

**Current Good Manufacturing Practices
(CGMPs), Quality Control Procedures,
Quality Factors, Notification Requirements,
and Records and Reports, for Infant Formula**

Docket No. FDA-1995-N-0063

**Final Regulatory Impact Analysis
Final Regulatory Flexibility Analysis
Unfunded Mandates Reform Act Analysis**

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I. Introduction and Summary

A. Introduction

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). We believe that the final rule is not a significant regulatory action as defined by Executive Orders 12866 and 13563.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. According to our analysis, the final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is \$141 million, using the most current (2013) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

The analyses that we have performed to examine the impacts of this final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act, and the Unfunded Mandates Reform Act of 1995 are included in this Regulatory Impact Analysis (RIA).

B. Summary of Costs and Benefits

The estimated cost of the final rule is \$7.29 million in the first year and \$4.06 million in subsequent years. The estimated benefit to public health from this final rule is \$10.00 million annually, resulting in total net benefits of \$2.71 million in the first year and \$5.94 million in subsequent years.

Table 1--Benefit and Cost Overview (in millions)

	Benefits	Costs	Net Benefits
Total First Year	\$10.00	\$7.29	\$2.71
Annual Total After the First Year	\$10.00	\$4.06	\$5.94

II. Regulatory Impact Analysis for the Final Rule

In the Regulatory Impact Analysis of the interim final rule, we described the need for this regulation, the characteristics of the infant formula industry, and a summary of the economic analysis of the proposed rule. Please refer to the Regulatory Impact Analysis to the interim final rule for a full discussion of these topics.

In reviewing the Regulatory Impact Analysis of the interim final rule, in preparation for the publication of the final rule, we discovered an editing error in the text regarding the range of years used to calculate the average number of yearly *Cronobacter* cases in the United States. While Table 1 in the RIA presented data from 1988-2009, the text in the analysis should have indicated that the calculation of average cases was based on data from 2000-2009. This editing error had no impact on any of the calculations, including the estimate of benefits for the final rule.

A. Economic Analysis for the Final Rule

In this section of the document we respond to comments submitted to the interim final rule that raised concerns regarding our cost-benefit analysis. For a full discussion of all costs and benefits associated with this final rule, see the regulatory impact analyses for the proposed and interim final rules.

To make it easier to identify comments and FDA's responses, the word "Comment," in parentheses, appears before the comment's description, and the word "Response," in parentheses, appears before FDA's response. Each comment is numbered to help distinguish between different comments. The number assigned to each comment is purely for organizational purposes and does not signify the comment's value or importance.

1. Production and In-Process Control System (§ 106.6)

The final rule requires manufacturers to implement a system of production and in-process controls that covers all stages of processing. The system must be set out in a written plan or set of procedures that includes establishment of specifications and corrective action plans, documented reviews and material disposition decisions for articles not meeting a specification, and the quarantine of any article that fails to meet a specification pending completion of a documented review and material disposition decision.

(Comment 1) As discussed in the preamble to the final rule, one comment requested that FDA clarify whether additional non-process-related specifications beyond what manufacturers currently do are required and, if so, which non-process-related specifications, or the criteria to make this determination, are needed. The comment said that manufacturers need this information to assess their ability to comply and determine related costs. The comment said that, if additional specifications need to be developed for areas not critical to preventing product adulteration, much more time than 150 days will be required to draft, finalize, implement, and train employees.

(Response) The comment did not define non-process-related specifications or provide additional examples of non-process—related specifications beyond what manufacturers currently do. In the absence of such information, we cannot respond to the comment’s request for clarification and have no basis to agree that there would be additional costs or additional time required for compliance associated with § 106.6(a), beyond our conclusions reached in the regulatory impact analysis document included with the interim final rule. Note also that the final rule adopts a compliance of 60 days after the effective date of this final rule for requirements of § 106.6(a) to facilitate manufacturer compliance. This delay does not affect the cost estimates.

2. Controls to prevent adulteration caused by facilities (§ 106.20)

The final rule requires infant formula manufacturers to establish controls to ensure that

formula does not become adulterated as a result of the design and maintenance of formula production facilities. These controls include separating incompatible operations; establishing a system of segregation for raw materials, in-process materials, and final product; providing adequate lighting and ventilation; and providing appropriate toilet and hand washing facilities. This section also requires that the agents used within the facility, such as rodenticides, insecticides, and cleaning and sanitizing agents, be held and used so as not to contaminate formula, that culinary steam be used at certain production points, and that boiling water additives be used in conformance with the applicable food additive regulation (21 CFR 173.310). Finally, this section requires that potable water used in formula manufacturing meet EPA's Primary Drinking Water regulations, and that the water be tested for chemical, bacterial, and radiological contaminants at intervals specified in the final rule.

(Comment 2) One comment said that the requirements of § 106.20(i), which addresses controls to prevent adulteration from in-plant toilet facilities, are more restrictive than the provisions for toilet facilities in the food GMPs (21 CFR §110.37(d)(4)), which allows for doors in in-plant toilet facilities to open into certain areas if "alternate means have been taken to protect against ... contamination (such as double doors or positive air-flow systems)." The comment continued that FDA did not establish a public health need for the more restrictive requirements and claimed that infant formula manufacturers will have to move or otherwise reconfigure their in-plant toilet facilities if the interim final rule is interpreted not to permit the alternate means in the food GMPs or exempt facilities in areas where product is not subject to airborne contamination.

(Response) We agree with the aspect of the comment that suggests that it should be permissible for doors in in-plant toilet facilities to open into certain areas if alternate means have been taken to protect against contamination. However, we disagree that airborne contamination is the only source of contamination from toilet facilities. Contamination can come from hands,

clothing, and footwear of employees exiting the toilet facilities, and it is likely that measures such as foot baths and footwear and garment changes in addition to double doors and positive air-flow systems will be needed to prevent contamination from in-plant toilet facilities.

We are revising § 106.20(i) to permit doors to toilet facilities to open into the plant facilities if alternate means have been taken to protect against such contamination. It is estimated that, given this language is consistent with existing GMP language, infant formula manufacturers have practices that are already in alignment with this requirement, and no additional cost is estimated.

(Comment 3) One comment stated if that modification of toilet facilities must be implemented by the interim final rule's July effective date, it could require closing off certain toilet areas and rerouting traffic to other parts of the facility, which could increase the potential risk for contamination. Such modifications would require capital costs and it would be unreasonable to expect manufacturers to be able to complete such construction before the July effective date.

(Response) Because we have revised § 106.20(i) to allow alternate means of protection against contamination, consistent with existing regulations, it is expected that manufacturers will already be in alignment with this requirement, and no additional cost is estimated. Note also that the final rule adopts a compliance date of 60 days after the effective date of this final rule for the requirements of § 106.20(i) to facilitate manufacturer compliance. This delay does not affect the cost estimates.

3 Controls to prevent adulteration caused by equipment or utensils (§ 106.30)

The final rule requires manufacturers to clean, sanitize, and maintain all equipment and utensils at regular intervals, have a qualified individual check that this activity has been done satisfactorily each time, and make and retain records that this activity has been completed.

