all automatic equipment, including mechanical and electronic equipment (such as computers), that is used in production or quality control of infant formula.

(2) ''Software'' means any programs, procedures, rules, and associated documentation used in the operation of a system.

(3) ''System'' means a collection of components (including software and hardware) organized to accomplish a specific function or set of functions in a specified environment.

(4) ''Validation'' means establishing documented evidence that provides a high degree of assurance that a system will consistently produce a product meeting its predetermined specifications and quality characteristics. Validation can be accomplished through any suitable means, such as verification studies or modeling.

(b) All systems shall be designed, installed, tested, and maintained in a manner that will ensure that they are capable of performing their intended function and of producing or analyzing

infant formula in accordance with this subpart and subpart C of this part.

(1) A manufacturer shall ensure, at any point, step, or stage where control is necessary to prevent adulteration of the infant formula, that all hardware is routinely inspected and checked according to written procedures and that hardware that is capable of being calibrated is routinely calibrated according to written procedures.

(2) A manufacturer shall check and document the accuracy of input into, and output generated by, any system used in the production or quality control of an infant formula to ensure that the infant formula is not adulterated. The degree and frequency of input/output verification shall be based on the complexity and reliability of the system and the level of risk associated with the safe operation of the system.

(3) A manufacturer shall ensure that each system is validated prior to the release for distribution of any infant formula manufactured using the system.

(4) A manufacturer shall ensure that any system that is modified is revalidated following the modification and prior to the release for distribution of any infant formula manufactured using the modified system. All modifications to software shall be made by a designated individual and shall be checked by the infant formula manufacturer to ensure that infant formula that is produced or analyzed using the modified software complies with this subpart and with subpart C of this part.

(c) A manufacturer shall make and retain records, in accordance with § 106.100(f)(5), concerning mechanical or electronic equipment.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33071, June 10, 2014]

§ 106.40 Controls to prevent adulteration caused by ingredients, containers, and closures.

(a) The only substances that may be used in an infant formula are substances that are safe and suitable for use in infant formula under the applicable food safety provisions of the Federal Food, Drug, and Cosmetic Act; that is, a substance is used in accordance with the Agency's food additive regulations, is generally recognized as safe (GRAS) for such use, or is authorized by a prior sanction.

(b) Infant formula containers and closures shall not be reactive or absorptive so as to affect the safety of the infant formula. The following substances may be used as packaging material that comes in contact with an infant formula:

(1) A food additive that is the subject of a regulation issued under section 409(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 348(c)) and is used consistent with the conditions of use of that regulation;

(2) A food contact substance that is the subject of an effective notification under section 409(h) of the Federal Food, Drug, and Cosmetic Act and is used consistent with the conditions of use in that notification;

(3) A substance that is exempt from regulation as a food additive under § 170.39 of this chapter and its use conforms to the use identified in the exemption letter;

(4) A substance that is generally recognized as safe for use in or on infant formula or for use in infant formula packaging;

(5) A substance the use of which is authorized by a prior sanction from the Food and Drug Administration or from the U.S. Department of Agriculture; and

(6) A substance that is not a food additive within the meaning of section 201(s) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(s)) because the substance is not reasonably expected to become a component of food or otherwise affect the characteristics of food.

(c) Ingredients, containers, and closures used in the manufacture of infant formula shall be identified with a lot number to be used in recording their disposition.

(d) A manufacturer shall develop written specifications for ingredients, containers, and closures used in manufacturing infant formula and shall develop and follow written procedures to determine whether all ingredients, containers, and closures meet these specifications. When any specification is not met, an individual qualified by education, training, or experience shall

conduct a documented review, shall determine whether a failure to meet such a specification could result in an adulterated infant formula, and shall make and document a material disposition decision to reject the ingredient, container, or closure or the affected infant formula; to reprocess or otherwise recondition the ingredient, container, or closure or the affected infant formula; or to approve and release the ingredient, container, or closure or the affected infant formula for use.

(e) Ingredients, containers, and closures shall be stored in separate areas or separated by a system of segregation, such as a computerized inventory control, a written card system, or an automated system of segregation, clearly designated for materials pending release for use; materials released for use; or materials rejected for use in infant formula production.

(1) Any lot of an ingredient, a container, or a closure that does not meet the manufacturer's specifications shall be quarantined under a system designed to prevent its use in the manufacture of infant formula until an individual qualified by education, training, or experience has conducted a documented review, has determined whether such failure could result in an adulterated infant formula, and has made and documented a material disposition decision to reject the ingredient, container, closure, or the affected infant formula; to reprocess or otherwise recondition the ingredient, container, closure, or the affected infant formula; or to approve and release the ingredient, container, closure, or the affected infant formula for use.

(2) Any ingredient, container, or closure that has been reprocessed or otherwise reconditioned shall be the subject of a documented review and material disposition decision by an individual qualified by education, training, or experience to determine whether it may be released for use.

(3) A manufacturer shall not reprocess or otherwise recondition an ingredient, container, or closure rejected because it is contaminated with microorganisms of public health significance or other contaminants, such as heavy metals.

(f) If an ingredient, container, or closure that complies with a manufacturer's specifications, or that has been released for use following a material review and disposition decision, is subsequently exposed to air, heat, or other conditions that may adversely affect it, or if a manufacturer reasonably believes that an ingredient, container, or closure that complies with a manufacturer's specifications, or that has been released for use following a material review and disposition decision, has been exposed to air, heat, or other conditions that may adversely affect it, the ingredient, container, or closure shall be quarantined under a system designed to prevent its use in the manufacture of infant formula until an individual qualified by education, training, or experience has conducted a documented review and has made and documented a material disposition decision to reject the ingredient, container, or closure; to reprocess or otherwise recondition the ingredient, container, or closure; or to approve and release the ingredient, container, or closure for use.

(1) Any ingredient, container, or closure that is reprocessed or otherwise reconditioned shall be retested or reexamined and be the subject of a documented review and material disposition decision by an individual qualified by education, training, or experience to determine whether the ingredient, container, or closure should be rejected, further reprocessed or otherwise further reconditioned, or approved and released for use.

(2) Any rejected ingredient, container, or closure shall be clearly identified as having been rejected for use in infant formula manufacturing or processing operations and shall be controlled under a quarantine system designed to prevent its use in infant formula manufacturing or processing operations.

(3) Any ingredient, container, or closure that has not been manufactured, packaged, labeled, or held under conditions to prevent adulteration under section 402(a)(1) through (a)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 342(a)(1) through (a)(4)) shall not be approved and released for use.

(g) A manufacturer shall make and retain records, in accordance with §106.100(f)(6), on the ingredients, containers, and closures used in the manufacture of infant formula.

§ 106.50 Controls to prevent adulteration during manufacturing.

(a) A manufacturer shall prepare and follow a written master manufacturing order that establishes controls and procedures for the production of an infant formula.

(1) The manufacturer shall make and retain records, in accordance with §106.100(e), that include complete information relating to the production and control of the production aggregate. An individual qualified by education, training, or experience shall conduct an investigation of any deviations from the master manufacturing order and document any corrective action taken.

(2) Changes made to the master manufacturing order shall be reviewed and approved by a responsible official and include an evaluation of the effect of the change on the nutrient content and the suitability of the formula for infants.

(b) A manufacturer shall establish controls to ensure that each raw or in-process ingredient required by the master manufacturing order is examined by one person and checked by a second person or system. This checking shall ensure that the correct ingredient is added during the manufacturing process, that the ingredient has been released for use in infant formula, and that the correct weight or measure of the ingredient is added to the production unit.

