Infant Formula Requirements
OMB Control No. 0910-0256
RIN: 0910-AF27

SUPPORTING STATEMENT, Part A

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

Statutory requirements for infant formula under the Federal Food, Drug, and Cosmetic Act (the FD&C Act) are intended to protect the health of infants and include a number of reporting and recordkeeping requirements. Among other things, section 412 of the FD&C Act (21 U.S.C. 350a) requires manufacturers of infant formula to establish and adhere to quality control procedures, notify FDA when a batch of infant formula that has left the manufacturers' control may be adulterated or misbranded, and keep records of distribution. We have issued regulations to implement the FD&C Act's requirements for infant formula in 21 CFR parts 106 and 107, which covers the labeling of infant formula under the authority of section 403 of the FD&C Act (21 U.S.C. 343). Under our regulations, the label of an infant formula must include nutrient information and directions for use. The purpose of these labeling requirements is to ensure that consumers have the information they need to prepare and use infant formula appropriately.

This information collection approval request is for all information requirements imposed by the regulations listed below:

21 CFR part 106, *Infant Formula Requirements Pertaining To Current Good Manufacturing Practice, Quality Control Procedures, Quality Factors, Records And Reports, And Notifications*; and

21 CFR part 107, *Infant Formula*.

2. Purpose and Use of the Information Collection

This information is used by the agency and industry to ensure the availability of safe infant formula through compliance with the requirements associated with infant formula development, production, and distribution. The information is also used by consumers when purchasing, storing, and preparing infant formula as well as to confirm that the nutrient requirements of the FD&C Act have been met.

Description of Respondents: Respondents to this information collection are manufacturers of infant formula. Respondents are from the private sector (for-profit businesses).

3. Use of Improved Information Technology and Burden Reduction

We expect that 100% of the infant formula manufacturers will use electronic means for the required recordkeeping. For petitions or notifications, we expect that 50% will be electronically submitted. Because such submissions contain technical material specifically related to the infant formula, respondents may choose their preferred format for submission as long as the required information is included.

4. Efforts to Identify Duplication and Use of Similar Information

There is no duplicative information collection as a result of the infant formula regulations. The data recorded are specific to the individual processing facilities. No other regulation or information collection duplicates this effort. There are no similar data that can be used or modified for use.

5. Impact on Small Businesses or Other Small Entities

Using the Small Business Administration's definition of small business for food manufacturers of 500 employees or fewer (up to 1,000 employees for some industries), and Dun & Bradstreet data on firm size, FDA estimates that no small firms will be affected by the provisions in this information collection. However, FDA does aid small businesses in complying with its regulatory requirements through the agency's Regional Small Business Representatives and through the scientific and administrative staffs within the agency. FDA has provided a Small Business Guide on the agency's website at http://www.fda.gov/oc/industry/.

6. Consequences of Collecting the Information Less Frequently

FDA has concluded that the recordkeeping and reporting requirements are necessary to ensure compliance with the current good manufacturing practice and quality control procedures (including production aggregate control and distribution), quality factors, audits, and registration and notification provisions. Records of actions taken due to each requirement are essential for manufacturers to implement these provisions effectively. We believe these burdens are the minimum necessary to meet the requirements of the FD&C Act.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There are no special circumstances for this collection of information.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

8a. Publication in the Federal Register

In accordance with 5 CFR 1320.8(d), FDA provided opportunity for public comment on the information collection requirements associated with its infant formula regulations in a proposed rule that published July 9, 1996 (61 FR 36154). Another opportunity for public

comment on the information collection requirements came April 28, 2003 (68 FR 22341). Still another opportunity for public comment was provided February 10, 2014 (79 FR 7934) regarding the information collection provisions associated with infant formula. Finally, on June 10, 2014 (79 FR 33057), again provided opportunity for public comment regarding its infant formula regulations, including the information collection requirements. Although some comments were received, none pertained to the information collection provisions covered by the PRA and are therefore not discussed in this document.

8b. Outside Consultation

Given the lack of data on current practices in the infant formula industry, we identified individuals with experience who could inform us on industry's current good manufacturing practice and aide in the estimation of the burden of information collection. This information served to supplement agency expertise regarding burden estimates associated with the regulatory impact of the infant formula regulations. Specifically, on November 24, 2009, a phone meeting was conducted between the infant formula GMP rule working group and a representative of Fujitsu America with extensive experience in infant formula manufacturing. The meeting consisted of a question and answer discussion on general issues regarding the manufacturing of infant formula. Subsequent e-mail communications on follow up issues, including questions on information collection, were made on 04/08/2011, 08/01/2011, and 09/02/2011. Furthermore, one of CFSAN's internal experts contacted three former colleagues in the infant formula industry to anonymously answer a questionnaire regarding practices in infant formula manufacturing.

