



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 107

[Docket No. FDA-2013-N-0067]

Infant Formula: The Addition of Minimum and Maximum Levels of Selenium to Infant Formula and Related Labeling Requirements

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA or we) is amending the regulations on nutrient specifications and labeling for infant formula to add the mineral selenium to the list of required nutrients and to establish minimum and maximum levels of selenium in infant formula.

DATES: This final rule is effective June 22, 2016. See section VII of this document for information on the filing of objections. Submit either electronic or written objections and requests for a hearing by July 23, 2015.

ADDRESSES: You may submit either electronic or written objections and/or requests for a hearing, identified by Docket No. FDA-2013-N-0067, by any of the following methods:

Electronic Submissions

Submit electronic objections in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.

## Written Submissions

Submit written objections in the following ways:

- Mail/Hand delivery/Courier (for paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Docket No. FDA-2013-N-0067 for this rulemaking. All objections received may be posted without change to <http://www.regulations.gov>, including any personal information provided. For additional information on submitting objections, see the "Objections" heading of the SUPPLEMENTARY INFORMATION section of this document.

Docket: For access to the docket to read background documents, comments, or objections received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Leila Beker, Center for Food Safety and Applied Nutrition (HFS-850), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, 240-402-1451.

### SUPPLEMENTARY INFORMATION:

#### I. What Is the Background and Legal Authority of This Final Rule?

##### A. Background

Section 412(i) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 350a(i)) establishes requirements for the nutrient content of infant formulas. Under section 412(i)(2) of the FD&C Act, the Secretary of Health and Human Services (the Secretary) is

authorized to revise the list of required nutrients and the required level for any required nutrient. This authority has been delegated to the Commissioner of Food and Drugs (the Commissioner). The table in section 412(i) of the FD&C Act, and in FDA regulations at § 107.100(a) (21 CFR 107.100(a)), specifies that infant formulas must contain 29 nutrients; minimum levels for each nutrient and maximum levels for 9 of the nutrients are also specified. In 1989, the Food and Nutrition Board of the National Research Council established a Recommended Dietary Allowance for selenium for infants 0 to 6 months of age of 10.0 micrograms per day ( $\mu\text{g}/\text{day}$ ), a level extrapolated from adult values on the basis of body weight and with a factor allowed for growth (Ref. 1).

In the Federal Register of April 16, 2013 (78 FR 22442), we proposed to amend the nutrient specifications for infant formula to include selenium as a required nutrient in § 107.100(a). We also proposed to establish minimum and maximum levels for selenium in infant formulas because evidence exists for both deficiency and toxicity of selenium. We proposed 2.0  $\mu\text{g}$  selenium per 100 kilocalories (/100 kcal) as the minimum level of selenium in infant formulas and 7.0  $\mu\text{g}/100$  kcal as the maximum level of selenium in infant formulas.

Scientific evidence from multiple sources supported the proposed levels. Specifically, for the proposed requirements, we considered scientific evidence in: (1) The Institute of Medicine's (IOM) "Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids" (Ref. 2); (2) the Life Sciences Research Office's "Assessment of Nutrient Requirements for Infant Formulas" by Raiten et al. (Ref. 3); (3) "Global Standard for the Composition of Infant Formula. Recommendations of an ESPGHAN [European Society for Paediatric Gastroenterology, Hepatology and Nutrition] Coordinated International Expert Group" by Koletzko et al. (Ref. 4); and (4) "Selenium Status of Term Infants Fed Selenium-

Supplemented Formula in a Randomized Dose-Response Trial" by Daniels et al. (Ref. 5). We also searched the scientific literature from 1998 through 2012 for published studies not included in these reports.

In addition, we proposed to amend the labeling requirements for infant formula in § 107.10(a)(2) to add selenium to the list of nutrients along with the requirement to list the amount of selenium per 100 kcal in the formula.

#### B. Legal Authority

Section 412(i) of the FD&C Act contains a table of nutrients (including minimum and, in some cases, maximum levels for nutrients) that are required to be in an infant formula. Section 412(i)(2) of the FD&C Act authorizes the Secretary to revise the statutory table of nutrients and to revise the level of any required nutrient. The Secretary has delegated this authority to the Commissioner. Our regulations establishing the table of nutrients are codified at § 107.100.

