4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-0044]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Recommended Recordkeeping for Exempt Infant Formula Production

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-7285, or emailed to oira_submission@omb.eop.gov. All comments should be identified with the OMB control number 0910-NEW. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Rd., COLE-14526, Silver Spring, MD 20993-0002, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Recommended Recordkeeping for Exempt Infant Formula Production--OMB Control Number 0910-NEW

I. Background

Section 412(h)(1) (21 U.S.C. 350a(h)(1)) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) exempts an infant formula which is represented and labeled for use by an infant with an inborn error of metabolism, low birth weight, or who otherwise has an unusual medical or dietary problem from the requirements of section 412(a), (b), and (c) of the FD&C Act (21 U.S.C. 350a(a), (b), and (c)). These formulas are customarily referred to as "exempt infant formulas." In the Federal Register of June 10, 2014 (79 FR 33057), we published a final rule that adopted, with some modifications, an interim final rule published on February 10, 2014 (79 FR 7934), that established requirements for quality factors for infant formulas and current good manufacturing practices (CGMPs), including quality control procedures, under section 412 of the FD&C Act. The final rule will help prevent the manufacture of adulterated infant formula, ensure the safety of infant formula, and ensure that the nutrients in infant formula are present in a form that is bioavailable.

In the Federal Register of February 10, 2014 (79 FR 7610), we published a notice of availability of the draft guidance document entitled, "Guidance for Industry: Exempt Infant Formula Production: Current Good Manufacturing Practices, Quality Control Procedures, Conduct of Audits, and Records and Reports" (the draft guidance). The draft guidance, when finalized, will describe our current thinking on the manufacturing of exempt infant formula in relation to the requirements in part 106 (21 CFR part 106) for CGMPs, quality control

procedures, conduct of audits, and records and reports that apply to nonexempt infant formulas. Persons with access to the Internet may obtain the draft guidance at http://www.fda.gov/FoodGuidances.

II. Analysis of the Proposed Information Collection

The proposed information collection seeks OMB approval of the recordkeeping recommendations of the draft guidance. Our estimate of the burden of the recordkeeping recommendations includes the one-time burden of developing production and in-process control systems and the annual burdens of developing and maintaining production aggregate production and control records, records pertaining to the distribution of infant formula, and records pertaining to regularly scheduled audits. 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.

Description of Respondents: The respondent recordkeepers are manufacturers of exempt infant formula.

Description: The records recommended, to the extent practicable, in the draft guidance include records required by part 106, subparts A, B, C, D, and F for non-exempt infant formulas. Because the records and reporting requirements related to part 106 subparts E and G are not generally applicable to exempt infant formula manufacturers, FDA is not recommending in the draft guidance that exempt infant formula manufacturers follow these requirements. As such, the records and reporting requirements in part 106 subparts E and G are not part of this new information collection.

In the Federal Register of March 18, 2015 (80 FR 14134), FDA published a 60-day notice requesting public comment on the proposed collection of information. We received one letter responsive to the notice, which contained comments.

(Comment 1) One comment suggested that we clarify the action level for end-of-shelf-life verification testing and how this testing differs for exempt infant formulas as compared to non-exempt infant formulas.

(Response) We appreciate the concerns discussed in the comment. The exempt infant formula guidance recommends that manufacturers of exempt infant formulas follow, to the extent practicable, subparts A, B, C, D, and F of 21 CFR part 106, as amended or established by the final rule published on June 10, 2014 (79 FR 33057), in the production of their formula products. We do not plan to establish an action level for end-of-shelf-life verification testing in the exempt infant formula guidance. Furthermore, our guidance documents do not establish legally enforceable requirements and therefore cannot include mandatory language such as "shall, must, required, or requirement," unless specific regulatory or statutory requirements are cited.

To the extent that the comment requests us to engage in rulemaking, the comment is outside the scope of the comment request on the four collection of information topics as they relate to the provisions of the draft guidance document.

(Comment 2) One comment asserted that we may have underestimated the time it would take to test weekly for bacteriological contaminants, as reported in Table 1. The comment noted our estimate of 5 minutes per test, once a week, for each of three infant formula plants and added that including the performance of the test would significantly increase the time needed.