(c) A manufacturer shall establish a system of identification for the contents of all compounding and storage containers, processing lines, and major equipment used during the manufacture of a production aggregate of an infant formula. The system shall permit the identification of the processing stage and the unique identification number for the particular production unit or production aggregate of infant formula.

(d) A manufacturer shall establish controls to ensure that the nutrient levels required by §107.100 of this chapter are maintained in the formula, and that the formula is not contaminated with microorganisms or other contaminants. Such controls shall include:

(1) The mixing time; the speed, temperature, and flow rate of product; and other critical parameters necessary to ensure the addition of required ingredients to, and the homogeneity of, the formula;

(2) The spray-drying process for powdered infant formula, including the filtering of the intake air before heating, to prevent microbial and other contamination;

(3) The removal of air from the finished product to ensure that nutrient deterioration does not occur;

(4) Ensuring that each container of finished product is properly sealed. Such controls shall involve use of established procedures, specifications, and intervals of examination that are designed by qualified individuals and are sufficient to:

(i) Detect visible closure or seal defects, and

(ii) Determine closure strength through destructive testing. A manufacturer of a liquid infant formula that is a thermally processed low-acid food packaged in a hermetically sealed container shall perform such closure integrity testing in accordance with §113.60(a) of this chapter.

(e) A manufacturer shall establish controls that ensure that the equipment used at points where control is deemed necessary to prevent adulteration is monitored, so that personnel will be alerted to malfunctions.

(f) A manufacturer shall establish controls for in-process material as follows:

(1) For any specification established in accordance with §106.6(c)(1) that a manufacturer fails to meet for in-process material, an individual qualified by education, training, or experience shall conduct a documented review and shall make a material disposition decision to reject the affected in-process material, to reprocess or otherwise recondition the affected in-process material, or to approve and release the affected in-process material for use or distribution;

(2) Pending a documented review and material disposition decision, any in-process material that fails to meet any

specification established in accordance with §106.6(c)(1) shall be clearly identified as such and shall be controlled under a quarantine system designed to prevent its use in manufacturing or processing operations until completion of the documented review and material disposition decision;

(3) Any in-process material that has been reprocessed or otherwise reconditioned shall be the subject of a documented review and material disposition decision by an individual qualified by education, training, or experience to determine whether it may be released for use; and

(4) Any rejected in-process material shall be clearly identified as having been rejected for use in infant formula and shall be controlled under a quarantine system designed to prevent its use in infant formula manufacturing or processing operations.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33071, June 10, 2014]

§ 106.55 Controls to prevent adulteration from microorganisms.

(a) A manufacturer of infant formula shall establish a system of process controls covering all stages of processing that is designed to ensure that infant formula does not become adulterated due to the presence of microorganisms in the formula or in the processing environment.

(b) A manufacturer of liquid infant formula shall comply, as appropriate, with the procedures specified in part 113 of this chapter for thermally processed low-acid foods packaged in hermetically sealed containers and part 114 of this chapter for acidified foods.

(c) A manufacturer of powdered infant formula shall test representative samples of each production aggregate of powdered infant formula at the final product stage, before distribution, to ensure that each production aggregate meets the microbiological quality standards in the table in paragraph (e) of this section.

(d) A manufacturer shall make and retain records, in accordance with §106.100(e)(5)(ii) and (f)(7), on the testing of infant formulas for microorganisms.

(e) A powdered infant formula that contains any microorganism that exceeds the M value listed for that microorganism in the table in paragraph (e) of this section shall be deemed adulterated under sections 402(a)(1), 402(a)(4), and 412(a)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(a)(3)). The Food and Drug Administration will determine compliance with the M values listed below using the latest edition of the *Bacteriological Analytical Manual* (BAM) (*http://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/BacteriologicalAnalyticalManualBAM/default.htm*) (accessed April 8, 2013).

Microorganism	n[1]	Sample size	M value
Cronobacter spp.	30	10 g (grams)	[2]0.
Salmonella spp.	60	25 g	[2]0.

[1] Number of samples.
[2] None detected.

§ 106.60 Controls to prevent adulteration during packaging and labeling of infant formula.

(a) A manufacturer shall examine packaged and labeled infant formula during finishing operations to ensure that all containers and packages in the production aggregate have the correct label, the correct use-by date, and the correct code established under §106.80.

(b) Labels shall be designed, printed, and applied so that the labels remain legible and attached during the conditions of processing, storage, handling, distribution, and use.

(c) Packaging used to hold multiple containers of an infant formula product shall be labeled as follows:

(1) Where all containers are the same infant formula product and all bear the same code established under §106.80, the packaging label shall include the product name, the name of the manufacturer, distributor, or shipper, and the code established under §106.80.

(2) Where the containers are not the same infant formula product or do not

all bear the same code established under §106.80, the packaging label shall:

(i) Include the product name of each product, the name of the manufacturer, distributor, or shipper of each product, the code established under §106.80 for each product, and a ''use by'' date that is no later than the ''use by'' date of the container exhibiting the closest ''use by'' date applied to satisfy the requirement of §107.20(c) of this chapter; or

(ii) Include a unique identification number assigned by the packager, provided that the distributor of the package maintains a record linked to such unique number that identifies the product name of each product, the name of the manufacturer, distributor, or shipper of each product, the code established under §106.80 for each product, and the ''use by'' date for each product applied to satisfy the requirement of §107.20(c) of this chapter.

§106.70 Controls on the release of finished infant formula.

(a) A manufacturer shall control under a quarantine system designed to prevent use or distribution of each production aggregate of infant formula until it determines that the production aggregate meets all of the manufacturer's specifications, including those adopted to meet the standards of §106.55 on microbiological contamination and of §106.91(a) on quality control procedures, or until the documented review of the failure to meet any of the manufacturer's specifications finds that the failure does not result in, or could not lead to, adulteration of the product.

(b) Any production aggregate of infant formula that fails to meet any of the manufacturer's specifications shall be quarantined under a system designed to prevent its use in the manufacture of infant formula or its distribution until an individual qualified by education, training, or experience has conducted a documented review and has made and documented a material disposition decision to reject the infant formula; to reprocess or otherwise recondition the infant formula; or to approve and release the infant formula. Any production aggregate of infant formula that is reprocessed or otherwise reconditioned shall be the subject of a documented review and material disposition decision by an individual qualified by education, training, or experience to determine whether it may be released for use or distribution.

(c) Any rejected infant formula shall be clearly identified as having been rejected for use and shall be controlled under a quarantine system designed to prevent its release or distribution.

(d) A production aggregate of infant formula, including a reprocessed or reconditioned production aggregate, that does not meet the nutrient requirements of section 412(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(i)) or that has not been manufactured, packaged, labeled, and held under conditions to prevent adulteration under sections 402(a)(1) through (a)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 342(a)(1) through (a)(4)) shall not be approved and released for distribution.

§106.80 Traceability.

Each production aggregate of infant formula shall be coded with a sequential number that identifies the product and the establishment where the product was packed and that permits tracing of all stages of manufacture of that production aggregate, including the year, the days of the year, and the period during those days that the product was packed, and the receipt and handling of raw materials used.

§106.90 Audits of current good manufacturing practice.

(a) A manufacturer of an infant formula, or an agent of such manufacturer, shall conduct regularly scheduled audits to determine whether the manufacturer has complied with the current good manufacturing practice regulations in this subpart. Such audits shall be conducted at a frequency that is required to ensure compliance with such regulations.

(b) The audits required by paragraph (a) of this section shall be performed by an individual or a team of individuals who, as a result of education, training, or experience, is knowledgeable in all aspects of infant formula production

and of the Agency's regulations concerning current good manufacturing practice that such individual or team is responsible for auditing. This individual or team of individuals shall have no direct responsibility for the matters that such individual or team is auditing and shall have no direct interest in the outcome of the audit.