The final rule amends § 107.100 to add selenium to the list of nutrients required for infant formula. The legal authority for the amendment to § 107.100 comes from section 412(i)(2) of the FD&C Act.

The final rule also requires adding selenium to the statement of the amounts of nutrients required for infant formula labeling in § 107.10(a)(2). "Infant formula" is defined as a food for "special dietary use" under section 201(z) of the FD&C Act (21 U.S.C. 321(z)). Under sections 403(j) and 701(e) of the FD&C Act (21 U.S.C. 343(j) and 21 U.S.C. 371(e)), the Secretary, and by delegation the Commissioner, may prescribe regulations concerning the vitamin and mineral content of foods for special dietary uses to fully inform purchasers as to the value of the food for such uses. As such, FDA has the authority to revise the statement of the amounts of nutrients

required for infant formula labeling in § 107.10(a)(2) under sections 201(z), 403(j), 412(i), and 701(e) of the FD&C Act.

## II. What Issues Did the Comments Raise? What Are FDA's Responses to the Comments?

We invited public comment on the proposed rule. The comment period closed on July 1, 2013. We received fewer than 20 comments. Overall, the comments supported the addition of selenium to infant formula and agreed that selenium is an essential nutrient. We summarize and respond to the comments on the proposed rule and describe the final rule in this section. For ease of reading, we preface each comment discussion with a numbered "Comment," and each response by a corresponding numbered "Response." We have numbered each comment to help distinguish among different topics. The number assigned is for organizational purposes only and does not signify the comment's value, importance, or the order in which it was received.

### A. The Addition of Selenium to the Statement of the Amounts of Nutrients (§ 107.10(a)(2))

The proposed rule would amend the infant formula nutrient labeling and nutrient specification regulations at §§ 107.10 and 107.100, respectively. Proposed § 107.10(a)(2) would add selenium to the statement of the amounts of nutrients required for infant formula labeling.

We did not receive any comments on proposed § 107.10(a)(2). However, we note that we have revised § 107.10(a)(2) in this final rule to correspond to changes resulting from an interim final rule that appeared in the Federal Register on February 10, 2014 (79 FR 7934), and later affirmed in a final rule that appeared in the Federal Register on June 10, 2014 (79 FR 33057). In brief, § 107.10(a)(2) was reworded by replacing "A statement of the amount of each of the following nutrients supplied by 100 kilocalories" with "A statement of the amount, supplied by 100 kilocalories, of each of the following nutrients and of any other nutrient added by the manufacturer."

### B. Minimum and Maximum Levels of Selenium (§ 107.100)

Proposed § 107.100(a) would add selenium to the list of required nutrients in infant formula. The proposal also would establish minimum and maximum levels for selenium in infant formula because evidence exists for both deficiency and toxicity of selenium, and there is no room for error in production of a food that serves as the sole source of nutrition for infants. We proposed to set 2.0 µg selenium/100 kcal as the minimum level of selenium in infant formulas and 7.0 µg/100 kcal as the maximum level of selenium in infant formulas. Since the publication of the proposed rule, we have conducted a search of the scientific literature to identify whether additional studies on selenium requirements of infants were published after we issued our proposal. We did not find any relevant studies in our search.

(Comment 1) One comment suggested we decrease the minimum level of selenium to 1.6 µg/100 kcal. The comment pointed to analytical variability that can occur between laboratories when testing the levels of selenium. According to the comment, due to this analytical variability, a minimum selenium level of 1.6 µg/100 kcal will likely result in manufacturers' formulating to deliver selenium levels close to 2.0 µg/100 kcal to ensure products do not fall below the minimum.

(Response 1) We decline to lower the minimum level of selenium in infant formula to 1.6 µg/100 kcal to accommodate analytical variability that can occur between laboratories as the comment suggested. The level of any substance (including nutrients, food additives, or contaminants) established for regulatory purposes must be a value that is based on and true to the available scientific evidence. We recognize that analytical variability is always present and manage this matter under our compliance program. We also note that lowering the minimum level of selenium would not change the analytical variability, and the tested level of selenium

might fall below whatever minimum level is set, due to analytical variability. For example, if the minimum level was lowered to 1.6 µg/100 kcal, the tested level of selenium might fall below 1.6 µg/100 kcal due to analytical variability. However, on our own initiative we have revised proposed § 107.100(a) to insert the word "level" between the words "minimum" and "specified" in light of an inadvertent omission in the proposed rule.