(Response) We appreciate the information provided in the comment. However, the comment did not provide us data or information to support a different estimate. In the absence of

such data, we lack a basis on which to revise our estimates. In addition, we note that our estimate of 5 minutes per test, once a week, reflects the amount of time needed to fulfill the recordkeeping burdens associated with this requirement, not the time needed to conduct the testing that is subject to the recordkeeping requirement. In preparation for the next regular information collection request, we will consult with several establishments to obtain additional data on the recordkeeping burdens and reevaluate our estimates. We will then publish the revised estimates for comment and consider additional information submitted in response.

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

The total one-time estimated burden imposed by this collection of information is 19,320 hours. The total annual estimated burden imposed by this collection of information is 6,328.06 hours. There are no capital costs or operating and maintenance costs associated with this collection of information. The estimated burden for the draft guidance 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.

As of the beginning of 2015, five manufacturers produce exempt infant formulas that are marketed in the United States. Four out of these five infant formula manufacturers produce both exempt and non-exempt infant formulas, with both types of infant formula produced using the same production lines and equipment. Our experts believe that manufacturing practices are similar for both exempt and non-exempt infant formulas. Furthermore, given expert estimations of industry standard practices, it is estimated that the manufacturer that only produces exempt infant formula has practices comparable to those manufacturers producing both exempt and non-

exempt infant formulas (Ref. 1). Together, these 5 manufacturers produce exempt infant formula at 12 plants.

The number of recordkeepers in column 3 of Table 1 is based on FDA's expert estimation of the number of plants that may not already be adhering to the relevant recordkeeping provisions of the final rule. The Regulatory Impact Analysis for the final rule (79 FR 33057) estimated that 25 percent of all infant formula plants manufacturing non-exempt infant formula were not currently adhering to the recordkeeping provisions under § 106.100 (21 CFR 106.100). Although such recordkeeping requirements are now effective for manufacturers of non-exempt infant formulas, and manufacturers of exempt infant formulas may have implemented similar procedures for their exempt infant formulas, it is estimated conservatively that this same proportion (25 percent, or 3 out of 12 plants that manufacture exempt infant formula) are not currently adhering to the recordkeeping provisions, and unless otherwise specified, burdens are estimated based on these 3 plants. Furthermore, we estimate that plants will collect the same information across the various exempt infant formulas produced by each firm.

For records pertaining to production and in-process controls, FDA estimates that, at most, three plants do not currently develop production records as specified under §§ 106.6(c)(5) and 106.100(e)(1) and (3). A team of two senior validation engineers (or other similarly skilled employees) per plant (2 workers per plant × 3 plants = 6 workers) would each need to work 20 hours to provide sufficient initial baseline records and documentation to develop records pertaining to production and in-process controls, for an industry total of 120 hours (2 workers per plant × 3 plants × 20 hours per worker = 120 hours), as presented in line 1 of Table 1.

For the recordkeeping specified under § 106.35(c), in accordance with § 106.100(f)(5), FDA estimates that a team of 10 senior validation engineers (or other similarly skilled

employees) per plant would need to work full time for the 16 weeks (16 weeks/person × 40 work hours/week = 640 work hours per person) to provide sufficient initial records and documentation pertaining to controls intended to prevent adulteration due to automatic equipment. The total burden for 10 senior validation engineers each working 640 hours is 6,400 per plant in the first year (10 senior validation engineers × 640 hours = 6,400). For three plants, the total one-time hourly burden is 3 plants × 6,400 hours per plant = 19,200 hours, as presented in line 2 of Table 1.

For the testing specified under § 106.20(f)(3), manufacturers of exempt infant formulas should conduct water testing with appropriate frequency to meet Environmental Protection Agency primary standards for drinking water (40 CFR parts 9, 141, and 142), but shall conduct these tests 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 exempt infant formula plants to test for chemical contaminants and keep records of those tests on a regular basis; therefore, this is a new collection of information that does not present a burden (Ref. 1).

It is estimated that the recommendation to manufacturers of exempt infant formulas to test at least every 4 years for radiological contaminants would represent a new burden for all 12 infant formula plants (Ref. 1). In addition, it is estimated that collecting water for this testing 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 × 12 plants = 18 total hours, every 4 years, or 4.5 hours per year, as seen in line 3 of Table 1.