Subpart C—Quality Control Procedures

§ 106.91 General quality control.

(a) During manufacture, a manufacturer shall test each production aggregate for nutrients as follows:

(1) Each nutrient premix used in the manufacture of an infant formula shall be tested for each nutrient (required under §107.100 of this chapter or otherwise added by the manufacturer) that the manufacturer is relying on the premix to provide, to ensure that the premix is in compliance with the manufacturer's specifications;

(2) During the manufacturing process, after the addition of the premix, or at the final product stage but before distribution, each production aggregate of infant formula shall be tested for at least one indicator nutrient for each of the nutrient premixes used in the infant formula to confirm that the nutrients supplied by each of the premixes are present, in the proper concentration, in the production aggregate of infant formula.

(3) At the final product stage, before distribution of an infant formula, each production aggregate shall be tested for vitamins A, C, E, and thiamin.

(4) During the manufacturing process or at the final product stage, before distribution, each production aggregate shall be tested for all nutrients required to be included in such formula under §107.100 of this chapter for which testing is not conducted for compliance with paragraphs (a)(1) or (a)(3) of this section and for any nutrient added by the manufacturer for which testing is not conducted for compliance with paragraph (a)(1) of this section.

(b) A manufacturer shall test each production aggregate of finished product for nutrients as follows:

(1)(i) For an infant formula that is a new infant formula the manufacturer shall collect, from each manufacturing site and at the final product stage, a representative sample of the first production aggregate of packaged, finished formula in each physical form (powder, ready-to-feed, or concentrate) and evaluate the levels of all nutrients required under §107.100 of this chapter and all other nutrients added by the manufacturer. The manufacturer shall repeat such testing every 4 months thereafter throughout the shelf life of the product.

(ii) The Food and Drug Administration will exempt the manufacturer from the requirements of paragraph (b)(1)(i) of this section if the manufacturer of a new infant formula requests an exemption and provides analytical data, as required under §106.120(b)(7), that demonstrates that the stability of the new infant formula will likely not differ from the stability of formulas with similar composition, processing, and packaging for which there are extensive stability data. A manufacturer exempt from the requirements of paragraph (b)(1)(i) of this section would be required to test the first production aggregate according to the requirements of §106.91(b)(2).

(2) The manufacturer shall collect, from each manufacturing site and at the final product stage, a representative sample of each subsequent production aggregate of packaged, finished formula in each physical form (powder, ready-to-feed, or concentrate) and evaluate the levels of all nutrients required under §107.100 of this chapter and all other nutrients added by the manufacturer. The manufacturer shall repeat such testing at the end of the shelf life of the product.

(3) If the results of the testing required by paragraph (b)(1) of this section do not substantiate the shelf life of the infant formula, the manufacturer shall address, as appropriate, all production aggregates of formula released and pending release for distribution that are implicated by the testing results, such as by conducting the testing required by paragraph (b)(1) of this section on a subsequently produced production aggregate to substantiate the shelf life of the infant formula or

revising the use by date for such product so that such date is substantiated by the stability testing results.

(4) If results of the testing required by paragraph (b)(2) of this section show that any required nutrient is not present in the production aggregate of infant formula at the level required by § 107.100 of this chapter or that any nutrient added by the manufacturer is not present at the level declared on the label of the production aggregate of infant formula, the manufacturer shall:

(i) Investigate the cause of such variance in the level of any required or added nutrient;

(ii) Evaluate the significance, if any, of the results for other production aggregates of the same formula that have been released for distribution;

(iii) Address, as appropriate, all production aggregates of formula released and pending release for distribution that are implicated by the testing results; and

(iv) Determine whether it is necessary to conduct the testing required by paragraph (b)(1) of this section.

(5) The testing required by paragraphs (b)(1) and (b)(2) of this section is not required to evaluate the level of minerals present in the infant formula.

(c) All quality control testing shall be conducted using appropriate, scientifically valid test methods.

(d) A manufacturer shall make and retain quality control records in accordance with § 106.100(e)(5)(i).

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33071, June 10, 2014]

§ 106.92 Audits of quality control procedures.

(a) A manufacturer of an infant formula, or an agent of such a manufacturer, shall conduct regularly scheduled audits to determine whether the manufacturer has complied with the requirements for quality control procedures that are necessary to ensure that an infant formula provides nutrients in accordance with section 412(b) and (i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(b) and (i)) and is manufactured in a manner designed to prevent adulteration of the infant formula under section 412(a)(1) and (a)(3) of the Federal Food, Drug, and Cosmetic Act. Such audits shall be conducted at a frequency that is required to ensure compliance with the requirements for quality control procedures.

(b) The audits required by paragraph (a) of this section shall be performed by an individual or a team of individuals who, as a result of education, training, or experience, is knowledgeable in all aspects of infant formula production and of the regulations concerning quality control procedures that such individual or team is responsible for auditing. This individual or team of individuals shall have no direct responsibility for the matters that such individual or team is auditing and shall have no direct interest in the outcome of the audit.

Subpart D—Conduct of Audits

§ 106.94 Audit plans and procedures.

(a) A manufacturer shall develop and follow a written audit plan that is available at the manufacturing facility for Food and Drug Administration inspection.

(b) The audit plan shall include audit procedures that set out the methods the manufacturer uses to determine whether the facility is operating in accordance with current good manufacturing practice, with the quality control procedures that are necessary to ensure that an infant formula provides nutrients in accordance with sections 412(b) and (i) of the Federal Food, Drug, and Cosmetic Act, and in a manner designed to prevent adulteration of the infant formula.

(c) The audit procedures shall include:

(1) An evaluation of the production and in-process control system established under § 106.6(b) by:

(i) Observing the production of infant formula and comparing the observed process to the written production and in-process control plan required under § 106.6(b);

(ii) Reviewing records of the monitoring of points, steps, or stages where control is deemed necessary to prevent adulteration; and

(iii) Reviewing records of how deviations from any specification at points, steps, or stages where control is deemed necessary to prevent adulteration were handled; and

(2) A review of a representative sample of all records maintained in accordance with §106.100(e) and (f).

Subpart E—Quality Factors for Infant Formulas

§106.96 Requirements for quality factors for infant formulas.

The regulations set forth in this subpart define the minimum requirements for quality factors for infant formulas:

(a) An infant formula shall meet the quality factor of normal physical growth.

(b) A manufacturer of an infant formula that is not an eligible infant formula shall demonstrate that a formula supports normal physical growth in infants when fed as a sole source of nutrition by conducting, in accordance with good clinical practice, an adequate and well-controlled growth monitoring study of the infant formula that:

(1) Is no less than 15 weeks in duration, enrolling infants no more than 2 weeks old at time of entry into the study;

(2) Includes the collection and maintenance of data on formula intake and anthropometric measures of physical growth, including body weight, recumbent length, head circumference, average daily weight increment, and average daily recumbent length increment;

(3) Includes anthropometric measurements made at the beginning and end of the study, and at least four additional measurements made at intermediate time points with three of the six total measurements made within the first 4 weeks of the study and three measurements made at approximately 4-week intervals over the remaining 11 weeks of the study;

(4) Compares the anthropometric data for the test group to a concurrent control group or groups at each time point and compares the anthropometric data for each infant (body weight for age, body length for age, head circumference for age, and weight for length) in the test group and the control group to the 2009 CDC growth charts, which are incorporated by reference at §106.160; and

(5) Compares the data on formula intake of the test group with a concurrent control group or groups and a scientifically appropriate reference.