9. Explanation of Any Payment or Gift to Respondents

FDA does not provide any payment or gift to respondents.

10. Assurance of Confidentiality Provided to Respondents

Information submitted to FDA under the infant formula regulations may contain trade secret and commercial confidential information. Only information that is releasable under the agency's regulations in 21 CFR part 20 would be released to the public. This information is also safeguarded by Section 301(j) of the FD&C Act and would be protected from disclosure under the Freedom of Information Act (FOIA) under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)).

11. Justification for Sensitive Questions

This collection of information does not involve questions that are of a personally sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

FDA estimates the burden of this collection as follows:

Table 1.—Estimated Annual Reporting Burden[1]

Row No.	Activity; 21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response (in hours)	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	34	34	12	408
3	New Infant Formula Registration; 106.110	4	9(8.5)	35	.5 (30 min.)	18
4	New Infant Formula Submission; 106.120	4	9 (8.5)	35	10	350
	TOTAL					1,456 (1455.5)

[1] Where necessary, numbers have been rounded to the nearest whole number.

It is estimated that that 34 exemptions will be submitted annually and that each exemption will take 20 hours to assemble (Silverman Statement 2011). Therefore, 34 exemptions x 20 hours = 680 hours is the total estimated burden for §106.96(c), as presented in row 1 of Table 1.

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 (Silverman Statement 2011). 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 (Silverman Statement 2011). Therefore, 34 exemptions x 12 hour per exemption = 408 hours to fulfill the requirements of §106.96(g), as presented in row 2 of Table 1.

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 pursuant to §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 (Silverman Statement 2011), or an average of about nine (8.5) registrations per firm. Therefore, to comply with §106.110, the total annual industry burden is 35 registrations x 30 minutes per registration = 17.5 (18) hours, as presented in row 3 of Table 1.

FDA estimates that, for each of the four firms in the infant formula industry, one senior scientist or regulatory affairs professional will need ten hours to gather and record information needed for infant formula submissions made pursuant to §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 (8.5) submissions per firm (Silverman Statement 2011). 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 row 4 of Table 1. Thus, the total annual submission burden is 1,455.5 (rounded to 1,456) hours.

Table 2. –Estimated Annual Recordkeeping Burden[1]

First Year Hourly Burden						
Row No.	Activity; 21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Avg. Burden per Recordkeeping	Total Hours
1	Production and In-Process Control System; 106.6(c)(5) and 106.100(e)(1) and (e)(3)	5	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	5	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)(4), 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)	672	4	2688	0.5 (30 min.)	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)	672	4	2688	0.25 (15 min.)	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)	672	4	2,688	0.08 (5 min.)	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)	672	4	2,688	0.08 (5 min.)	215

8	Quality Factors—Records; 106.96(i)(1)(iii) and 106.100(p)(2)	46	1	46	20	920
TOTAL (first year only)						35,630
Recurring Hourly Burden						
Row No.	21 CFR Section	Number 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 (90 min.)	32
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 (5 min.)	2
11	Controls to prevent adulteration caused by facilities – testing for bacteriological contaminants 106.20(f)(3)	5	52	260	.08 (5 min.)	21
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	08 (5 min.)	21
13	Controls to prevent adulteration by equipment or utensils; 106.30(d) and 106.100(f)(2)	5	52	260	0.21 (13 min.)	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 (13 min.)	55
15	Controls to prevent adulteration by equipment or utensils; 106.30(f) and 106.100(f)(4)	5	52	260	0.19 (12 min.)	49
16	Controls to prevent adulteration due to automatic (mechanical or electronic) equipment; 106.35(c) and 106.100(f)(5)	5	1	5	520	2,600