(Comment 2) One comment said that the minimum level of selenium should be in the range reported in breast milk and specifically recommended the level of 1.6 µg selenium/100 kcal, consistent with the mean concentration of selenium in breast milk reported by Daniels et al. (2008). The comment continued, saying it was not aware of any reports of selenium deficiency in breast-fed infants or at this concentration of selenium in infant formula. The comment also stated that we did not consider the data from the breast-fed control group in the Daniels et al. study.

(Response 2) With regard to this comment suggesting that the selenium concentration in human milk (and more specifically, the level of 1.6 µg/100 kcal reported in the Daniels et al. study) be used as the basis for the required minimum selenium level in infant formula, the scientific evidence we discussed in the proposed rule (78 FR 22442 at 22444) was more broadly based. The discussion in the proposed rule considered the levels of selenium in human milk from the studies used to establish the adequate intake (AI) for selenium by the IOM and the levels of selenium in infant formulas fed in the randomized and double-blinded dose-response study in infants by Daniels et al. (2008).

Specifically, as discussed in the proposed rule (78 FR 22442 at 22444), the IOM established an AI for selenium of 15.0 µg/day (approximately 2.1 µg/kg body weight/day) for infants 0 to 6 months of age based on the average concentration of selenium in human milk from

healthy women from 2 to 6 months of lactation as reported in four studies. The study by Daniels et al. was published after the IOM established the AI for selenium for infants 0 to 6 months of age, and the concentration of selenium in human milk reported in that study was not among the studies considered in the establishment of the AI. We note that the mean concentration of selenium in human milk in the studies included by the IOM in setting the AI for infants 0 to 6 months of age was 18 µg/L and that reported by Daniels et al. was 10.7 µg/L.

The study by Daniels et al. provides direct evidence of the effect of selenium concentration of infant formula on the circulating biochemical indicators of selenium status in infants. As described in the proposed rule (78 FR 22442 at 22444), this study included a control formula that contained 0.9 µg selenium/100 kcal (considered by the investigators to be a low-selenium formula) and two test formulas that contained 1.9 µg selenium/100 kcal or 3.1 µg selenium/100 kcal. The level of selenium in the formula containing 1.9 µg/100 kcal was somewhat higher than the level in human milk reported in the Daniels et al. study and close to the AI set by the IOM. In our consideration of the study by Daniels et al., we regarded the data from the human milk-fed infants as reference data, with the direct comparators being the indicators of selenium status of infants fed the formulas containing the three levels of selenium. The plasma and erythrocyte indicators of selenium status for both test formulas did not differ from each other but differed with statistical significance from the control formula. Compared to the infants fed the formula containing 1.9 µg selenium/100 kcal, infants fed the formula containing 3.1 µg selenium/100 kcal excreted more selenium in the urine. This increase in urinary selenium was found to be statistically significant. Combined with the finding of no dose-related changes in the circulating indicators of selenium status in infants fed formulas containing 1.9 µg selenium/100 kcal or 3.1 µg selenium/100 kcal, this dose-related increase in urinary



selenium suggests that infants fed the formula containing a level of 1.9 µg selenium/100 kcal received sufficient selenium to meet their nutritional needs. Much of the selenium intake above the level of 1.9 µg selenium/100 kcal was apparently eliminated from the body through the body's homeostatic mechanisms.

As effects on indicators of selenium status have not been evaluated in infants fed formulas with concentrations of selenium between 0.9 µg selenium/100 kcal and 1.9 µg selenium/100 kcal, there are no data to support lowering the minimum level of selenium in infant formula from 2.0 µg/100 kcal to 1.6 µg/100 kcal. The scientific evidence discussed previously and in section III.A. of the proposed rule (78 FR 22442 at 22443) continues to justify 2.0 µg selenium/100 kcal as the minimum level for selenium in infant formulas.