(c) The Food and Drug Administration will exempt a manufacturer from the requirements of paragraph (b) of this section, if:

(1) The manufacturer requests an exemption and provides assurances, as required under §106.121(b), that the changes made by the manufacturer to an existing infant formula are limited to changing the type of packaging of an existing infant formula (e.g., changing from metal cans to plastic pouches); or

(2) The manufacturer requests an exemption and provides assurances, as required under §106.121, which demonstrate that:

(i) An alternative method or study design that is based on sound scientific principles is available to show that the formula supports normal physical growth in infants when the formula is fed as the sole source of nutrition;

(ii) The change made by the manufacturer to an existing formula does not affect the ability of the formula to support normal physical growth; or

(iii) The manufacturer markets a formulation in more than one form (e.g., liquid and powdered forms) and the quality factor requirements are met by the form of the formula that is processed using the method that has the greatest potential for adversely affecting nutrient content and bioavailability.

(d) A manufacturer of a new infant formula that is not an eligible infant formula shall, in accordance with §106.100(p)(1), make and retain records demonstrating that the formula meets the quality factor of normal physical growth.

(e) An infant formula shall meet the quality factor of sufficient biological quality of protein.

(f) A manufacturer of an infant formula that is not an eligible infant formula shall demonstrate that a formula meets the quality factor of sufficient biological quality of protein by establishing the biological quality of the protein in the infant formula when fed as the sole source of nutrition using an

appropriate modification of the Protein Efficiency Ratio (PER) rat bioassay described in the ''Official Methods of Analysis of AOAC International,'' 18th ed., sections 45.3.04 and 45.3.05, ''AOAC Official Method 960.48 Protein Efficiency Ratio Rat Bioassay,'' which is incorporated by reference at §106.160. The PER rat bioassay shall be conducted on a formula and the results evaluated prior to the initiation of a growth monitoring study of the formula that is required under paragraph (b) of this section.

(g) The Food and Drug Administration will exempt a manufacturer from the requirements of paragraph (f) of this section, if:

(1) The manufacturer requests an exemption and provides assurances as required under §106.121(g) that the changes made by the manufacturer to an existing infant formula are limited to changing the type of packaging of an existing infant formula (e.g., changing from metal cans to plastic pouches); or

(2) The manufacturer requests an exemption and provides assurances, as required under §106.121(h), that demonstrate that the change made by the manufacturer to an existing formula does not affect the bioavailability of the protein.

(3) The manufacturer requests an exemption and provides assurances, as required under §106.121(i), that demonstrate that an alternative method to the PER that is based on sound scientific principles is available to demonstrate that the formula supports the quality factor for the biological quality of the protein.

(h) A manufacturer of a new infant formula that is not an eligible infant formula shall, in accordance with §106.100(q), make and retain records demonstrating that the formula meets the quality factor of sufficient biological quality of protein.

(i) The following provisions for requirements for quality factors apply only to an ''eligible infant formula'' as defined in §106.3:

(1) An eligible infant formula that fulfills one or more of the following criteria meets the quality factor of normal physical growth:

(i) The scientific evidence on such infant formula meets the requirements of paragraph (b) of this section that apply to infant formula that is not an eligible infant formula;

(ii) The scientific evidence on such infant formula meets the following provisions:

(A) The evidence is an adequate and well-controlled growth study, conducted in accordance with good clinical practice, to determine whether an infant formula supports normal physical growth in infants when the formula is fed as the sole source of nutrition;

(B) The growth study is no less than 4 months in duration, enrolling infants no more than 1 month old at time of entry into the study;

(C) The growth study collects from the study subjects data on anthropometric measures of physical growth, including body weight, recumbent length, head circumference, and average daily weight increment, and plots the data on the following charts from ''Physical Growth: National Center for Health Statistics Percentiles'' for body weight, body length, and head circumference, which are incorporated by reference at §106.160:

(*1*) *Figure 1*. Length by age percentiles for girls aged birth–36 months (p. 609);

(*2*) *Figure 2*. Length by age percentiles for boys aged birth–36 months (p. 610);

(*3*) *Figure 3*. Weight by age percentiles for girls aged birth–36 months (p. 611);

(*4*) *Figure 4*. Weight by age percentiles for boys aged birth–36 months (p. 612);

(*5*) *Figure 5*. Head circumference by age percentiles for girls aged birth–36 months (p. 613);

(*6*) *Figure 6*. Weight by length percentiles for girls aged birth–36 months (p. 613);

(*7*) *Figure 7*. Head circumference by age percentiles for boys aged birth–36 months (p. 614); and

(*8*) *Figure 8*. Weight by length percentiles for boys aged birth–36 months (p. 614); and

(D) The growth study collects anthropometric measurements at the beginning of the growth study, at 2 weeks, at 4 weeks, at least monthly thereafter, and at the conclusion of the study; or

(iii) The scientific evidence on such infant formula otherwise demonstrates that such formula supports normal physical growth.

(2) An eligible infant formula that fulfills one or more of the following criteria meets the quality factor of sufficient biological quality of the protein:

(i) The scientific evidence on such infant formula meets the requirements of paragraph (f) of this section that apply to infant formula that is not an eligible infant formula;

(ii) The scientific evidence on such infant formula is a study that establishes the biological quality of the protein in an infant formula by demonstrating that the protein source supports adequate growth using the Protein Efficiency Ratio (PER) rat bioassay described in sections 45.3.04 and 45.3.05 of the ''Official Methods of Analysis of the Association of Official Analytical Chemists,'' 16th ed., which are incorporated by reference at §106.160; or

(iii) The scientific evidence on such infant formula otherwise demonstrates that the protein in such infant formula is of sufficient biological quality.

(3) The manufacturer of an eligible infant formula may, not later than November 12, 2015, submit a petition to the Food and Drug Administration under §10.30 of this chapter that:

(i) Demonstrates that such formula fulfills one or more of the criteria in paragraph (i)(1) of this section; or

(ii) Demonstrates that such formula fulfills one or more of the criteria in paragraph (i)(2) of this section.

(4) A petition filed under paragraph (i)(3) of this section shall address only one infant formula formulation and shall contain all data and information relied upon by the manufacturer to demonstrate that such formulation fulfills one or more of the criteria in paragraph (i)(1) or in paragraph (i)(2) of this section. A manufacturer may combine petitions submitted under paragraphs (i)(3)(i) and (i)(3)(ii) of this section that relate to the same formulation.

(5) The manufacturer of each eligible infant formula shall make and retain, in accordance with §106.100(p)(2), records to demonstrate that such formula supports normal physical growth in infants when fed as the sole source of nutrition and shall make and retain, in accordance with §106.100(q)(2), records to demonstrate that that the protein in such infant formula is of sufficient biological quality. The records required by this paragraph shall include all relevant scientific data and information and a narrative explanation of why the data and information demonstrate that the formula supports normal physical growth and a narrative explanation of why the data and information demonstrate that the protein in such infant formula is of sufficient biological quality.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33071, June 10, 2014]

Subpart F—Records and Reports

§106.100 Records.

(a) Every manufacturer of infant formula shall maintain the records specified in this regulation in order to permit the Food and Drug Administration to determine whether each manufacturer is in compliance with section 412 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a)).

(b) The manufacturer shall maintain all records that pertain to food-packaging materials subject to §174.5 of this chapter and that bear on whether such materials would cause an infant formula to be adulterated within the meaning of section 402(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 342(a)(2)(C)).

(c) The manufacturer shall maintain all records that pertain to nutrient premix testing that it generates or receives. Such records shall include, but are not limited to:

(1) Any results of testing conducted to ensure that each nutrient premix is in compliance with the premix certificate and guarantee and specifications that have been provided to the manufacturer by the premix supplier, including tests conducted when nutrients exceed their expiration date or shelf life (retest date).