17	Controls to prevent adulteration due to automatic (mechanical or electronic) equipment 106.35(c) and 106.100(f)(5)	5	2	10	640	6,400
18	Controls to prevent adulteration caused by ingredients, containers, and closures; 106.40(g) and 106.100(f)(6)	5	52	260	0.17 (10 min.)	44
19	Controls to prevent adulteration during manufacturing; 106.50 and 106.100(e)	5	52	260	0.2 (14 min.)	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 (15 min.)	65
21	Controls to prevent adulteration during packaging and labeling of infant formula; 106.60(c)	1	12	12	.25 (15 min.)	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 (9 min.)	31
24	General quality control; 106.91(b)(2) 106.91(d), and 106.100(e)(5)(i)	4	52	208	0.15 (9 min.)	31
25	General quality control; 106.91(b)(3) 106.91(d), and 106.100(e)(5)(i)	4	52	208	0.15 (9 min.)	31
26	Audit plans and procedures; ongoing review and updating of audits; 106.94	5	1	5	8	40
27	Audit plans and procedures – regular audits; 106.94	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)	112	6	672	0.5 (30 min.)	336

30	Requirements for quality factors for infant formulas—formula intake 106.96(b)(3) and 106.96(d), and 106.100(p)(1)	112	6	672	0.25 (15 min.)	168
31	Requirements for quality factors for infant formulas—data plotting; 106.96(b)(4), 106.96(d), and 106.100(p)(1)	112	6	672	0.08 (5 min.)	54
32	Requirements for quality factors for infant formulas—data comparison; 106.96(b)(5), 106.96(d), and 106.100(p)(1)	112	6	672	0.08 (5 min.)	54
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 Burden					11,225 (11,225.05)
	TOTAL					46,855 (46,855.05)

[1] Where necessary, numbers have been rounded to the nearest whole number.
[2] This testing only occurs every four years.

The total one-time estimated burden imposed by this collection of information is 35,630 hours. Thereafter, the total annual estimated burden imposed by this collection of information is 12,680.55 (11,225.05 recordkeeping hours + 1, 455.5) hours. 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.

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), §106.100(e)(1), and §106.100(e)(3) (Zink Statement 2010). 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 row 1 of Table 2. For the purposes of this table, the number of recordkeepers is shown as 5 (teams).

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 row 2 of Table 2. For the purposes of this table, the number of recordkeepers is shown as 5 (teams).

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)(4), 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 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 row 3 of Table 2.

A clinical growth 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 .25 hours = .5 hour per infant, per visit, and .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 row 4 of Table 2.

In addition, it is estimated that one nurse will need 15 minutes per infant to collect and record the formula intake information. That is, .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 row 5 of Table 2.

Section §106.96(b)(4) requires plotting each infant's anthropometric measurements on the CDC-recommended WHO 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 .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 row 6 of Table 2.

Finally, section §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 .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 row 7 of Table 2.

Final §106.100(p)(2) and §106.100(q)(2) require that, in accordance with §106.96(i)(4), 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 (Silverman Statement 2011). 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 21 CFR 106.30(c)(2) to conduct a PER study, and thus, this requirement does not represent an additional quantifiable hourly burden (Silverman Statement 2011). 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 row 8 of Table 2. 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.

Accordingly, as shown in Table 2, FDA estimates a total first year only hourly burden of 35,630 hours.

It is estimated that the requirement to test at least every four years for radiological contaminants will represent a new collection of information for 21 infant formula plants (Zink Statement 2010). In addition, it is estimated that collecting water for all testing in §106.20(f)(3) takes between one and two hours (Zink Statement 2013). 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 four years. Therefore, 1.5 hours per plant x 21 plants = 31.5 total hours, every four years, as seen in row 9 of Table 2. 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 five minutes per record every four years. Therefore, .08 hour per record x 21 plants = 1.68 hours, every four years for the maintenance of records of radiological testing, as seen on row 10 of Table 2.

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 five minutes per test once a week. Annually, this burden is .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 row 11 of Table 2. Furthermore, for the five plants that are estimated to not currently test weekly for bacteriological contaminants, this burden is estimated to be five minutes per record, every week. Therefore, .08 hour per record x 52 weeks =4.16hours, per plant for the maintenance of records of bacteriological testing. Accordingly, 4.16 hours x 5 plants = 20.8 annual hours, as seen on row 12 of Table 2.

The regulations require 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 record keepers x 52 weeks = 260 records; 260 records x .21 hour per record = 55 hours as the total industry annual burden, as presented in row 13 of Table 2.

The regulations under §106.30(e)(3)(iii) and §106.100(f)(3)) require 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 record keepers x 52 weeks = 260 records; 260 records x .21 hours per record = 55 hours as the total industry annual burden, as presented in row 14 of Table 2.

Sections §106.30(f) and §100.100(f)(4) require 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 record keepers x 52 weeks = 260 records; 260 records x .19 hours per record = 49.4 hours as the total industry annual burden, as presented in row 15 of Table 2.