(Comment 4) One comment requested that FDA align § 106.30(e)(2)(ii) with the

Pasteurized Milk Ordinance, which specifies a maximum 45° F storage temperature for pasteurized milk and milk products. The comment said that if FDA does not concur with this revision, the capital costs to one or more manufacturers will be extensive, and that such costs were obviously not considered in the economic analysis of the regulation. Additionally, the comment stated that any capital improvements to facilities needed to comply will take considerably longer than the 150 days until the effective date.

(Response) As mentioned in the preamble to the final rule, the changes made in § 106.30(e)(2)(ii) allow the 45°F temperature permitted for pasteurized milk and milk products for in-process or final infant formula for a defined period of time provided that the manufacturer has scientific 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. Therefore, we do not estimate a need to make capital improvements related to complying with the requirements of § 106.30(e)(2)(ii) of the final rule, and no additional cost is estimated. Note that the final rule adopts a compliance date of 60 days after the effective date of this final rule for the requirements of § 106.30(e)(2)(ii) to facilitate manufacturer compliance. This delay does not affect the cost estimates.

4. Controls to prevent adulteration due to automatic equipment (§ 106.35)

The final rule requires that manufacturers validate automatic (mechanical and electronic) equipment and make and retain records concerning the proper functioning of automatic equipment.

(Comment 5) One comment stated that a “full” revalidation of a “system” for one plant would cost upwards of \$3 million. The comment claimed that, with multiple plants per company and possible inclusion of third party manufacturers, total costs would be significantly higher. The

comment also asserted that it would take approximately two years to complete a “full” system revalidation. The comment said that due to the nature of recurring validations, this is expected to be an ongoing cost recurring periodically. The comment stated that FDA may have underestimated the cost of these requirements.

(Response) As mentioned in the preamble to the final rule, we have revised § 106.35(b)(4) to clarify that validation can be accomplished through any suitable means, such as verification studies or modeling. It was not our intent to require “full” revalidations of a “system”; the RIA for the interim final rule already including the cost estimates for revalidation, therefore, no cost estimations will be added to the economic analysis for this activity.

5. General quality control (§ 106.91)

This section establishes requirements for two types of quality control testing for infant formulas: nutrient testing on the production aggregate and stability testing on packaged finished product.

(Comment 6) One comment stated that testing nutrient premixes, as required by § 106.91(a)(1), would result in formulas being tested twice: once by the premix supplier prior to the release of the premix and once by the infant formula manufacturer upon receipt of the premix. The comment asserted that this requirement adds cost without commensurate benefit.

(Response) As discussed in the interim final rule and the final rule, the requirement to test the premix, even if the manufacturer possesses a COA from the supplier, is required under the FD&C Act. The comment did not provide any data or evidence that demonstrates this requirement would result in costs not accounted for by the economic analysis in the interim final rule. Therefore, the costs are not reestimated in this final rule.

(Comment 7) One comment stated that the requirement in § 106.91(b) to conduct stability testing on every subsequent production aggregate is overly burdensome and unnecessary. The

comment stated that this requirement would generate redundant data and would add considerable costs for formulas.

(Response) As discussed in the preamble, the purpose of stability testing of subsequent production aggregates for nutrients, as required by § 106.91(b)(2), is to confirm that the nutrients present in an infant formula at the finished product stage do not degrade below minimum levels over the shelf life of the product. Every production aggregate must be at or above such minimum levels at the end of the shelf life of the product. The evidence that nutrient levels have been maintained at or above such minimum levels in each production aggregate is provided by the results of stability testing at the end of the shelf life of each production aggregate. This testing requirement will provide direct evidence that nutrient levels are maintained throughout the shelf life of infant formula products. We do note that the critical data are the nutrient levels present at the end of shelf life and that the midpoint data are not essential in subsequent production aggregates. Therefore, we have deleted the requirement to conduct stability testing at the midpoint of the shelf life for infant formulas tested under § 106.91(b)(2). To be conservative, the mean cost estimate presented in the analysis of the interim final rule for § 106.91, \$31,000 in the first year and in subsequent years, has not been reestimated.

6. Assurances of quality factors in new infant formulas, new infant formula submissions, and quality factor submissions (§§ 106.96, 106.120, and 106.121)

This final rule requires that a manufacturer of a new infant formula conduct a growth monitoring study to demonstrate that an infant formula supports normal physical growth, unless the manufacturer qualifies for an exemption from the need to conduct such a study (§ 106.96(b)). A manufacturer may request an exemption from the requirement for a growth monitoring study under certain circumstances. For example, a manufacturer may consider submitting such a request to FDA if it can provide assurances that an alternative method or study

design is based on sound scientific principles and can be shown to support normal physical growth in infants, or that the change made by the manufacturer to an existing formula does not affect the bioavailability of the nutrients in the formula.

(Comment 8) A comment estimated the cost of a 15-week clinical growth study to be \$2.5-\$3 million and questioned the source of the RIA estimate of \$500,000.

(Response) The comment did not provide any references to support the estimate of \$2.5-\$3 million per growth study. Furthermore, FDA's estimate of \$500,000 was based on information obtained by FDA from professionals who have designed and conducted clinical studies in infants and who have prepared budget estimates for grant proposals that included the activities described in the codified (Ref. 2). Therefore, we disagree that the estimate should be recalculated.

7. Comments on the Regulatory Impact Analysis of the Interim Final Rule

(Comment 9) One comment stated that FDA overstated the benefits presented in the RIA. The comment characterized the date range of the data used to calculate benefits as outdated and cited a reference (Ref 4) that provides worldwide average number of *Cronobacter* cases of 4.3 annually, as opposed to the upper bound average of four domestic cases per year, adjusted for underreporting, that was presented in the RIA. Based on the cited reference, the comment concluded that the RIA estimate of annual *Cronobacter* cases in the United States is likely to be overestimated.

(Response) It is correct that data after 2009 were not used in the estimate of average *Cronobacter* cases. However, we disagree with the comment for two reasons. First, the comment does not acknowledge that the estimate of mean annual benefits (\$10 million) acknowledges the possibility that benefits may be zero. Second, the comment's cited reference (Ref 4), while estimating a worldwide average of 4.3 annual cases of *Cronobacter*, states that the author could

only study available records of known cases of *Cronobacter* infections and that underestimation of infections in healthy, nonhospitalized infants may be one of several substantial limitations of the study. Due to this substantial limitation, we reject the reliance on this study as a sole basis for reestimating benefits, and we decline to change the estimation of mean annual benefits in the RIA.

B. Summary of Mean Costs and Mean Benefits of the Final Rule

Mean costs and mean benefits, estimated in the Regulatory Impact Analysis of the interim final rule, were not changed as a result of public comments. Table 2 presents mean costs and mean benefits of the final rule.