(2) All certificates and guarantees given by premix suppliers concerning the nutrients required by section 412(i) of the Federal Food, Drug, and Cosmetic Act and §107.100 of this chapter.

(d) The premix supplier shall maintain the results of all testing conducted to provide all certificates and guarantees concerning nutrient premixes for infant formulas. Such records shall include but are not limited to:

(1) The results of tests conducted to determine the purity of each nutrient required by section 412(i) of the Federal Food, Drug, and Cosmetic Act or §107.100 of this chapter and any other nutrient listed in the certificate and guarantee;

(2) The weight of each nutrient added;

(3) The results of any quantitative tests conducted to determine the amount of each nutrient certified or guaranteed; and

(4) The results of any quantitative tests conducted to identify the nutrient levels present when nutrient premixes exceed their expiration date or shelf life (retest date).

(e) For each production aggregate of infant formula, a manufacturer shall prepare and maintain records that include complete information relating to the production and control of the production aggregate. These records shall include:

(1) The master manufacturing order. The master manufacturing order shall include:

(i) The significant steps in the production of the production aggregate and the date on which each significant step occurred;

(ii) For a manufacturing facility that has more than one set of equipment or more than one processing line, the identity of equipment and processing lines for which the manufacturer has identified points, steps, or stages in the production process where control is necessary to prevent adulteration;

(iii) The identity of each lot of ingredients, containers, and closures used in producing the production aggregate of formula;

(iv) The amount of each ingredient to be added to the production aggregate of infant formula and a check (verification) that the correct amount was added; and

(v) A copy of each infant formula label used on a finished production aggregate of infant formula and the results of examinations conducted during the finishing operations to provide assurance that the containers and packages have the correct label.

(2) Any deviations from the master manufacturing order and any corrective actions taken because of the deviations.

(3) Documentation, in accordance with §106.6(c), of the monitoring at any point, step, or stage in the manufacturer 's production process where control is deemed necessary to prevent adulteration. These records shall include:

(i) A list of the specifications established at each point, step, or stage in the production process where control is deemed necessary to prevent adulteration, in accordance with §106.6(c)(1), including documentation of the scientific basis for each specification;

(ii) The actual values obtained during the monitoring operation, any deviations from established specifications, and any corrective actions taken; and

(iii) Identification of the person monitoring each point, step, or stage in the production process where control is deemed necessary to prevent adulteration.

(4) The conclusions and followup, along with the identity of the individual qualified by education, training, or experience who investigated:

(i) Any deviation from the master manufacturing order and any corrective actions taken;

(ii) A finding that a production aggregate or any of its ingredients failed to meet the infant formula manufacturer's specifications; and

(iii) A failure to meet any specification at any point, step, or stage in the production process where control is deemed necessary to prevent adulteration.

(5) The results of all testing performed on the production aggregate of infant formula, including testing on the in-process production aggregate, at the final product stage, and on finished product throughout the shelf life of the product. The results recorded shall include:

(i) The results of all quality control testing conducted in accordance with §106.91(a) and (b) to verify that each nutrient required by §107.100 of this chapter is present in each production

aggregate of infant formula at the level required by §107.100 of this chapter, and that all other nutrients added by the manufacturer are present at the appropriate level. The record of the results of the quality control testing shall include:

(A) A summary document identifying the stages of the manufacturing process at which the nutrient analysis for each required nutrient is conducted as required under §106.91(a); and

(B) A summary document on the stability testing program conducted under §106.91(b), including the nutrients tested and the frequency of nutrient testing throughout the shelf life of the product.

(ii) For powdered infant formula, the results of any testing conducted in accordance with §106.55(c) to verify compliance with the microbiological quality standards in §106.55(e).

(f) A manufacturer shall make and retain all records described in subparts B and C of this part, including:

(1) Records, in accordance with §106.20(f)(4), of the frequency and results of testing of the water used in the production of infant formula;

(2) Records, in accordance with §106.30(d), of accuracy checks of instruments and controls. A certification of accuracy of any known reference standard used and a history of recertification shall be maintained. At a minimum, such records shall specify the instrument or control being checked, the date of the accuracy check, the standard used, the calibration method used, the results found, any actions taken if the instrument is found to be out of calibration, and the initials or name of the individual performing the test. If calibration of an instrument shows that a specification at a point, step, or stage in the production process where control is deemed necessary to prevent adulteration has not been met, a written evaluation of all affected product, and any actions that need to be taken with respect to that product, shall be made.

(3) Records, in accordance with §106.30(e)(3)(iii).

(4) Records, in accordance with §106.30(f), on equipment cleaning, sanitizing, and maintenance that show the date and time of such cleaning, sanitizing, and maintenance and the production aggregate number of each infant formula processed between equipment startup and shutdown for cleaning, sanitizing, and maintenance. The person performing and checking the cleaning, sanitizing, and maintenance shall date and sign or initial the record indicating that the work was performed.

(5) Records, in accordance with §106.35(c), on all mechanical and electronic equipment used in the production or quality control of infant formula. These records shall include:

(i) A list of all systems used with a description of the computer files and the defined capabilities and inherent limitations of each system;

(ii) A copy of all software used;

(iii) Records that document installation, calibration, testing or validation, and maintenance of the systems used;

(iv) A list of all persons authorized to create or modify software;

(v) Records that document modifications to software, including the identity of the person who modified the software;

(vi) Records that document retesting or revalidation of modified systems; and

(vii) A backup file of data entered into a computer or related system. The backup file shall consist of a hard copy or alternative system, such as duplicate electronic records, tapes, or microfilm, designed to ensure that backup data are exact and complete, and that they are secure from alteration, inadvertent erasures, or loss.

(6) Records, in accordance with §106.40(g), on ingredients, containers, and closures used in the manufacture of infant formula. These records shall include:

(i) The identity and quantity of each lot of ingredients, containers, and closures;

(ii) The name of the supplier;

(iii) The supplier's lot numbers;

(iv) The name and location of the manufacturer of the ingredient, container, or closure, if different from the supplier;

(v) The date of receipt;

(vi) The receiving code as specified; and

(vii) The results of any test or examination (including retesting and reexamination) performed on the ingredients, containers, or closures and the conclusions derived there from and the disposition of all ingredients, containers, or closures.

(7) A full description of the methodology used to test powdered infant formula to verify compliance with the microbiological quality standards of § 106.55(c) and the methodology used to do quality control testing, in accordance with § 106.91(a).

(g) A manufacturer shall maintain all records pertaining to distribution of the infant formula, including records that show that formula produced for export only is exported. Such records shall include all information and data necessary to effect and monitor recalls of the manufacturer's infant formula products in accordance with subpart E of part 107 of this chapter.

(h) The manufacturer shall maintain all records pertaining to the microbiological quality and purity of raw materials and finished powdered infant formula.

(i) [Reserved]

(j) The manufacturer shall make and retain records pertaining to regularly scheduled audits, including the audit plans and procedures, the findings of the audit, and a listing of any changes made in response to these findings. The manufacturer shall make readily available for authorized inspection the audit plans and procedures and a statement of assurance that the regularly scheduled audits are being conducted. The findings of the audit and any changes made in response to these findings shall be maintained for the time period required under paragraph (n) of this section, but need not be made available to the Food and Drug Administration.

(k) The manufacturer shall maintain procedures describing how all written and oral complaints regarding infant formula will be handled. The manufacturer shall follow these procedures and shall include in them provisions for the review of any complaint involving an infant formula and for determining the need for an investigation of the possible existence of a hazard to health.