(Comment 3) In support of a lower minimum level for selenium in infant formula, one comment pointed out that the Codex Alimentarius infant formula standard and the European Union Directive on Infant Formulae and Follow-On Formulae recommend a minimum level of selenium in infant formula of 1.0 µg selenium/100 kcal.

(Response 3) The level of 1.0 µg/100 kcal as the minimum level for selenium in infant formula was adopted by the Codex Alimentarius in 2007 for its Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants (Codex Stan 72-1981) (Ref. 6) based on recommendation of this level by an International Expert Group (IEG) of the ESPGHAN (Ref. 4). The IEG recommended 1.0 µg selenium/100 kcal for infant formula based on the median selenium content of human milk and an established history of apparent safe use. However, as described in the proposed rule (78 FR 22442 at 22444), no information was provided regarding the details of how such information was used in making the recommendation for 1.0 µg selenium/100 kcal in infant formula. In addition, the recommendation of the IEG was made in

2005 before the dose-response study of Daniels et al. was published in 2008, and data from that study suggest that a level of 1.9 µg selenium/100 kcal in infant formula meets infants' selenium needs. Further, although, as noted in the comment, the level of 1.0 µg/100 kcal was also adopted as the minimum level for selenium by the European Union in 2006 for its Directive on Infant Formulae and Follow-On Formulae (Commission Directive 2006/141/EC), identification of a scientific basis for the selection of 1.0 µg selenium/100 kcal was not included in the European Union Commission Directive.

(Comment 4) One comment suggested raising the maximum level of selenium added to infant formula to 9.0 µg/100 kcal. The comment said that the 9.0 µg selenium/100 kcal would align the maximum level of selenium with the upper levels recommended in the Codex Alimentarius Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants, and with the European Union Directive on Infant Formulae and Follow-on Formulae. The comment also stated that 9.0 µg selenium/100 kcal is more aligned with the use of 8.0 µg/100 kcal as the maximum value for selenium in the FDA Compliance Program Guidance Manual (CPGM).

(Response 4) We decline to increase the maximum level of selenium in infant formula to 9.0 µg selenium/100 kcal as the comment suggested. As noted in the response to comment 1 concerning the minimum level of selenium in infant formula, the maximum level of any substance (including nutrients, food additives, or contaminants) established for regulatory purposes must also be a value that is based on and true to the available scientific evidence.

The level of 9.0 µg selenium/100 kcal suggested in the comment is the maximum level recommended by the ESPGHAN IEG for infant formula. The report of the IEG stated that its recommendation was based on a history of safe use (not further described) and did not identify

scientific data or other information relied upon for its recommendation for a maximum level of 9.0 µg selenium/100 kcal that was subsequently adopted by Codex Alimentarius in 2007 for its Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants (Codex Stan 72-1981). The level of 9.0 µg selenium/100 kcal was also listed in the European Union Directive on Infant Formulae and Follow-on Formulae. We considered the level of 9.0 µg selenium/100 kcal; however, we could not determine the scientific basis for this level.

Although we expressly invited comment regarding the proposed maximum level in infant formula of 7.0 µg selenium/100 kcal, including whether such a maximum level is needed and the scientific data or information that form the basis of any comments (78 FR 22442 at 22445), we did not receive any comments that disagreed with the need for a maximum level or that provided a scientific basis that would support a change from the proposed level. The report of the IOM, which we relied upon to propose the maximum level of 7.0 µg selenium/100 kcal, identified the data (concentration of selenium in human milk not associated with known adverse effects) and the method of calculation used to estimate a Tolerable Upper Intake Level (UL) of 7.0 µg/kg body weight/day for selenium intake of infants from 0 to 6 months of age. (As explained in the proposed rule (78 FR 22442 at 22444), a level of intake expressed as µg/kg body weight/day is consistent with an infant formula concentration expressed in µg/100 kcal.)

With regard to the use of 8.0 µg/100 kcal as a maximum in our CPGM, this level was incorporated into the CPGM when infant formula manufacturers in the United States began adding selenium to infant formulas starting as early as 1990 and preceded the establishment of the UL for infants 0 to 6 months of age by the IOM. We will update the minimum and maximum values for selenium in infant formula in our CPGM to align with the final rule.