Table 2--Summary of Mean Costs and Mean Benefits of This Final Rule

Provisions Related to Good Manufacturing Practices	First Year	Annual After the First Year
§ 106.20--Controls to prevent adulteration caused by facilities	\$15,625	\$15,625
§ 106.30--Controls to prevent adulteration caused by equipment or utensils	\$3,100,000	\$3,100,000
§ 106.60--Controls to Prevent Adulteration During Packaging and Labeling of Infant Formula	\$39	\$39
§ 106.91--General quality control	\$31,000	\$31,000
§106.94--Audit plans and procedures	\$925	\$925
§ 106.100--Records pertaining to CGMP provisions	\$1,227,996	\$339,804
Administrative costs	\$298,000	\$0
Total Mean CGMP Provision Costs	\$4,673,585	\$3,487,393
<u>Provisions Related to Quality Factors</u>	<u>First Year</u>	<u>Annual After the First Year</u>
§§ 106.96, 106.120, and 106.121--Assurances of quality factors in new infant formulas, new infant formula submissions, and quality factor submissions	\$2,619,282	\$568,719
<u>Total Costs</u> ¹	\$7,292,867	\$4,056,112
<u>Mean quantified benefits</u> ²	\$10,000,000	\$10,000,000

¹Annualized first year mean costs are \$1,170,551 discounted at a rate of 3% over 7 years.

²Mean quantified benefits represent a range of benefits from \$0 to \$20 million.

Net quantified benefits are estimated to be about \$2.70 million in the first year and about \$6 million annually thereafter. The present value of annual net benefits is about \$74 million or \$116.54 million, given a 7 percent or 3 percent discount rate over 30 years. If this rule prevents nutritional deficiencies, then net benefits will be larger, as illustrated by the benefits of preventing human capital losses associated with developmental deficiencies for the 141 children with documented hypochloremic metabolic alkalosis in 1978 (Ref. 3). As presented in the discussion of benefits, preventing those effects would have resulted in benefits of about \$5.5 million or \$3.5 million, discounted at 3 percent or 7 percent, in addition to those benefits estimated from averted cases of *Cronobacter*.

III. Regulatory Flexibility Analysis for Final Rule

FDA has examined the economic implications of this final rule as required by the Regulatory Flexibility Act, 5 U.S.C. 601-612. If a rule has a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would lessen the economic effect of the rule on small entities. Because none of the manufacturers subject to this rule is a small entity, as defined by a firm that employs fewer than 500 employees, we certify that this final rule will not have a significant economic impact on a substantial number of small entities.

IV. Paperwork Reduction Act of 1995

This final rule contains information collection requirements that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520) (the PRA). The title, description, and respondent description of the information collection requirements are given in the following paragraphs, including estimates of

the one-time burden of developing an audit plan and audit procedures, developing production and in-process control systems, audit plans, one-time growth studies, and petitions submitted for eligible infant formulas. Annual burdens of batch production and control records, records pertaining to the distribution of infant formula, records pertaining to regularly scheduled audits, quality factor requirements, and registration and submission requirements are also estimated. Included in the burden 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.

In the July 9, 1996, proposed rule, FDA included an analysis of the information collection provisions of the proposal under the PRA and requested comments on four questions relevant to that analysis (61 FR at 36205-36206). Subsequently, in 2003, we reopened the comment period to update comments and to receive any new information on all issues, including on the PRA analysis (68 FR 22341). In response to these requests, FDA received no comments specifically referring to our 1996 PRA analysis or otherwise referring to the PRA. FDA did receive comments on the substantive provisions of the proposed rule, including comments on the proposed recordkeeping and other provisions of the proposal that would result in information collections. FDA has summarized and responded to these comments in this document.

As noted, the 1996 proposal included a PRA analysis. FDA is re-estimating the burden of this final rule using current burden analysis methodology. We had included a section titled "Paperwork Reduction Act of 1995" in the preamble to the interim final rule (79 FR 7934 at 8055 to 8056). Any comments on our analysis of the burdens presented in that section were submitted to OMB. We will not address these comments in this document. We are resubmitting the information collection provisions of this final rule to OMB because the final rule provides additional modifications and clarifications to 21 CFR Part 106.

We invite comments on new issues relating to the following topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Infant Formula Requirements--21 CFR Parts 106 and 107 (OMB Control Number 0910-0256)--Revision

These estimated annual recordkeeping burdens have changed from the burdens estimated for the OMB control number 0910-0256 (75 FR 67983; November 4, 2010). The estimated recurring burden for § 106.100 has decreased from 20,000 hours estimated in OMB Control No. 0910-0256 to 11,225.05 hours due to a revised estimate of the industry's current recordkeeping practices. In the interim final rule, and affirmed by the final rule, current § 106.120 was consolidated with current § 107.240 and recodified as § 106.150.

Description: This new collection of information will be performed by manufacturers of infant formula. The records requirements of this final rule include records pertaining to (1) production aggregate production and control; (2) growth studies and Protein Efficiency Ratio (PER) studies; (3) current good manufacturing practice and quality control; (4) distribution of infant formula; and (5) regularly scheduled audits, including audit plans and procedures. In addition, this final rule includes reporting requirements pertaining to (1) registration of new infant formula; (2) submission requirements for new infant formulas; (3) submissions before the

first production and introduction into interstate commerce to verify that the formula complies with the requirements of the FD&C Act; (4) submission requirements when there is a change in the formulation or processing of the formula that may affect whether the formula is adulterated; and (5) voluntary petition relating to eligible infant formulas.

FDA has concluded that recordkeeping and reporting are necessary for the success of the current good manufacturing practice and quality control procedures (including production aggregate control and distribution), quality factors, audits, and registration and notification requirements. Records of actions taken due to each requirement are essential for manufacturers to implement this rule effectively. Further, records and reports are essential for FDA to be able to determine whether a firm is in compliance with the rule.

Analysis of Burden Estimates Resulting from this Final Rule

Description of Respondents: Infant Formula Manufacturers

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

The total one-time estimated burden imposed by this collection of information is 35,630 hours. The total annual estimated burden imposed by this collection of information is 12,680.55 (11,225.05 recordkeeping hours + 1, 455.5) hours. There are no capital costs or operating and maintenance costs associated with this collection of information. The estimated burden for this final rule is based on "Evaluation of Recordkeeping Costs for Food Manufacturers," Eastern Research Group Task Order No. 5, Contract No. 223-01-2461. FDA estimates that firms will be able to fulfill recordkeeping requirements with existing record systems; that is, FDA estimates that it will not be necessary for infant formula firms to invest in new recordkeeping systems.

For records relating to CGMP requirements, the number of record keepers in column 2 of table 3 and table 4 is based on our expert estimation of the number of plants that may not already be adhering to the recordkeeping provisions of this final rule. The RIA estimated that 25 percent of

all infant formula plants were not currently adhering to the CGMP provisions under § 106.100 (5 out of 21 plants) and, unless otherwise specified, burdens are estimated based on these five plants. Furthermore, we estimate that plants will collect the same information across the various infant formulas produced by each firm. For records relating to quality factor requirements, the number of record keepers in column 2 of table 3 and table 4 varies according to the nature of the requirement and other factors identified in the discussion that follows.