(1) For purposes of this section, every manufacturer shall interpret a ''complaint'' as any communication that contains any allegation, written or oral, expressing dissatisfaction with a product for any reason, including concerns about the possible existence of a hazard to health and about appearance, taste, odor, and quality. Correspondence about prices, package size or shape, or other matters that could not possibly reveal the existence of a hazard to health shall not, for compliance purposes, be considered a complaint and therefore need not be made available to a Food and Drug Administration investigator.

(2) When a complaint shows that a hazard to health possibly exists, the manufacturer shall conduct an investigation into the validity of the complaint. Where such an investigation is conducted, the manufacturer shall include in its file on the complaint the determination as to whether a hazard to health exists and the basis for that determination. No investigation is necessary when the manufacturer determines that there is no possibility of a hazard to health. When no investigation is necessary, the manufacturer shall include in the record the reason that an investigation was found to be unnecessary and the name of the responsible person making that determination.

(3) When there is a reasonable possibility of a causal relationship between the consumption of an infant formula and an infant's death, the manufacturer shall, within 15 days of receiving such information, conduct an investigation and notify the Agency as required in § 106.150.

(4) The manufacturer shall maintain in designated files all records pertaining to the complaints it receives. The manufacturer shall separate the files into two classes:

(i) Those complaints that allege that the infant became ill from consuming the product or required treatment by a physician or health care provider and

(ii) Those complaints that may involve a possible existence of a hazard to health but do not refer to an infant becoming ill or the need for treatment by physician or a health care provider.

(5) The manufacturer shall include in a complaint file the following information concerning the complaint:

(i) The name of the infant formula;

(ii) The production aggregate number;

(iii) The name of complainant;

(iv) A copy of the complaint or a memo of the telephone conversation or meeting and all correspondence with the complainant;

(v) By reference or copy, all the associated manufacturing records and complaint investigation records needed to evaluate the complaint. When copies of such records are not maintained in the complaint file, they must be available within 24 hours when requested by a Food and Drug Administration official.

(vi) All actions taken to followup on the complaint; and

(vii) All findings and evaluations of the complaint.

(6) The manufacturer should maintain the files regarding infant formula complaints at the establishment where the infant formula was manufactured, processed, or packed. When the manufacturer wishes to maintain all consumer complaints for the entire firm at one location other than at the facility where an infant formula was manufactured, processed, or packed, the manufacturer may do so as long as all records required by this section are available within 24 hours of request for inspection at that facility. However, all records of consumer complaints, including summaries, any reports, and any files, maintained at the manufacturing facility or at any other facility shall be made available to investigators for review and copying upon request.

(l) The manufacturer shall make readily available for authorized inspection all records required under this part or copies of such records. Records shall be available at any reasonable time at the establishment where the activities described in such records occurred. (Infant formula complaint files may be maintained at one facility, as provided in paragraph (k)(6) of this section, if all required records are readily available at that facility.) These records or copies thereof shall be subject to photocopying or other means of reproduction as part of such inspection. Records that can be immediately retrieved from another location by electronic means shall be considered as meeting the requirements of this paragraph.

(m) A manufacturer shall maintain all records required under this part in a manner that ensures that both the manufacturer and the Food and Drug Administration can be provided with access to such records within 24 hours. The manufacturer may maintain the records required under this part as original records, as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records, or as electronic records. Where reduction techniques, such as microfilming, are used, suitable reader and photocopying equipment shall be readily available. All electronic records maintained under this part shall comply with part 11 of this chapter.

(n) Production control, product testing, testing results, complaints, and distribution records necessary to verify compliance with parts 106, 107, 109, 110, 113, and 117 of this chapter, or with other appropriate regulations, shall be retained for 1 year after the expiration of the shelf life of the infant formula or 3 years from the date of manufacture, whichever is greater.

(o) The manufacturer shall maintain quality control records that contain sufficient information to permit a public health evaluation of any production aggregate of infant formula.

(p) A manufacturer shall make and retain records that demonstrate that the formula meets the quality factor of normal physical growth.

(1) For an infant formula that is not an eligible infant formula, in accordance with §106.96(d), these records shall include:

(i) Records demonstrating compliance with the requirements in §106.96(b), including records made in compliance with §106.121; or

(ii) Records demonstrating satisfaction of an applicable exemption under §106.96(c), including records made in compliance with §106.121.

(2) For an eligible infant formula, in accordance with §106.96(i)(5), these records shall include records demonstrating that the formula fulfills one or more of the criteria listed in §106.96(i)(1).

(q) A manufacturer shall make and retain records that demonstrate that a formula meets the quality factor of sufficient biological quality of protein.

(1) For an infant formula that is not an eligible infant formula, in accordance with §106.96(h), these records shall include:

(i) Records demonstrating compliance with the requirements in §106.96(f), including records made in compliance with §106.121; or

(ii) Records demonstrating satisfaction of an applicable exemption under §106.96(g), including records made in compliance with §106.121.

(2) For an eligible infant formula, in accordance with §106.96(i)(5), these records shall include records demonstrating that the formula fulfills one or more of the criteria listed in §106.96(i)(2).

(r) The failure to comply with the records requirements in this section applicable to the quality factors shall render the formula adulterated under section 412(a)(2) of the Federal Food, Drug, and Cosmetic Act. The failure to comply with the records requirements in this section applicable to the good manufacturing practices and quality control procedures, including distribution and audit records requirements, with respect to an infant formula shall render the formula adulterated under section 412(a)(3) of the Federal Food, Drug, and Cosmetic Act. A failure to retain or make available records applicable to the quality factor requirements, quality control procedures, or current good manufacturing practices requirements in compliance with paragraph (l), (m), or (n) of this section with respect to a formula shall render the formula adulterated under section 412(a)(2) or (a)(3) of the Federal Food, Drug, and Cosmetic Act, as applicable.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33072, June 10, 2014; 80 FR 56144, Sept. 17, 2015]

Subpart G—Registration, Submission, and Notification Requirements

§ 106.110 New infant formula registration.

(a) Before a new infant formula may be introduced or delivered for introduction into interstate commerce, including a new infant formula for export only, the manufacturer of the formula shall register with the Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Nutrition, Labeling, and Dietary Supplements, Infant Formula and Medical Foods Staff (HFS–850), 5001 Campus Dr., College Park, MD 20740–3835.

(b) The new infant formula registration shall include:

(1) The name of the new infant formula;

(2) The name of the manufacturer;

(3) The street address of the place of business of the manufacturer; and

(4) The name and street address of each establishment at which the manufacturer intends to manufacture such new infant formula.

§ 106.120 New infant formula submission.

(a) At least 90 days before a new infant formula is introduced or delivered for introduction into interstate commerce, a manufacturer shall submit notice of its intent to do so to the Food and Drug Administration at the address given in §106.110(a). An original and two paper copies of such notice of intent shall be submitted, unless the notice is submitted in conformance with part 11 of this chapter, in which case a single copy shall be sufficient.

(b) The new infant formula submission shall include:

(1) The name and description of the physical form (e.g., powder, ready-to feed, or concentrate) of the infant formula;

(2) An explanation of why the formula is a new infant formula;

(3) The quantitative formulation of each form of the infant formula that is the subject of the notice in units per volume or units per weight for liquid formulas, specified either as sold or as fed, and units per dry weight for powdered formulas, and the weight of powder to be reconstituted with a specified volume of water, and, when applicable, a description of any reformulation of the infant formula, including a listing of each new or changed ingredient and a discussion of the effect of such changes on the nutrient levels in the formulation;

(4) A description, when applicable, of any change in processing of the infant formula. Such description shall identify the specific change in processing, including side-by-side, detailed schematic diagrams comparing the new processing to the previous processing and processing times and temperatures;

(5) Assurance that the infant formula will not be marketed unless the formula meets the requirements for quality factors of section 412(b)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(b)(1)) and the nutrient content requirements of section 412(i) of the Federal Food, Drug, and Cosmetic Act.