(Comment 5) One comment said that setting 7.0 µg selenium/100 kcal as the maximum level of selenium, which is the amount we proposed, would mean some manufacturers would need to reformulate their products that currently meet the 8.0 µg selenium/100 kcal level that is listed in the FDA CPGM.

(Response 5) Although the comment said that some manufacturers whose products currently meet the 8.0 µg selenium/100 kcal level listed in the FDA CPGM would need to reformulate, it did not specify how many manufacturers or products would likely be affected or whether label changes would be required following any reformulations. It also did not provide estimates of possible costs resulting from establishing a maximum of 7.0 µg selenium/100 kcal. Other comments indicated that any formula changes could be made in a cost effective and timely manner with an effective date 12 months after publication of the final rule (see comment 7).

If some manufacturers who currently meet the 8.0 µg selenium/100 kcal level need to reformulate their products to avoid exceeding a selenium level of 7.0 µg/100 kcal, such a reformulation would involve only a small reduction in the amount of selenium added to the formula. Manufacturers routinely make such small changes in the rates of addition of ingredients (which may or may not result in the need for label changes) as a fundamental part of their current good manufacturing practices and quality control programs to ensure the consistent production of infant formulas of high quality. These types of changes are generally not considered to be major changes and are reported to FDA in a "before first processing" submission by the manufacturers if the change may adulterate the product, as required by section 412(d)(3) of the FD&C Act and our regulations in 21 CFR 106.140.

### C. Allowance for Analytical Variability

(Comment 6) One comment suggested that, in the absence of setting a higher maximum selenium level, FDA would need to establish a specific allowance for method bias to ensure that manufacturers can meet both the minimum and maximum selenium levels. The comment suggested an allowance of 30 percent to account for analytical variability.

(Response 6) As noted in the response to comment 4, the maximum level of any substance must be a value that is based on and true to the available scientific evidence. For this reason, we are not setting a higher maximum value that would include an allowance for analytical variability or method bias. We are not aware of method bias (consistent over- or under-measurement of the actual concentration) in the analysis of selenium in infant formula. We acknowledge that analytical variability occurs between laboratories when testing the levels of nutrients in infant formula, and we manage this matter under our compliance program as necessary. Further, we decline to set a 30 percent allowance for analytical variation for the chemical analysis of selenium in infant formula. The comment did not provide a reason for setting such a high allowance for analytical variation, and 30 percent variability is much higher than performance requirements for commonly used methods for chemical analysis of minerals in infant formula, which typically is about 10 to 15 percent.

### D. Effective Date

In the Regulatory Impact Analysis of the proposed rule, we analyzed three options with respect to an effective date: (1) Take no new regulatory action (baseline); (2) require the provisions of this proposed rule and make the provisions of the rule effective 180 days after publication; and (3) require the provisions of this proposed rule, but make the provisions of the rule effective 12 months after publication (78 FR 22442 at 22446).

(Comment 7) Two comments supported FDA's option 3 in the proposed rule to make the final rule effective 12 months after publication to allow for cost effective and timely changes with no anticipated impact on infant health. One comment explained that because there have been no reports of full-term, breast-fed infants in the United States with evidence of selenium deficiency, there would be no anticipated impact to infant health due to a 6-month delay in the rule's effective date (from 6 months in option 2 to 12 months in option 3 of the Regulatory Impact Analysis of the proposed rule).

(Response 7) The final rule will be effective 12 months after publication of this document (see DATES). This will allow the industry to make any needed reformulations and label changes to their infant formula products in the 12-month period that the comment identified as cost effective and timely for needed changes.

#### E. Miscellaneous Comments

Several comments addressed matters that were not specific to a particular provision in the proposed rule and/or that were not covered by the rule. We summarize and address those comments here.

(Comment 8) One comment suggested that FDA recommend or encourage the use of the organic form of selenium, selenomethionine, rather than the inorganic forms, sodium selenite or sodium selenate. The comment explained that selenomethionine is the selenium compound incorporated into body proteins and is available in dietary supplements or from brewer's yeast.