The one-time burdens result from the need to develop production and in-process control systems, validation records, one-time growth studies, and petitions submitted to us for eligible infant formulas, and are presented in table 3. Development of in-process control systems and audit plans will both likely occur on the plant level. Petitions regarding eligible infant formulas will be developed per formulation. It is possible that one or more manufacturers of an eligible infant formula will choose to conduct a growth study of an infant formula formulation, and the information collection and recordkeeping for such studies, as well as any petitions developed for these eligible infant formulas, will also represent one-time burdens.¹

For records pertaining to production and in-process controls, FDA estimates that, at most, five plants will be required to develop production records to comply with § 106.6(c)(5) and § 106.100(e)(1) and (e)(3) (Ref. 1). A team of two senior validation engineers (or other similarly skilled employees) per plant (2 x 5 plants = 10 workers) will each need to work 20 hours to provide sufficient initial baseline records and documentation to develop records pertaining to production and in-process controls in order to comply with § 106.6(c)(5) and § 106.100(e)(1) of the final rule, for an industry total of 200 hours (2 workers x 5 plants x 20 hours = 200 hours), as presented in line 1 of table 3.

¹ Hourly burdens for infant formulas that are not eligible infant formulas are estimated on an annual basis.

For the recordkeeping requirement of § 106.35(c), in accordance with § 106.100(f)(5), FDA estimates that a team of ten senior validation engineers (or other similarly skilled employees) per plant will need to work full time for the 16 weeks (640 work hours per person) to provide sufficient initial records and documentation to comply with this section. The total burden for ten senior validation engineers each working 640 hours is 6,400 per plant in the first year (10 senior validation engineers x 640 hours = 6,400). For five plants, the total one-time hourly burden is 5 plants x 6,400 hours = 32,000 hours, as presented in line 2 of table 3.

Section 106.96(i) of the final rule outlines certain requirements for eligible infant formulas; these include the requirement that such infant formulas meet the quality factor of normal physical growth. It is estimated that among all eligible infant formulas, there are 50 formulations currently on the market that must satisfy the quality factor of normal physical growth (Ref. 2). It is likely that some eligible infant formulas will be the subject of a growth monitoring study; it is estimated that, for eligible infant formulas, industry will perform four growth studies one time as a result of the requirement of § 106.96(i)(1) (Ref. 2). It is assumed that the balance of the 50 eligible infant formulations (46 formulations) will comply with § 106.96(i)(1)(iii) by assembling from existing studies, data, and information a record that demonstrates that the formulation supports normal physical growth.

It is estimated that the data collection associated with a growth study performed to comply with § 106.96(i)(1) will be assembled into a written study report and that the study report will be kept as a record in compliance with § 106.96(i)(1)(i) or § 106.96(i)(1)(ii), § 106.96(i)(5), and § 106.100(p)(2). As noted, four growth studies of eligible infant formulas are estimated as a result of this final rule. Therefore, it is estimated that four growth study reports will be generated as a result of this final rule. It is estimated that one report will require one senior scientist to work 16 hours to compile these data into a comprehensive report. Therefore, four growth study reports x

16 hours = 64 hours for compliance with § 106.96(i)(1)(i) or § 106.96(i)(1)(ii), as presented in line 3 of table 3. Once prepared, the maintenance of the growth study report will also fulfill the requirements of §§ 106.96(i)(5) and 106.100(p)(2) without any additional quantifiable hourly burden.

The estimates for the information collection burden assume that the growth studies for eligible formulas will be conducted consistent with the requirements of § 106.96(b) of the final rule. The final rule (§ 106.96(b)(2)) requires that several pieces of data be collected and maintained for each infant at six visits during each such study. The burden estimates for these specific collections, as applied to eligible infant formulas, are discussed below.

A study conducted according to the requirements of § 106.96(b)(2) must include the collection of anthropometric measurements of physical growth and formula intake, and § 106.96(b)(3) requires that the anthropometric measurements be taken six times during the growth study. It is estimated that, in a growth study of 112 infants, two nurses or other health professionals with similar experience will need 15 minutes each per infant at each of the required six times to collect and record the required anthropometric measurements. Therefore, 2 nurses x 0.25 hours = 0.5 hour per infant, per visit, and 0.5 hour x 6 visits = 3 hours per infant. For 112 infants in a study, 3 hours x 112 infants = 336 hours to collect anthropometric information for one growth study. For four growth studies, this burden is 1,344 hours (336 hours x 4 studies), as presented in line 4 of table 3. In addition, it is estimated that one nurse will need 15 minutes per infant to collect and record the formula intake information. That is, 0.25 hour x 6 visits = 1.5 hour per infant, and 1.5 hour per infant x 112 infants = 168 hours to collect information on formula intake for one growth study. For four growth studies, this burden is 672 hours (168 hours x 4 studies), as presented in line 5 of table 3.

Section 106.96(b)(4) requires plotting each infant's anthropometric measurements on the

2009 CDC growth charts. This task is estimated to take five minutes per infant at each study visit. Therefore, six data plots x 112 infants = 672 total data plots, and 672 data plots x 0.08 hour per comparison = 53.75 total hours. For four growth studies, this burden is 215 hours (53.75 hours x 4 studies), as presented in line 6 of table 3.

Finally, § 106.96(b)(5) requires that data on formula intake by the test group be compared to that of the concurrent control group. FDA estimates that one nurse or other health care professional with similar experience will need five minutes per infant, for each of the six study visits, to fulfill the requirements of this section. Therefore, six comparisons of data x 112 infants = 672 data comparisons, and 672 data comparisons x 0.08 hour per comparison = 53.75 total hours. For four growth studies, this burden is 215 hours (53.75 hours x 4 studies), as presented in line 7 of table 3.

Section 106.100(p)(2) and (q)(2) require that, in accordance with § 106.96(i)(5), a manufacturer keep records demonstrating that an eligible infant formula fulfills one or more of the criteria listed in § 106.96(i)(1) and one or more of the criteria in § 106.96(i)(2). It is estimated that, for an eligible infant formula for which a growth study is performed, the records required by § 106.100(p)(2) are fulfilled by the growth study data collection and the study report and do not represent an additional quantifiable hourly burden to these manufacturers (Ref. 2). In addition, it is estimated that the records required by § 106.100(q)(2) are fulfilled by an infant formula firm by virtue of the current requirement in § 106.30(c)(2) to conduct a PER study, and thus, this requirement does not represent an additional quantifiable hourly burden (Ref. 2). For an eligible infant formula for which no growth study is performed, the recordkeeping burden of § 106.100(p)(2) is estimated to be 20 hours per record for each of 46 estimated formulations due to the need for manufacturers to compile existing data into a record. Therefore, 20 hours x 46

formulations = 920 hours for this subset of manufacturers to comply with § 106.100(p)(2), as presented in line 8 of table 3. This 920 hours represents the total industry burden for compliance with § 106.100(p)(2). This burden is estimated also to cover the requirements of § 106.96(i)(1)(iii), which state that an eligible infant formula meets the quality factor of normal physical growth if the scientific evidence on such infant formula otherwise demonstrates that such formula supports normal physical growth.