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 ten 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 row 16 of Table 2. 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 four 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 =1280 total work hours), per plant. Therefore, 1280 hours per plant x 5 plants = 6,400 annual hours, as shown on row 17 of Table 2.

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 (Zink Statement 2013). 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 record keepers x 52 weeks = 260 records and 260 records x .17 hour = 45 total annual hours, as presented in row 18 of Table 2.

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 record keepers x 52 weeks = 260 records; 260 records x .23 hour = 60 hours as the total annual industry burden, as presented in row 19 of Table 2.

Sections §106.55(d), §106.100(e)(5)(ii), and §106.100(f)(7)) require infant formula manufacturers to make and retain records of the testing of infant formula for microorganisms. Based on expert opinion, the agency estimates that these recordkeeping requirements represent a new collection of information for, at most, five plants (Zink Statement 2013) 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 .25 hour per record = 65 hours as the total annual industry burden, as presented in row 20 of Table 2.

Section §106.60 establishes requirements for the labeling of mixed-lot packages of infant formula. The agency estimates 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. 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 (.25 x 12 months = 3 annual hours), to meet the requirements of §106.60(c)(2), as presented in row 21 of Table 2.

The regulations also establish on-going stability testing requirements (§106.91(b)(1), §106.91(b)(2), and §106.91(b)(3)). It is estimated that the systems and processes of the formula industry partially adhere to these provisions in that 80% of infant formula plants (17 of 21 plants) conduct stability testing as specified in these provisions (Zink Statement 2013). For the 20% 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 (Zink Statement 2013). 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 hours x 4 plants = 8 annual hours to fulfill the testing requirements of §106.91(b) as shown in row 22 of Table 2.

The requirements of §106.91(d) and §106.100(e)(5) to keep records of tests required under §106.91(b)(1), §106.91(b)(2), and §106.91(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) (Zink Statement 2013). 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 record keepers x 52 weeks = 208 records; 260 records x .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 2.

It is estimated that the ongoing review and updating of audit plans will require a senior validation engineer eight hours per year, per plant. Therefore, 8 hours x 5 plants = 40 annual hours to regularly review and update audit plans as shown in row 26 of Table 2.

The regulations do 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 four 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 row 27 of Table 2.

FDA estimates that, as a result of the regulations, the industry as a whole will perform one additional growth study per year (Silverman Statement 2011), in accordance with §106.96. The regulations require 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 the regulations, 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 row 28 of Table 2.

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 .25 hours = .5 hour per infant, per visit, and .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 row 29 of Table 2. In addition, it is estimated that one nurse will need 15 minutes per infant to collect and record the formula intake information. That is, .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 row 30 of Table 2.

Section §106.96(b)(4) requires plotting each infant's anthropometric measurements on the CDC-recommended WHO Child Growth Standards. 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 .08 hour per comparison = 53.75 total hours, as presented in row 31 of Table 2.

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 five 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 .08 hour per comparison = 53.75 total hours, as presented in row 32 of Table 2.

The requirements of §106.96(f) state 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 §106.100(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 (Silverman Statement 2011).

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. Therefore, 20 rats x 5 records = 100 records; 100 records x .08 hour minutes 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 2. Therefore, the total recurring recordkeeping burden is 11,225.05 hours.

12b. Annualized Cost Burden Estimate

Table 3.—Annualized Cost Burden Estimate

First Year Only				
21 CFR Part	**Type of Respondent**	**Total Burden Hours**	**Hourly Wage Rate**	**Total Respondent Costs**
§106.35(c), §106.100(f)(5)	Senior Validation Engineer	32,000	$46.26	$1,480,320
§106.100(e)(1), (e)(3)	Senior Validation Engineer	200	$46.26	$9,252
§106.96	Scientist	3,430	$54.96	$188,512.80
Total				$1,678,084.80
Annual Cost				
21 CFR Part	**Type of Respondent**	**Total Burden Hours**	**Hourly Wage Rate**	**Total Respondent Costs**
§106.20	Scientist	74.78	$46.26	$3,459.32
§106.30(f), §106.100(f)(5)	Senior Validation Engineer	159.4	$46.26	$7,373.84
§106.35(c), §106.100(f)(5)	Senior Validation Engineer	9,000	$46.26	$416,340
§106.40(g), §106.100(f)(6)	Senior Validation Engineer	45	$46.26	$2,081.70
§106.50, §106.100(e)	Senior Validation Engineer	60	$46.26	$2,775.60
§106.55, §106.100(e)(5)(ii), (f)(7)	Senior Validation Engineer	65	$46.26	$3,006.90
§106.60	Line Worker	3	$26.24	$78.42
§106.91(b),§106.91(d), §106.100(e)	Scientist	101.6	$46.26	$4,700.02
§106.94	Senior Validation Engineer	1,080	$46.26	$49,960.80
§106.96(b),(d), §1006.100(p)	Scientist	627.5	$54.96	$34,487.40
§106.96(c)	Scientist	680	$54.96	$37,372.80
§106.96(f)	Scientist	9	$54.96	$494.64
§106.96(g)	Support Staff	408	$27.23	$11,109.84
§106.110	Support Staff	17.5	$27.23	$476.53
§106.120	Scientist	350	$54.96	$19,236
Total Cost				$592,953.81