(Response 8) FDA's specifications for infant formula composition in § 107.100 identify nutrients that must be included in the formula. The regulations do not specify ingredients that can serve as sources of the nutrients, except for vitamin K in § 107.100(c). We decline to specify the form of selenium in infant formula because we do not have information that indicates

that any specific source of selenium should be used in infant formula. Our recently published current good manufacturing practices for infant formulas require that ingredients used in infant formulas be safe and suitable for use in infant formula. Specifically, under § 106.40(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 FD&C Act; that is, a substance is used in accordance with the Agency's food additive regulations, is generally recognized as safe for such use, or is authorized by a prior sanction.

(Comment 9) One comment agreed with the proposed selenium levels "unless a pediatrician otherwise recommends an alternative dosage because of a peculiar deficiency of selenium." The comment did not explain the circumstances under which a pediatrician would recommend an "alternative dosage."

(Response 9) The final rule adds selenium to the list of required nutrients in infant formula and establishes minimum and maximum levels of selenium in infant formula. Manufacturers will be required to add selenium to infant formula within the established bounds as of the effective date of this rule. The rule does not apply to what physicians may do within the practice of medicine. Thus, matters pertaining to the practice of pediatric medicine are outside the scope of this rulemaking.

(Comment 10) Another comment suggested that FDA consider establishing a higher maximum for vitamin D based on recent American Academy of Pediatrics and IOM recommendations.

(Response 10) The final rule adds selenium to the list of required nutrients in infant formula and establishes minimum and maximum levels of selenium in infant formula. With

respect to vitamin D and infant formula, we may, as resources permit, reevaluate all the minimum and maximum required nutrient levels for infant formula in separate rulemakings.

(Comment 11) One comment supported the proposal to require the addition of selenium in infant formula. The comment stated that a child that does not receive enough selenium in the diet is at risk of developing Keshan disease.

(Response 11) FDA agrees that Keshan disease is linked to selenium deficiency. The preamble to the proposed rule discussed the known biological functions of selenium and Keshan disease (a cardiomyopathy that occurs almost exclusively in children) (see 78 FR 22442 at 22443).

### III. What Is the Environmental Impact of This Final Rule?

FDA has determined under 21 CFR 25.32(n) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

### IV. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. We have determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we have concluded that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.



## V. Executive Order 12866 and Executive Order 13563: Cost Benefit Analysis

On April 16, 2013, we proposed to amend our regulations on nutrient specifications and labeling for infant formula to add the mineral selenium to the list of required nutrients and to establish minimum and maximum levels of selenium in infant formula (78 FR 22442). The Economic Impact Analysis in the proposed rule explained the economic impact of the changes to regulations at part 107. We did not receive any comments on the economic analysis of the proposed rule.

FDA has examined the impacts of this final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct Agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). FDA has developed a regulatory impact analysis that presents the benefits and costs of this proposed rule (Ref. 7). We believe that the final rule will not be a significant regulatory action as defined by Executive Order 12866.

## VI. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3520). The title, description, and respondent description of the information collection provisions are shown in the following paragraphs with an estimate of the annual third-party disclosure burden. Included in the estimate is the time for reviewing instructions,

searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Third-Party Disclosure Requirements for Selenium in Infant Formula

Description of Respondents: The respondents to this information collection are manufacturers of infant formula marketed in the United States.

Description: The final rule revises § 107.10(a)(2) to require that selenium be listed in the nutrient list on the label for all infant formulas. In particular, in the nutrient list, selenium must be listed between iodine and sodium and the amount per 100 calories declared; and because selenium is a required ingredient in infant formula, selenium is required to be declared in the formula's ingredient statement by its common or usual name and positioned according to the descending order of its predominance in the formula, under § 101.4 (21 CFR 101.4). The present version of § 107.10(a)(2) is approved by OMB in accordance with the PRA and has been assigned OMB control number 0910-0256. This final rule modifies the information collection associated with the present version of § 107.10(a)(2) by adding 23 hours to the burden associated with the collection. A manufacturer not in compliance with the new minimum and maximum levels for selenium in infant formula would be required to make a one-time change to the nutrient list information disclosed to consumers on the label of its infant formula, to account for the required change in the amount of selenium in its products. The nutrient information disclosed by manufacturers on the infant formula label is necessary to inform purchasers of the value of the infant formula. As discussed previously in this document, FDA has the authority to revise the statement of the amounts of nutrients required for infant formula labeling in § 107.10(a)(2).