Section 106.96(i)(3), which establishes a voluntary petition process for eligible infant formulas, is estimated to be a one-time burden. Under § 106.96(i)(3), the manufacturer of an eligible infant formula may submit a citizen petition in accordance with 21 CFR 10.30 that demonstrates that such formula meets the quality factor of normal physical growth, demonstrates that such formula meets the quality factor of sufficient biological quality of the protein, or both. Each petition may address both quality factors but may only address one infant formula formulation. It is estimated that one petition will be submitted for each eligible infant formula formulation, including the four eligible infant formulas formulations for which growth studies are performed (Ref. 2). Section 106.96(i)(3) of the final rule refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by OMB under the PRA. The collections of information in § 10.30 have been approved under OMB control number 0910-0183 (General Administrative Procedures: Citizen Petitions; Petition for Reconsideration or Stay of Action; Advisory Opinions).

Accordingly, as shown in table 3, FDA estimates a total first-year only hourly burden of 35,630 hours.

Section 106.20(f)(3) requires that manufacturers conduct water testing at least annually for chemical contaminants, every 4 years for radiological contaminants, and weekly for bacteriological contaminants. FDA estimates that it is part of normal business practice for infant

formula plants to test for chemical contaminants and keep records of those tests on a regular basis; therefore, this requirement is not a new collection of information (Ref. 1).

However, it is estimated that the requirement to test at least every 4 years for radiological contaminants will represent a new collection of information for 21 infant formula plants (Ref. 1). In addition, it is estimated that collecting water for all testing in § 106.20(f)(3) takes between 1 and 2 hours (Ref. 1). For the purposes of this analysis, it is conservatively estimated that water collection takes, on average 1.5 hours and that water collection occurs separately for each type of testing. It is estimated that performing the test (collecting the information) will take 1.5 hours per test, every 4 years. Therefore, 1.5 hours per plant x 21 plants = 31.5 total hours, every 4 years, as seen in line 9 of table 3. Furthermore, § 106.20(f)(4) and § 106.100(f)(1) require firms to make and retain records of the frequency and results of water testing. For the 21 plants that are estimated not to currently test for radiological contaminants, this burden is estimated to be 5 minutes per record every 4 years. Therefore, 0.08 hour per record x 21 plants = 1.68 hours, every 4 years for the maintenance of records of radiological testing, as seen on line 10 of table 3.

It is estimated that the requirement to test weekly for bacteriological contaminants is a new burden for five infant formula plants. It is estimated that performing the test (collecting the information) will take 5 minutes per test once a week. Annually, this burden is 0.08 hours x 52 weeks = 4.16 hours per year, per plant, and 4.16 hours per plant x 5 plants = 20.8 total annual hours, as seen on line 11 of table 3. Furthermore, for the five plants that are estimated to not currently test weekly for bacteriological contaminants, this burden is estimated to be 5 minutes per record, every week. Therefore, 0.08 hour per record x 52 weeks = 4.16 hours per plant for the maintenance of records of bacteriological testing. Accordingly, 4.16 hours x 5 plants = 20.8 annual hours, as seen on line 12 of table 3.

The final rule requires that certain instruments be calibrated against a known reference standard, and that records of these calibration activities be made and retained (§§ 106.30(d) and 100.100(f)(2)); these records will be kept at the plant level. FDA estimates that one senior validation engineer (or other similarly skilled employee) for each of the five (at most) plants will need to spend about 13 minutes per week to satisfy the ongoing calibration recordkeeping requirements of §§ 106.30(d) and 100.100(f)(2). Therefore, 5 recordkeepers x 52 weeks = 260 records; 260 records x 0.21 hour per record = 55 hours as the total industry annual burden, as presented in line 13 of table 3

The final rule (§§ 106.30(e)(3)(iii) and 106.100(f)(3)) requires the making and retaining records of the temperatures of each cold storage compartment. Based on expert opinion, FDA estimates that five (at most) plants are not currently adhering to this recordkeeping provision, and that at each of these five plants, compliance will require one senior validation engineer (or other similarly skilled employee) about 13 minutes per week. Therefore, 5 recordkeepers x 52 weeks = 260 records; 260 records x 0.21 hours per record = 55 hours as the total industry annual burden, as presented in line 14 of table 3.

The final rule (§§ 106.30(f) and 100.100(f)(4)) requires the making and retention of records of ongoing sanitation efforts. Based on expert opinion, FDA estimates that five (at most) plants are not currently adhering to this recordkeeping provision, and that at each of these five plants, compliance will require one senior validation engineer (or other similarly skilled employee) about 12 minutes per week. Therefore, 5 recordkeepers x 52 weeks = 260 records; 260 records x 0.19 hours per record = 49.4 hours as the total industry annual burden, as presented in line 15 of table 3.

There will be annual recordkeeping associated with §§ 106.35(c) and 106.100(f)(5). It is estimated that one senior validation engineer (or other similarly skilled employee) per plant will

need to work 10 hours per week (520 work hours per year) to meet the ongoing recordkeeping requirements of this section. For the estimated five (at most) plants not adhering to the recordkeeping provisions of § 106.35, the total annual burden for this provision is 520 hours per plant x 5 plants = 2,600 annual hours, as shown in line 16 of table 3. In addition, an infant formula manufacturer will need to revalidate its systems when it makes changes to automatic equipment. FDA estimates that such changes are likely to occur twice a year to any aspect of the plant's system, and that on each of the two occasions, a team of four senior validation engineers (or other similarly skilled employees) per plant will need to work full time for 4 weeks (4 weeks x 40 hours per week = 160 work hours per person) to provide revalidation of the plant's automated systems sufficient to comply with this section. The total annual burden for four senior validation engineers each working 160 hours twice a year is 1,280 hours ((160 hours x 2 revalidations) x 4 engineers = 1,280 total work hours), per plant. Therefore, 1,280 hours per plant x 5 plants = 6,400 annual hours, as shown on line 17 of table 3.

Section 106.40(d) requires written specifications for ingredients, containers, and closures, and is considered a collection of information. FDA estimates that the infant formula industry already establishes written specifications for these components. However, the requirements of §§ 106.40(g) and 106.100(f)(6) may represent new recordkeeping for five (at most) plants (Ref. 1). It is not possible to predict how often a specification will not be met or how often documented reviews of reconditioned ingredients, closures, or containers will occur. FDA estimates that, on average, one senior validation engineer per plant will work about 10 minutes a week to fulfill the recordkeeping requirements of §§ 106.40(g) and 106.100(f)(6). Therefore, 5 recordkeepers x 52 weeks = 260 records and 260 records x 0.17 hour = 45 total annual hours, as presented in line 18 of table 3.

Records pertaining to § 106.50, the master manufacturing order and any changes to it,

will be kept at the plant level. It is not possible to predict how often changes to the master manufacturing order will be made or how often deviations from the master manufacturing order will occur. Based on expert opinion, FDA estimates that each year, 5 (at most) plants will change a master manufacturing order and that, on average, one senior validation engineer for each of the 5 (at most) plants will spend about 14 minutes per week on recordkeeping pertaining to the master manufacturing order, as required by §§ 106.50(a)(1) and 106.100(e). Thus, 5 recordkeepers x 52 weeks = 260 records; 260 records x 0.23 hour = 60 hours as the total annual industry burden, as presented in line 19 of table 3.