One-Time Costs

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 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. FDA estimates average compensation for a senior validation engineer to be about $46.26 per hour, including overhead (Bureau of Labor Statistics a). The total cost for ten senior validation engineers each working 640 hours at $46.26 per hour is $301,760 per plant in the first year (10 senior validation engineers x 640 hours = 6,400, and 6,400 work hours x 5 (at most)plants = 32,000 hours, and $46.26/hour x 32,000 hours= $1,480,320.

It is estimated that a senior engineer will need a total of 200 hours to establish records that include complete information relating to the production and control of the production aggregate, (§106.100(e)(1)). A manufacturer is required to maintain records pertaining to current good manufacturing practice, (§106.100(e)(3)). At a wage rate of $46.26 per hour (Bureau of Labor Statistics a), this cost is estimated to be $46.26 x 200 = $9,252. It is estimated that the one-time recordkeeping burden of 106.96(i)(4) is fulfilled by scientists working for a total of 3,215 hours to gathering data into records. At a wage rate of $54.96 per hour, the total one-time cost for scientists is 3,215 work hours x $54.96 = $188,512.80 (Bureau of Labor Statistics b). Accordingly, the total one-time labor cost is $1,678,084.80.

Recurring Costs

It is estimated that scientists will have to work 74.78 total hours to comply with the testing requirements of §106.20. At a wage rate of $46.26/hour (Bureau of Labor Statistics a), the labor cost of this information collection is estimated to be $46.26 x 74.78 hours = $3,459.32.

It is estimated that fulfilling the recordkeeping requirements of §106.30(f) will require senior validation engineers to spend 159.4 hours on these requirements. At a wage rate of $46.26/hour, the labor cost of this information collection is estimated to be $46.26 x 159.4 = $7,373,84.

It is estimated that fulfilling the recordkeeping requirements of §106.35 will require senior validation engineers to work a total of 9,000 hours annually. At a wage of $46.26/per hour), this cost is estimated to be 9,000 hours x $46.26/hour = $416,340.

It is estimated that fulfilling the recordkeeping requirements of §106.40(g) will require senior validation engineers to work a total of 46.26 hours annually. At a wage of $46.26/per hour, this cost is estimated to be 446.26 hours x $46.26/hour = $2,081.70.

It is estimated that fulfilling the recordkeeping requirements of §106.50 will require senior validation engineers to work a total of 60 hours annually. At a wage of $46.26/per hour, this cost is estimated to be 60 hours x $46.26/hour = $2,775.60.

It is estimated that fulfilling the recordkeeping requirements of §106.55 will require senior validation engineers to work a total of 65 hours annually. At a wage of $46.26/per hour, this cost is estimated to be 65 hours x $46.26/hour = $3,006.90.

It is estimated that it may take one worker, at most, 15 minutes to re-label one case of infant formula, one time each month (.25 x 12 months = 3 annual hours), using manual methods, to meet the requirements of §106.60(c)(2). At a wage of $26.24 per hour, including overhead (Bureau of Labor Statistics c), the maximum cost of meeting the requirement of §106.60(c)(2) is $26.24 x 3 = $78.42 per year.

It is estimated that the testing requirements of §106.91 will require scientists to work at total of 101.6 hours to fulfill the information collection requirements of this section. At a wage of $46.26/hour, the total cost is $46.26 x 101.6 = $4,700.02. It is estimated that the ongoing review and updating of audit plans will require senior validation engineers to spend 1,080 hours annually at $46.26 per hour to fulfill the requirements of §106.94. Therefore, 1.080 hours x $46.26/hour = $49,960.80

It is estimated that it will take scientists 627.5 hours annually at $54.96 per hour to fulfill the requirements of §106.96(b) and (d). Therefore, 627.5 hours x $54.96/hour = $34,487.40.