FDA estimates the burden of this collection of information as follows:

Table 1.--Estimated Annual Third-Party Disclosure Burden<sup>1</sup>

21 CFR Section	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours	Total Capital Cost
§107.10(a)(2)--Nutrient labeling for infant formula	1	46	46	0.5 (30 minutes)	23	\$792,439

<sup>1</sup> There are no operating and maintenance costs associated with this collection of information.

FDA concludes that there will be no additional burden associated with the requirement to disclose selenium in the ingredient statement as required under § 101.4 because all infant formula manufacturers currently add selenium as an ingredient to their infant formula products that are sold in the United States, and all manufacturers currently disclose selenium in the ingredient statement, as specified by § 101.4. Additionally, all manufacturers currently disclose selenium in the nutrient list, as required by § 107.10(b)(5). Under §107.10(a)(2), only one manufacturer would need to make a one-time labeling change to modify the amount of selenium shown in the nutrient list on the labels of its infant formula.

The third-party disclosure burden consists of the setup time required to design a revised label and incorporate it into the manufacturing process. Based upon our knowledge of food and dietary supplement labeling, we estimate that the affected manufacturer would require less than 0.5 hour per product to modify the label's nutrient list to reflect the addition of more selenium to the product. We estimate that this manufacturer produces 46 separate infant formulas that would require relabeling. The one-time third-party disclosure burden is estimated in table 1 of this document.

The final column of table 1 gives the estimated capital cost associated with relabeling. This is the cost of designing a revised label and incorporating it into the manufacturing process. The cost stated in table 1, \$792,439, is estimated based on an effective date of 1 year after publication. These costs are based on the cost model estimate that, over a longer period of time,

any labeling change is more likely to be coordinated with a change in a label that may already be scheduled, and will diminish the need to, for example, purchase and apply stickers to packages affected by the change.

The information collection provisions in this final rule have been submitted to OMB for review as required by section 3507(d) of the PRA. The requirements were approved and assigned OMB control number 0910-0256. This approval expires on 04/30/2018.

An Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

## VII. Objections

This rule is effective as shown in the DATES section, except as to any provisions that may be stayed by the filing of proper objections. If you will be adversely affected by one or more provisions of this regulation, you may file with the Division of Dockets Management (see ADDRESSES) either electronic or written objections. You must number each objection separately, and, within each numbered objection, you must specify with particularity the provision(s) to which you object, and the grounds for your objection. Within each numbered objection, you must specifically state whether you are requesting a hearing on the particular provision that you specify in that numbered objection. If you do not request a hearing for any particular objection, we will consider the absence of such a request as waiving the right to a hearing on that objection. If you request a hearing, your objection should include a detailed description and analysis of the specific factual information you intend to present in support of the objection in the event that a hearing is held.

It is only necessary to send one set of documents. Identify documents with the docket number found in brackets in the heading of this document. Any objections received in response

to the regulation may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>. We will publish notice of the objections that we have received or lack thereof in the Federal Register.

### VIII. References

The following references have been placed on display in the Division of Dockets Management (see ADDRESSES) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at <http://www.regulations.gov>.

1. Food and Nutrition Board, National Research Council, "Recommended Dietary Allowances," 10th ed., Washington, DC: The National Academies Press, p. 221, 1989.
2. Food and Nutrition Board, Institute of Medicine, "Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids," Washington, DC: The National Academies Press, pp. 21-33; 292-299; 315-316, 2000.
3. Raiten, D. J., J. M. Talbot, and J. H. Waters, "Assessment of Nutrient Requirements for Infant Formulas," Journal of Nutrition, 128:2059S-2249S, 1998.
4. Koletzko, B., S. Baker, G. Cleghorn, U.F. Neto, et al., "Global Standard for the Composition of Infant Formula. Recommendations of an ESPGHAN Coordinated International Expert Group," Journal of Pediatric Gastroenterology and Nutrition, 41:584-599, 2005.
5. Daniels, L., R. A. Gibson, K. Simmer, P. Van Dael, and M. Makrides, "Selenium Status of Term Infants Fed Selenium-Supplemented Formula in a Randomized Dose-Response Trial," American Journal of Clinical Nutrition, 88:70-76, 2008.