The final rule (§ 106.55(d) and § 106.100(e)(5)(ii) and (f)(7)) requires infant formula manufacturers to make and retain records of the testing of infant formula for microorganisms. Based on expert opinion, we estimate that these recordkeeping requirements represent a new collection of information for, at most, five plants (Ref. 1) and that one senior validation engineer per plant will spend 15 minutes per week on recordkeeping pertaining to microbiological testing. Thus, 5 record keepers x 52 weeks = 260 records; 260 records x 0.25 hour per record = 65 hours as the total annual industry burden, as presented in line 20 of table 3.

The final rule (§ 106.60) establishes requirements for the labeling of mixed-lot packages of infant formula. We estimate that § 106.60 will require infant formula diverters to label infant formula packaging (such as packing cases) to facilitate product tracing and to keep specific records of the distribution of these mixed lot cases. (A diverter is considered to be a business or individual that purchases food, including occasionally infant formula, in a geographic area where a special allowance or deal is being offered and then resells that food at a lower price to wholesale or retail grocery, drug and mass merchandise chains in an area where the deal is not being offered.) There will be some cost associated with this recordkeeping and labeling, but we estimate that this burden will be minimal as it is estimated that less than 1 percent of infant

formula is handled by diverters. For the purposes of this analysis, it is estimated that it may take one worker using manual methods 15 minutes, at most, to relabel one case of infant formula, one time each month ($0.25 \times 12 \text{ months} = 3 \text{ annual hours}$), to meet the requirements of § 106.60(c)(2), as presented in line 21 of table 3.

The final rule establishes nutrient testing requirements (§ 106.91(a)(1), (a)(2), (a)(3), and (a)(4)). It is estimated that the systems and processes of 100 percent of the formula industry adhere to these provisions. Therefore, nutrient testing does not represent a new collection of information or a new recordkeeping burden as nutrient testing is estimated to be common business practice in the infant formula industry. Thus, no burden is estimated for the requirements of § 106.91(a) (Ref. 1).

The final rule also establishes on-going stability testing requirements (§ 106.91(b)(1), (b)(2), and (b)(3)). It is estimated that the systems and processes of the formula industry partially adhere to these provisions in that 80 percent of infant formula plants (17 of 21 plants) conduct stability testing as specified in these provisions (Ref. 1). For the 20 percent of plants (4 of 21 plants) that do not conduct stability testing as specified in this provision, it is estimated that these plants do conduct initial stability testing, but may not do so at the intervals specified in this provision (Ref. 1). For the purposes of this analysis, it is estimated that the stability testing requirements of § 106.91(b) represent a new burden of 2 annual hours, per plant. Therefore, $2 \text{ hours} \times 4 \text{ plants} = 8 \text{ annual hours}$ to fulfill the testing requirements of § 106.91(b) as shown in line 22 of table 3.

The requirements of §§ 106.91(d) and 106.100(e)(5) to keep records of tests required under § 106.91(b)(1), (b)(2), and (b)(3) represent new information collections for the four plants that are estimated not to be conducting all of the stability testing specified in § 106.91(b) (Ref. 1). For the purposes of this analysis, FDA estimates that, for the testing requirements in §

106.91(b), one senior validation engineer per plant will spend about nine minutes per week maintaining records to be in compliance with § 106.91(d) and § 106.100(e)(5). Thus, 4 recordkeepers x 52 weeks = 208 records; 260 records x 0.15 hour per record = 31.2 hours, per testing requirement, as the annual total industry burden, as presented in lines 23, 24, and 25 of table 3.

FDA estimates that all infant formula manufacturers currently conduct audits in accordance with § 106.94, but that 25 percent of infant formula plants (5 of 21 plants) do not conduct audits that include all four elements required by this final rule (Ref. 1). It is estimated that the ongoing review and updating of audit plans will require a senior validation engineer 8 hours per year, per plant. Therefore, 8 hours x 5 plants = 40 annual hours to regularly review and update audit plans as shown in line 26 of table 3.

The final rule does not mandate a frequency of auditing. For the purposes of this analysis, FDA estimates that a manufacturer will choose to audit once per week. Each weekly audit is estimated to require a senior validation engineer 4 hours, or 52 weeks x 4 hours = 208 hours per plant. Therefore, the total annual burden for the estimated five plants not currently adhering to this provision to update audit plans is 208 hours x 5 plants = 1,040 hours, as shown in line 27 of table 3.

The final rule requires (§ 106.96) that a manufacturer of a new infant formula establish that the new infant formula supports normal physical growth. This will require that the manufacturer either conduct a growth monitoring study (§ 106.96(b)) or demonstrate to FDA's satisfaction that the formula is entitled to an exemption from the growth monitoring study requirement (§ 106.96(c)). FDA estimates that, as a result of the final rule, the industry as a whole will perform one additional growth study per year (Ref. 2). The final rule requires that

several pieces of data be collected and maintained for each infant in the growth study. It is estimated that the data collection associated with the growth study performed to comply with § 106.96(b) will be assembled into a written report and kept as a record in compliance with § 106.96(d) and § 106.100(p)(1). Thus, it is estimated that one additional growth study report will be generated as a result of this rule, and that this report will require one senior scientist to work 16 hours to compile the data into a study report. Therefore, one growth study report x 16 hours = 16 annual hours for compliance with § 106.96(d) and § 106.100(p)(1), as presented in line 28 of table 3.

The data required to be collected in a growth monitoring study will be collected for each infant at each of six visits of the study. The burden estimates for these collections have been calculated in a manner identical to that used to calculate the burden estimates for the one time burden for growth studies of eligible infant formulas.

A study conducted according to the requirements of § 106.96(b)(2) must include the collection of anthropometric measurements of physical growth and information on formula intake and § 106.96(b)(3) requires that the anthropometric measurements be made at six times during the growth study. It is estimated that in a growth study of 112 infants, two nurses or other health professionals with similar experience will need 15 minutes per infant at each of the required six times to collect and record the required anthropometric measurements. Therefore, 2 nurses x 0.25 hours = 0.5 hour per infant, per visit, and 0.5 hour x 6 visits = 3 hours per infant. For 112 infants in a study, 3 hours x 112 infants = 336 hours to collect anthropometric measurement information, as presented in line 29 of table 3. In addition, it is estimated that one nurse will need 15 minutes per infant to collect and record the formula intake information. That is, 0.25 hour x 6 visits = 1.5 hour per infant, and 1.5 hour per infant x 112 infants = 168 hours to collect information on formula intake, as presented in line 30 of table 3.

Section 106.96(b)(4) requires plotting each infant's anthropometric measurements on the 2009 CDC growth charts. It is estimated that it will take five minutes per infant to record the anthropometric data on the growth chart at each study visit. Therefore, 112 infants x 6 data plots = 672 total data plots, and 672 data plots x 0.08 hour per comparison = 53.75 total hours, as presented in line 31 of table 3.