(i) Assurance that the formula meets the requirements for quality factors, which are set forth in §106.96, shall be provided by a submission that complies with §106.121;

(ii) Assurance that the formula complies with the nutrient content requirements, which are set forth in §107.100 of this chapter, shall be provided by a statement that the formula will not be marketed unless it meets the nutrient requirements of §107.100 of this chapter, as demonstrated by testing required under subpart C of this part; and

(6) Assurance that the processing of the infant formula complies with section 412(b)(2) of the Federal Food, Drug, and Cosmetic Act. Such assurance shall include:

(i) A statement that the formula will be produced in accordance with subparts B and C of this part; and

(ii) The basis on which each ingredient meets the requirements of §106.40(a), e.g. that it is an approved food additive, that it is authorized by a prior sanction, or that it is generally recognized as safe (GRAS) for its intended use. Any claim that an ingredient is GRAS shall be supported by a citation to the Agency's regulations or by an explanation, including a list of published studies and a copy of those publications, for why, based on the published studies, there is general recognition of the safety of the use of the ingredient in infant formula.

(7) If the manufacturer is requesting an exemption under §106.91(b)(1)(ii), the manufacturer shall include the scientific evidence that the manufacturer is relying on to demonstrate that the stability of the new infant formula will likely not differ from the stability of formulas with similar composition, processing, and packaging for which there are extensive stability data.

(c) For a new infant formula for export only, a manufacturer may submit, in lieu of the information required under paragraphs (b)(5) and (b)(6) of this section, a statement certifying that the infant formula meets the specifications of the foreign purchaser, the infant formula does not conflict with the laws of the country to which it is intended for export, the infant formula is labeled on the outside of the shipping package to indicate that it is intended for export only, and the infant formula will not be sold or offered for sale in domestic commerce. Such manufacturer shall also submit a statement certifying that it has adequate controls in place to ensure that such formula is actually exported.

(d) The submission will not constitute notice under section 412 of the Federal Food, Drug, and Cosmetic Act unless it complies fully with paragraph (b) of this section, as applicable, and the information that it contains is set forth in a manner that is readily understandable. The Agency will notify the manufacturer if the notice is not complete because it does not meet the requirements in section 412(c) and (d) of the Federal Food, Drug, and Cosmetic Act.

(e) If a new infant formula submission contains all the information required by paragraph (b) of this section, as applicable, the Food and Drug Administration will acknowledge its receipt and notify the manufacturer of the date of receipt. The date that the Agency receives a new infant formula submission that is complete is the filing date for such submission. The manufacturer shall not market the new infant formula before the date that is 90 days after the filing date. If the information in the submission does not provide the assurances required under section 412(d)(1) of the Federal Food, Drug, and Cosmetic Act and the regulations of this chapter, the Food and Drug Administration will so notify the manufacturer before the expiration of the 90th day.

(f) If the manufacturer provides additional information in support of a new infant formula submission, the Agency will determine whether the additional information is a substantive amendment to the new infant formula submission. If the Agency determines that the new submission is a substantive amendment, the Food and Drug Administration will assign the new infant formula submission a new filing date. The Food and Drug Administration will acknowledge receipt of the additional information and, when applicable, notify the manufacturer of the new filing date, which is the date of receipt by the Food and Drug Administration of the information that constitutes the substantive amendment to the new infant formula submission.

(g) Submissions relating to exempt infant formulas are subject to the provisions of §107.50 of this chapter.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33072, June 10, 2014]

§ 106.121 Quality factor assurances for infant formulas.

To provide assurance that an infant formula meets the requirements for quality factors set forth in §106.96, the manufacturer shall submit the following data and information:

(a) Unless the manufacturer of a new infant formula can claim an exemption under §106.96(c)(1) or (c)(2), the following assurances shall be provided to ensure that the requirements of §106.96(a) and (b) have been met:

(1) An explanation, in narrative form, setting forth how requirements for quality factors in §106.96(b) have been met;

(2) Records that contain the information required by §106.96(b) to be collected during the study for each infant enrolled in the study. The records shall be identified by subject number, age, feeding group, gender, and study day of collection.

(3) Data, which shall include:

(i) Statistical evaluation for all measurements, including group means, group standard deviations, and measures of statistical significance for all measurements for each feeding group at the beginning of the study and at every point where measurements were made throughout the study, and

(ii) Calculations of the statistical power of the study before study initiation and at study completion.

(4) A report on attrition and on all occurrences of adverse events during the study, which shall include:

(i) Identification of the infant by subject number and feeding group and a complete description of the adverse event, including comparisons of the frequency and nature of occurrence in each feeding group and information on the health of the infant during the course of the study, including the occurrence and duration of any illness;

(ii) A clinical assessment by a health care provider of the infant's health during each suspected adverse event; and

(iii) A list of all subjects who did not complete the study, including the subject number and the reason that each subject did not complete the study.

(b) If the manufacturer is requesting an exemption from the growth monitoring study requirements under §106.96(c)(1), the manufacturer shall include a detailed description of the change made by the manufacturer to an existing infant formula and an explanation of why the change made by the manufacturer to an existing infant formula satisfies the criteria of §106.96(c)(1).

(c) If the manufacturer is requesting an exemption under §106.96(c)(2)(i), the manufacturer shall include a detailed description of the alternative method or alternative study design, an explanation of why the method or study design is based on sound scientific principles, and data that demonstrate that the formula supports normal physical growth in infants when the formula is fed as the sole source of nutrition.

(d) If the manufacturer is requesting an exemption under §106.96(c)(2)(ii), the manufacturer shall include a detailed description of the change and an explanation of why the change made by the manufacturer to an existing infant formula does not the affect the ability of the formula to support normal physical growth.

(e) If the manufacturer is requesting an exemption under §106.96(c)(2)(iii), the manufacturer shall include a detailed description of the two formulations and an explanation of why the

quality factor requirement of normal physical growth is met by the form of the formula that is processed using the method that has the greatest potential for adversely affecting nutrient content and bioavailability.

(f) Unless the manufacturer of a new infant formula is requesting an exemption under §106.96(g), the results of the Protein Efficiency Ratio bioassay shall be provided in accordance with §106.96(f).

(g) If the manufacturer is requesting an exemption under §106.96(g)(1), the manufacturer shall include a detailed description of the change made by the manufacturer to an existing infant formula and an explanation of why the change made by the manufacturer to an existing infant formula satisfies the criteria listed in §106.96(g)(1).

(h) If the manufacturer is requesting an exemption under §106.96(g)(2), the manufacturer shall include a detailed description of the change and an explanation of why the change made by the manufacturer to an existing infant formula does not affect the bioavailability of the protein.

(i) If the manufacturer is requesting an exemption under §106.96(g)(3), the manufacturer shall include a detailed explanation of the alternative method, an explanation of why the method is based on sound scientific principles, and the data that demonstrate that the quality factor for the biological quality of the protein has been met.

(j) A statement certifying that the manufacturer has collected and considered all information and data concerning the ability of the infant formula to meet the requirements for quality factors and that the manufacturer is not aware of any information or data that would show that the formula does not meet the requirements for quality factors.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33072, June 10, 2014]

§106.130 Verification submission.

(a) A manufacturer shall, after the first production and before the introduction into interstate commerce of a new infant formula (except for a new infant formula that is for export only for which a submission is received in compliance with §106.120(c)), verify in a written submission to the Food and Drug Administration at the address given in §106.110(a) that the infant formula complies with the requirements of the Federal Food, Drug, and Cosmetic Act and is not adulterated.