The agency estimates that scientists will spend 680 hours annually at a wage of $54.96 per hour to comply with the requirements of §106.96(c). Therefore, the cost to comply with §106.96(c) is 680 x $54.96 = $37,472.80.

For the submission of the PER exemption for non-eligible infant formulas, it is estimated that industry will submit 34 exemptions per year and that each exemption will take support staff 12 hours (Silverman Statement 2011) at a wage of $27.23 per hour (Bureau of Labor Statistics c). Therefore, 12 hours x $27.23 wage per hour = $324 per exemption; $324 per exemption x 34 exemptions = $11,109.84 annually to fulfill the requirements of §106.96(g). To comply with §106.110, the total annual industry burden is 35 registrations x 30 minutes per registration = 17.5 hours, and $27.23 per hour supporting staff wage x 17.5 hours = $476.53 .

It is estimated that, annually, the industry could make submissions for 35 new infant formulas, or an average of seven submissions per firm (Silverman Statement 2011), pursuant to §106.120. At a wage of $54.96 per hour, one submission is estimated to cost $549.60, or $54.96 hourly wage x 10 hours of work per submission = $549.60. Therefore, to comply with §106.120, the total annual industry burden is 35 submissions x $549.60 per submission = $19,236.
The total annual cost related to information collection is $592,953.81

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

The total cost to the Federal government is $860,473.90, calculated by adding the total labor cost of $163,800 for the information collection requirements imposed by the new regulations to the current cost of $696,673.90.

Specifically, each registration, new infant formula notification, infant formula submission, quality factor submission, or verification submission will require evaluation by subject matter experts who organize the evaluation and prepare the final documents. On average, there will be 2 subject matter experts (SME), a reviewer and a Consumer Safety Officer; the hours devoted will vary depending on the task. The reviewer would be a GS-14 or 15 level (a medical officer, a methods expert, etc.), with an average cost of $63/hour. The Consumer Safety Officer would be a GS-13 or 14 at an average cost of $5/hour. Further, the labor cost to review a registration submitted in accordance with §106.110 is estimated to be about $85.50 ((.5hour * $63/reviewer hour) + (1 hour * $54/CSO hour)). For an annual average of 35 registrations, the total labor cost is 35 registrations x $85.50 = $2,992.50 per year. The labor cost to review a new infant formula notification submitted in accordance with §106.120 is estimated to be about $4,680 (40 hours * $63/review hour) + (40 hours * $54/CSO hour)). For an annual average of 35 submissions, the total labor cost is $163,800 per year.

15. Explanation for Program Changes or Adjustments

This information collection request revises the currently approved collection under OMB Control No. 0910-0256. The new regulatory provisions impose a "first-year" burden of 35,630, and a subsequent recurring burden of 11,225. While this results in an immediate **increase of 48,311 burden hours**, ultimately the agency estimates that the recurring burden will result in a decrease of 18,977 hours. Similarly, the number of **annual responses is increased by 16,683**. Upon satisfaction of the "first-year" requirements, however, the agency estimates there will be a drop in the annual responses to 6,091.

16. Plans for Tabulation and Publication and Project Time Schedule

The agency has no plans for publication of information from this information collection.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

Approval to not display the expiration date of OMB approval is not being sought.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

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2. Bureau of Labor Statistics b. Occupational Employment and Wages, 19--1029 Biological Scientists, All Others. May 2010, Washington, DC; available at http://www.bls.gov/oes/current/oes191029.htm, accessed April 5, 2013.

3. Bureau of Labor Statistics c. Occupational Employment and Wages, 19-4011 Agricultural and Food Science Technicians. May 2012, Washington, DC (available at http://www.bls.gov/oes/current/oes194011.htm, accessed April 5, 2013.

4. Bureau of Labor Statistics d. Occupational Employment and Wages, 43-4199 Information and Record Clerks, All Other. May 2010, Washington, DC; available at http://www.bls.gov/oes/current/oes434199.htm, accessed April 5, 2013.

5. Silverman, Benson. Statement of Benson M. Silverman, M.D. "Industry Efforts to Meet Quality Factor Requirements," (2011).

6. Zink, Don. Statement of Donald L. Zink, Ph. D.: Infant Formula Manufacturing Practices 2010.