Section 106.96(b)(5) requires that data on formula intake by the test group be compared to the intake of a concurrent control group. FDA estimates that, to fulfill the requirements of this section, one nurse or other health care professional with similar experience will need 5 minutes per infant for each of the six times anthropometric data are collected. Therefore, 6 comparisons of data x 112 infants = 672 data comparisons and 672 data comparisons x 0.08 hour per comparison = 53.75 total hours, as presented in line 32 of table 3.

Under § 106.96(c)(1), an infant formula manufacturer may be exempt from the requirements of § 106.96(b) if the manufacturer requests an exemption and provides assurances, as required under § 106.121, that the changes to the infant formula are limited to changing the type of packaging. A manufacturer may also be exempt under § 106.96(c)(2), if the manufacturer requests an exemption and provides assurances, as required under § 106.121 that demonstrates, to FDA's satisfaction, that an alternative method or study design is available to show that the formula supports normal physical growth in infants, that the change to an existing formula does not affect the bioavailability of the formula (including the bioavailability of its nutrients), or that the formulation is marketed in more than one form 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 the nutrient content and bioavailability. We estimate that 34 exemptions will be submitted annually and that each exemption will take 20 hours to assemble (Ref. 2). Therefore, 34 exemptions x 20 hours = 680 hours is the total annual industry

burden for § 106.96(c), as presented in line 1 of table 4.

Section 106.96(f) states that a manufacturer shall meet the quality factor of sufficient biological quality of the 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. Under § 106.96(g)(1), a manufacturer of infant formula may be exempt from this requirement if the manufacturer requests an exemption and provides assurances, as required under § 106.121, that changes made by the manufacturer to an existing infant formula are limited to changing the type of packaging. A manufacturer may also be exempt from this requirement under § 106.96(g)(2), if the manufacturer requests an exemption and provides assurances, as required under § 106.121, that demonstrates, to FDA's satisfaction, that the change to an existing formula does not affect the bioavailability of the protein. Finally, a manufacturer of infant formula may be exempt from this requirement under § 106.96(g)(3) if 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 show that the formula supports the quality factor for the biological quality of the protein. It is estimated that these requirements represent two information collections: submission of the PER results or submission of a request for an exemption when appropriate. FDA estimates that annually the infant formula industry will submit a total of 35 PER submissions: 34 exemption requests and the results of one PER study (Ref. 2).

A PER study conducted according to AOAC Official Method 960.48 will be 28 days in duration. It is estimated that there will be 10 rats in the control and test groups (20 rats total) and that food consumption and body weight will be measured at day zero and at 7-day intervals during the 28-day study period (a total of five records per rat). It is further estimated that measuring and recording food consumption and body weight will take five minutes per rat (Ref.

2). Therefore, 20 rats x 5 records = 100 records; 100 records x 0.08 hour per record = 8 hours to fulfill the requirements of § 106.96(f). Furthermore, it is estimated that a report based on the PER study will be generated and that this study report will take a senior scientist one hour to generate. Therefore a total of 9 hours will be required to fulfill the requirements for § 106.96(f): 8 hours for the PER study and data collection, and 1 hour for the development of a report based on the PER study, as presented in lines 33 and 34 of table 3. Therefore, the total recurring recordkeeping burden is 11,225.05 hours.

For the submission of the PER exemption, it is estimated that infant formula industry will submit 34 exemptions per year and that each exemption will take supporting staff 12 hours to prepare (Ref. 2). Therefore, 34 exemptions x 12 hours per exemption = 408 hours to fulfill the requirements of § 106.96(g), as presented in line 2 of table 4.

Sections 106.100(p)(1) and § 106.100(q)(1) require that, in accordance with § 106.96(d) and § 106.96(h), the manufacturer of an infant formula that is not an eligible infant formula make and retain records that demonstrate that each infant formula meets the quality factors of normal physical growth and sufficient biological quality of protein. It is estimated that these recordkeeping requirements are fulfilled by the burden of the growth study report and PER exemption and, when necessary, the report resulting from a PER study. Thus, § 106.100(p)(1) and § 106.100(q)(1) do not represent an additional quantifiable hourly burden to manufacturers (Ref. 2).

The final rule implements the statutory requirement of section 412(c)(1)(A) of the FD&C Act that infant formula manufacturers register with FDA before introducing a new infant formula into interstate commerce. FDA estimates that, for each of the four firms in the infant formula industry, one senior scientist or regulatory affairs professional will need 30 minutes to gather and record the required information for an infant formula registration made under §

106.110. The annual number of registrations for a new infant formula and the number of firms that will make such registrations is not known. However, it is estimated that, annually, the industry could register 35 new infant formulas (Ref. 2), or an average of about nine registrations per firm. Therefore, to comply with § 106.110, the total annual industry burden is 35 registrations x 30 minutes per registration = 17.5 hours, as presented in line 3 of table 4.

The final rule implements the statutory requirement of section 412(c)(1)(B) of the FD&C Act that infant formula manufacturers make a submission complying with section 412(d)(1) of the FD&C Act to FDA before introducing a new infant formula into interstate commerce. FDA estimates that, for each of the four firms in the infant formula industry, one senior scientist or regulatory affairs professional will need 10 hours to gather and record information needed for infant formula submissions made under § 106.120. This estimate includes the time needed to gather and record the information the manufacturer uses to request an exemption under § 106.91(b)(1)(ii) of the final rule, which states that 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 formula with similar composition, processing, and packaging for which there are extensive stability data. The annual number of submissions for a new infant formula and the number of firms that will make such submissions is not known. However, it is estimated that, annually, the industry could make submissions for 35 new infant formulas, or an average of about nine submissions per firm (Ref. 2). Therefore, to comply with § 106.120, the total annual industry burden is 35 submissions x 10 work hours per submission = 350 hours, as presented in line 4 of table 4

Section 106.121 states that manufacturers shall submit data and information to FDA in order to provide assurances establishing that a new infant formula meets the requirements for quality factors set forth in § 106.96. FDA estimates that this requirement could be satisfied by

the submission of the written report of the growth monitoring study required by § 106.96(b), the burden of this provision is covered by the burden of developing the written report for a growth study. Accordingly, no additional quantifiable hourly burden is estimated for § 106.121.

The submissions under §§ 106.130, 106.140 and 106.150 must be made to satisfy the requirements of section 412(c) and (d) of the FD&C Act. Based on expert opinion, and because these submissions are currently made as required under the FD&C Act, it is estimated that the infant formula industry is adhering to these submission provisions. Furthermore, § 106.150 of the final rule is a consolidation recodification of current §§ 106.120 and 107.240(a) and (b), for which there is an existing OMB approval for the information collection. Therefore, no annual hourly burdens are estimated for these sections of this final rule.

Therefore, the total annual submission burden is 1,455.5 hours.

In compliance with the PRA, FDA has submitted the information collection provisions of this final rule to OMB for review. Prior to the effective date of this final rule, FDA will publish a notice in the Federal Register announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. 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.