(b) The verification submission shall include the following information:

(1) The name of the new infant formula; the filing date for the new infant formula submission, in accordance with §106.120, for the subject formula; and the identification number assigned by the Agency to the new infant formula submission:

(2) A statement that the infant formula to be introduced into interstate commerce is the same as the infant formula that was the subject of the new infant formula notification and for which the manufacturer provided assurances in accordance with the requirements of §106.120;

(3) A summary of test results of the level of each nutrient required by §107.100 of this chapter and any nutrient added by the manufacturer in the formula, presented in units per 100 kilocalories at the final product stage.

(4) A certification that the manufacturer has established current good manufacturing practices, including quality control procedures and in-process controls, and testing required by current good manufacturing practice, designed to prevent adulteration of this formula in accordance with subparts B and C of this part.

(c) The submission shall not constitute written verification under section 412(d)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(d)(2)) when any data prescribed in paragraph (b) of this section are lacking or are not set forth so as to be readily understood. In such circumstances, the Agency will notify the manufacturer that the notice is not adequate.

§106.140 Submission concerning a change in infant formula that may adulterate the product.

(a) When a manufacturer makes a change in the formulation or processing of the formula that may affect whether the formula is adulterated under section 412(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(a)), the manufacturer shall,

before the first processing of such formula, make a submission to the Food and Drug Administration at the address given in §106.110(a). An original and two copies shall be submitted.

(b) The submission shall include:

(1) The name and physical form of the infant formula (i.e., powder, ready-to-feed, or concentrate);

(2)(i) An explanation of why the change in formulation or processing may affect whether the formula is adulterated; and

(ii) What steps will be taken to ensure that, before the formula is introduced into interstate commerce, the formula will not be adulterated; and

(3) A statement that the submission complies with §106.120(b)(3), (b)(4), (b)(5), and (b)(6). When appropriate, a statement to the effect that the information required by §106.120(b)(3), (b)(4), (b)(5), or (b)(6) has been provided to the Agency previously and has not been affected by the changes that are the subject of the current submission, together with the identification number assigned by the Agency to the relevant infant formula submission, may be provided in lieu of such statement.

(c) The submission shall not constitute notice under section 412 of the Federal Food, Drug, and Cosmetic Act unless it complies fully with paragraph (b) of this section, and the information that it contains is set forth in a manner that is readily understandable. The Agency will notify the manufacturer if the notice is not adequate because it does not meet the requirements of section 412(d)(3) of the Federal Food, Drug, and Cosmetic Act.

§106.150 Notification of an adulterated or misbranded infant formula.

(a) A manufacturer shall promptly notify the Food and Drug Administration in accordance with paragraph (b) of this section when the manufacturer has knowledge (that is, actual knowledge that the manufacturer had, or the knowledge which a reasonable person would have had under like circumstances or which would have been obtained upon the exercise of due care) that reasonably supports the conclusion that an infant formula that has been processed by the manufacturer and that has left an establishment subject to the control of the manufacturer:

(1) May not provide the nutrients required by section 412(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a(i)) or by regulations issued under section 412(i)(2); or

(2) May be otherwise adulterated or misbranded.

(b) The notification made according to paragraph (a) of this section shall be made by telephone, to the Director of the appropriate Food and Drug Administration district office. After normal business hours (8 a.m. to 4:30 p.m.), the Food and Drug Administration's emergency number, 1–866–300–4374 shall be used. The manufacturer shall promptly send written confirmation of the notification to the Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Compliance, Division of Enforcement (HFS–605), Recall Coordinator, 5001 Campus Dr., College Park, MD 20740, and to the appropriate Food and Drug Administration district office.

[79 FR 8059, Feb. 10, 2014, as amended at 88 FR 17718, Mar. 24, 2023]

§106.160 Incorporation by reference.

(a) Certain material is incorporated by reference into this part with the approval of the Director of the Federal Register under 5 U.S.C. 552(a) and 1 CFR part 51. To enforce any edition other than that specified in this section, the Food and Drug Administration must publish notice of change in the FEDERAL REGISTER and the material must be available to the public. All approved material is available for inspection at the Food and Drug Administration library at 10903 New Hampshire Ave., Building 2, Third Floor, Silver Spring, MD 20993, 301–796–2039, and is available from the sources listed below. This material is also available for inspection at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202–741–6030 or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*

(b) 3–A Sanitary Standards, Inc., 6888 Elm St., Suite 2D, McLean, VA 22101–

3829, 703–790–0295, and may be ordered online at *http://www.3-a.org/*:

(1) 3–A Sanitary Standards, No. 609–03: A Method of Producing Culinary Steam, adopted November 21, 2004, into §106.20(h).

(2) [Reserved]

(c) American Society for Nutrition, 9650 Rockville Pike, Bethesda, MD 20814–3998, 301–634–7279, *http://www.nutrition.org*:

(1) *Physical growth: National Center for Health Statistics percentiles,* Hamill, P.V.V., T.A. Drizd, C.L. Johnson, R.B. Reed, A.F. Roche, and W.M. Moore, *American Journal of Clinical Nutrition,* vol. 32, pp. 607–614, dated March 1979, into §106.96(i)(1)(ii)(c).

(2) [Reserved]

(d) AOAC International, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877–2417, 301–924–7078:

(1) Official Methods of Analysis of AOAC International, 16th ed., dated 1995, into §106.96(i)(2)(ii):

(i) Section 45.3.04, AOAC Official Method 960.48 Protein Efficiency Ratio Rat Bioassay, and

(ii) Section 45.3.05, AOAC Official Method 982.30 Protein Efficiency Ratio Calculation Method.

(2) Official Methods of Analysis of AOAC International, 18th ed., dated 2005, into §106.96(f):

(i) Section 45.3.04, AOAC Official Method 960.48 Protein Efficiency Ratio Rat Bioassay, and

(ii) Section 45.3.05, AOAC Official Method 982.30 Protein Efficiency Ratio Calculation Method.

(e) Centers for Disease Control and Prevention, 1600 Clifton Rd., Atlanta, GA 30333, 1–800–232–4636, *http://www.cdc.gov/growthcharts/who_charts.htm.*

(1) *Birth to 24 months:* Boys Head circumference-for-age and Weight-for-length percentiles, dated November 1, 2009, into §106.96(b)(4).

(2) *Birth to 24 months:* Boys Length-for-age and Weight-for-age percentiles, dated November 1, 2009, into §106.96(b)(4).

(3) *Birth to 24 months:* Girls Head circumference-for-age and Weight-for-length percentiles, dated November 1, 2009, into §106.96(b)(4).

(4) *Birth to 24 months:* Girls Length-for-age and Weight-for-age percentiles, dated November 1, 2009, into §106.96(b)(4).

PART 107—INFANT FORMULA

Subpart A—General Provisions

Sec.

Subpart B—Labeling

Subpart C—Exempt Infant Formulas

Subpart D—Nutrient Requirements

Subpart E—Infant Formula Recalls

AUTHORITY: 21 U.S.C. 321, 343, 350a, 371.

SOURCE: 50 FR 1840, Jan. 14, 1985, unless otherwise noted.

EDITORIAL NOTE: Nomenclature changes to part 107 appear at 81 FR 49895, July 29, 2016.

Subpart A—General Provisions

§107.1 Status and applicability of the regulations in part 107.

(a) The criteria in subpart B of this part describe the labeling requirements applicable to infant formula under section 403 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C 343). Failure to comply with any regulation in subpart B of this part will render an infant formula misbranded under section 403 of the Federal Food, Drug, and Cosmetic Act.

(b) The criteria in subpart C of this part describe the terms and conditions