6. Codex Alimentarius Commission, "Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants, Codex Stan 72-1981," 1981. Revised 2007.

7. FDA/Center for Food Safety and Applied Nutrition, "Infant Formula: The Addition of Minimum and Maximum Levels of Selenium to Infant Formula and Related Labeling Requirements, Final Regulatory Impact Analysis and Regulatory Flexibility Analysis," 2015. Available at:

<http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/>.

#### List of Subjects in 21 CFR Part 107

Food labeling, Infants and children, Nutrition, Reporting and recordkeeping requirements, Signs and symbols.

For the reasons discussed in the preamble, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, the Food and Drug Administration amends 21 CFR part 107 as follows:

#### PART 107--INFANT FORMULA

1. The authority citation for 21 CFR part 107 continues to read as follows:

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

2. In § 107.10, revise paragraph (a)(2) to read as follows:

#### § 107.10 Nutrient information.

(a) \* \* \*

(2) A statement of the amount, supplied by 100 kilocalories, of each of the following nutrients and of any other nutrient added by the manufacturer:

Nutrients	Unit of measurement
Protein	Grams
Fat	Do.
Carbohydrate	Do.
Water	Do.
Linoleic acid	Milligrams
Vitamins:	
Vitamin A	International Units
Vitamin D	Do.
Vitamin E	Do.
Vitamin K	Micrograms
Thiamine (Vitamin B <sub>1</sub> )	Do.
Riboflavin (Vitamin B <sub>2</sub> )	Do.
Vitamin B <sub>6</sub>	Do.
Vitamin B <sub>12</sub>	Do.
Niacin	Do.
Folic acid (Folacin)	Do.
Pantothenic acid	Do.
Biotin	Do.
Vitamin C (Ascorbic acid)	Milligrams
Choline	Do.
Inositol	Do.
Minerals:	
Calcium	Milligrams
Phosphorus	Do.
Magnesium	Do.
Iron	Do.
Zinc	Do.
Manganese	Micrograms
Copper	Do.
Iodine	Do.
Selenium	Do.
Sodium	Milligrams
Potassium	Do.
Chloride	Do.

\* \* \* \* \*

3. In § 107.100, revise paragraph (a) to read as follows:

§ 107.100 Nutrient specifications.

(a) An infant formula shall contain the following nutrients at a level not less than the minimum level specified and not more than the maximum level specified for each 100

kilocalories of the infant formula in the form prepared for consumption as directed on the container:

Nutrients	Unit of measurement	Minimum level	Maximum level
Protein	Grams	1.8	4.5
Fat	Do.	3.3	6.0
	Percent calories	30	54
Linoleic acid	Milligrams	300	-----
	Percent calories	2.7	-----
Vitamins			
Vitamin A	International Units	250	750
Vitamin D	Do.	40	100
Vitamin E	Do.	0.7	-----
Vitamin K	Micrograms	4	-----
Thiamine (Vitamin B <sub>1</sub> )	Do.	40	-----
Riboflavin (Vitamin B <sub>2</sub> )	Do.	60	-----
Vitamin B <sub>6</sub>	Do.	35	-----
Vitamin B <sub>12</sub>	Do.	0.15	-----
Niacin <sup>1</sup>	Do.	250	-----
Folic acid (Folacin)	Do.	4	-----
Pantothenic acid	Do.	300	-----
Biotin <sup>2</sup>	Do.	1.5	-----
Vitamin C (Ascorbic acid)	Milligrams	8	-----
Choline <sup>2</sup>	Do.	7	-----
Inositol <sup>2</sup>	Do.	4	-----
Minerals			
Calcium	Do.	60	-----
Phosphorus	Do.	30	-----
Magnesium	Do.	6	-----
Iron	Do.	0.15	3.0
Zinc	Do.	0.5	-----
Manganese	Micrograms	5	-----
Copper	Do.	60	-----
Iodine	Do.	5	75
Selenium	Do.	2	7
Sodium	Milligrams	20	60
Potassium	Do.	80	200
Chloride	Do.	55	150

<sup>1</sup>The generic term "niacin" includes niacin (nicotinic acid) and niacinamide (nicotinamide).

<sup>2</sup>Required only for non-milk-based infant formulas.

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Dated: June 17, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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