Table 3.--Estimated Hourly Recordkeeping Burden¹

First Year Hourly Burden						
	21 CFR Section	No. of Record keepers	First Year Frequency of Recordkeeping	Total Records	Hours Per Record	Total Hours
1	Production and In-Process Control System 106.6(c)(5) and 106.100(e)(1) and (e)(3)	10	1	5	40	200
2	Controls to Prevent Adulteration due to Automatic (mechanical or electronic) Equipment 106.35(c) and 106.100(f)(5) 106.94	50	1	5	6,400	32,000
3	Requirements for Quality Factors For Eligible Infant Formulas-- Written Study Report 106.96(i)(1)(i) or 109.96(i)(1)(ii), 106.96(i)(5), and 106.100(p)(2)	4	1	4	16	64
4	Requirements for Quality Factors For Eligible Infant Formulas-- Anthropometric Data 106.96(i)(1), 106.96(i)(3), and 106.96(i)(4)	896	1	2688	0.5	1,344
5	Requirements for Quality Factors For Eligible Infant Formulas-- Formula Intake 106.96(i)(1), 106.96(i)(3), and 106.96(i)(4)	448	1	2,688	0.25	672
6	Requirements for Quality Factors For Eligible Infant Formulas-- Data Plotting 106.96(i)(1), 106.96(i)(3), and 106.96(i)(4)	4	1	2,688	0.08	215
7	Requirements for Quality Factors For Eligible Infant Formulas Data Comparison 106.96(i)(1), 106.96(i)(3), and 106.96(i)(4)	4	1	2,688	0.08	215
8	Quality Factors--Records 106.96(i)(1)(iii) and 106.100(p)(2)	5	1	46	20	920

Total First Year Only Hourly Recordkeeping Burden	-	-	-	-	<u>35,630</u>
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Recurring Hourly Burden

	21 CFR Section	No. of Record keepers	Annual Frequency of Recordkeeping	Total Records	Hours per Record	Total Hours
9	Controls to Prevent Adulteration Caused By Facilities-- Testing For Radiological Contaminants ² 106.20(f)(3)	21	1	21	1.5	31.5
10	Controls to Prevent Adulteration Caused By Facilities-- Recordkeeping of Testing For Radiological Contaminants ² 106.20(f)(4) and 106.100(f)(1)	21	1	21	.08	1.75
11	Controls to Prevent Adulteration Caused By Facilities--Testing For Bacteriological Contaminants 106.20(f)(3)	5	52	260	0.08	20.8
12	Controls to Prevent Adulteration Caused By Facilities-- Recordkeeping of Testing For Bacteriological Contaminants 106.20(f)(4) and 106.100(f)(1)	5	52	260	0.08	20.8
13	Controls to Prevent Adulteration By Equipment or Utensils 106.30(d) and 106.100(f)(2)	5	52	260	0.21	55
14	Controls to Prevent Adulteration By Equipment or Utensils 106.30(e)(3)(iii) and 106.100(f)(3)	5	52	260	0.21	55
15	Controls to Prevent Adulteration By Equipment or Utensils 106.30(f) and 106.100(f)(4)	5	52	260	0.19	49.4
16	Controls to Prevent Adulteration Due to Automatic (Mechanical or Electronic) Equipment 106.35(c) and 106.100(f)(5)	5	52	5	520	2,600
17	Controls to Prevent Adulteration Due to Automatic (Mechanical or Electronic) Equipment 106.35(c) and 106.100(f)(5)	20	2	10	640	6,400
18	Controls to Prevent Adulteration Caused By Ingredients, Containers, and Closures 106.40(g) and 106.100(f)(6)	10	52	260	0.17	45
19	Controls to Prevent Adulteration During Manufacturing 106.50 and 106.100(e)	10	52	260	0.2	60
20	Controls to Prevent Adulteration From Microorganisms 106.55(d), 106.100(e)(5)(ii), and 106.100(f)(7)	5	52	260	0.25	65

21	Controls to Prevent Adulteration During Packaging and Labeling of Infant Formula 106.60(c)	1	12	12	.25	3
22	General Quality Control-Testing 106.91(b)(1), 106.91(b)(2) and 106.91(b)(3)	4	1	4	2	8
23	General Quality Control 106.91(b)(1), 106.91(d), and 106.100(e)(5)(i)	4	52	208	0.15	31.2
24	General Quality Control 106.91(b)(2) 106.91(d), and 106.100(e)(5)(i)	4	52	208	0.15	31.2
25	General Quality Control 106.91(b)(3) 106.91(d), and 106.100(e)(5)(i)	4	52	208	0.15	31.2
26	Audit Plans and Procedures 106.94--Ongoing review and updating of Audits	5	1	5	8	40
27	Audit Plans and Procedures 106.94- Regular Audits	5	52	260	4	1040
28	Requirements for Quality Factors For Infant Formulas--Written Study Report 106.96(b), 106.96(d), 106.100(p)(1) , 106.100(q)(1), and 106.121	1	1	1	16	16
29	Requirements for Quality Factors For Infant Formulas--Anthropometric Data 106.96(b)(2), 106.96(d), and 106.100(p)(1)	2 2 4	6	672	0.5	336
30	Requirements for Quality Factors For Infant Formulas--Formula Intake 106.96(b)(3) and 106.96(d), and 106.100(p)(1)	1 1 2	6	672	0.25	168
31	Requirements for Quality Factors For Infant Formulas--Data Plotting 106.96(b)(4), 106.96(d), and 106.100(p)(1)	1	6	672	0.08	53.7 5
32	Requirements for Quality Factors For Infant Formulas--Data Comparison 106.96(b)(5), 106.96(d), and 106.100(p)(1)	1	6	672	0.08	53.7 5
33	Requirements for Quality Factors--PER Data Collection 106.96(f)	1	1	1	8.	8.
34	Requirements for Quality Factors--PER Written Report 106.96(f)	1	1	1	1	1
	Total Recurring Recordkeeping Burden					11,2 25.0 5
	Total Recordkeeping Burden					46,8 55.0 5

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

²This test is required no less frequently than once every 4 years.

Table 4.--Estimated Annual Submission Burden¹

	21 CFR Section	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Records	Hours per Record	Total Hours
1	Requirements for Quality Factors GMS Exemption 106.96(c)	4	9 (8.5)	34	20	680
2	Requirements for Quality Factors-- PER Exemption 106.96(g)	1	1	34	12	408
3	New Infant Formula Registration 106.110	4	9 (8.5)	35	.5	17.5
4	New Infant Formula Submission 106.120	4	9 (8.5)	35	10	350
	Total Annual Submission Hours					1,455.5

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

V. References

The following references have been placed on display in the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. We have verified all the Web site addresses in the References section, but we are not responsible for any subsequent changes to the Web sites after this document is uploaded to dockets.

1. Zink, Don. Statement of Donald L. Zink, Ph. D.: Infant Formula Manufacturing Practices, 2013.
2. Silverman, B. Statement of Benson M. Silverman, M.D. "Industry Efforts to Meet Quality Factor Requirements," 2013.
3. Dickinson, D.L. and R.L. Verbeek. "Wage Differentials Between College Graduates With and Without Learning Disabilities," Journal of Learning Disabilities 39: 175-184.
4. Jason, Janine. "Prevention of Invasive *Cronobacter* Infections in Young Infants Fed Powdered Infant Formulas," Pediatrics 130: 1076-1084, 2012.