Furthermore, the draft guidance recommends that manufacturers of exempt infant formula make and retain records of the frequency and results of water testing as specified under §§ 106.20(f)(4) and 106.100(f)(1). For the 12 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 × 12 plants = 0.96 hour every four years for the maintenance of records of radiological testing, or 0.24 hours per year, as seen on line 4 of Table 1.

It is estimated that the recommendation to test weekly for bacteriological contaminants is a new burden for three 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 hour × 52 weeks = 4.16 hours per year per plant, and 4.16 hours per plant × 3 plants = 12.48 total annual hours, as seen on line 5 of Table 1. Furthermore, for the three 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 × 52 weeks = 4.16 hours per plant for the maintenance of records of bacteriological testing. Accordingly, 4.16 hours per plant × 3 plants = 12.48 annual hours, as seen on line 6 of Table 1.

The draft guidance recommends that manufacturers of exempt infant formulas calibrate certain instruments against a known reference standard and that records of these calibration activities be made and retained, as specified in §§ 106.30(d)(1) and 106.100(f)(2). FDA estimates that one senior validation engineer (or other similarly skilled employee) for each of the three (at most) plants would need to spend about 13 minutes per week to conduct the ongoing calibration recordkeeping. Therefore, 3 recordkeepers × 0.21 hours per week per recordkeeper = 0.63 hours per week; 0.63 hours per week × 52 weeks per year = 32.76 hours as the total industry annual burden, as presented in line 7 of Table 1.

The draft guidance recommends that manufacturers of exempt infant formula make and retain records of the temperatures of each cold storage compartment as specified in §§ 106.30(e)(3)(iii) and 106.100(f)(3). Based on expert opinion, FDA estimates that three (at most) plants are not currently conducting recordkeeping, and that at each of these three plants, conducting this recordkeeping would take one senior validation engineer (or other similarly skilled employee) about 13 minutes per week. Therefore, 3 recordkeepers × 0.21 hours per week per recordkeeper = 0.63 hours per week; 0.63 hours per week × 52 weeks = 32.76 hours as the total industry annual burden, as presented in line 8 of Table 1.

The draft guidance recommends the making and retention of records of ongoing sanitation efforts as specified under §§ 106.30(f)(2) and 106.100(f)(4). Based on expert opinion, FDA estimates that three (at most) plants are not currently making and retaining these records, and that at each of these three plants, it would take one senior validation engineer (or other similarly skilled employee) 0.19 hours per week to make and retain these records. Therefore, 3 recordkeepers × 0.19 hours per week per recordkeeper = 0.57 hours per week; 0.57 hours per week × 52 weeks = 29.64 hours as the total industry annual burden, as presented in line 9 of Table 1.

There will be annual recordkeeping associated with recommendations for preventing adulteration from equipment, as specified under §§ 106.35(c) and 106.100(f)(5). It is estimated that one senior validation engineer (or other similarly skilled employee) per plant would need to work 10 hours per week (520 work hours per year) to meet the ongoing recordkeeping recommendation. For the estimated three (at most) plants not conducting this recordkeeping, the total annual burden is 520 hours per plant × 3 plants = 1,560 annual hours, as shown in line 10 of Table 1. In addition, this guidance recommends that an infant formula manufacturer 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 would need to work full time for 4 weeks (4 weeks × 40 hours per week = 160 work hours per person) to provide revalidation of the plant's automated systems sufficient to adhere to this section. The total annual burden for four senior validation engineers each working 160 hours twice a year is 1,280 hours ((160 hours × 2 revalidations) × 4 engineers = 1,280 total work hours) per plant. Therefore, 1,280 hours per plant × 3 plants = 3,840 annual hours, as shown on line 11 of Table 1.

The draft guidance recommends written specifications for ingredients, containers, and closures, as specified under §§ 106.40(g) and 106.100(f)(6). FDA estimates that the exempt infant formula industry already establishes written specifications for these components. However, the guidance regarding controls to prevent adulteration caused by ingredients, containers, and closures may represent new recordkeeping for three (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 would work about 10 minutes a week to complete this recordkeeping. Therefore, 3 recordkeepers × 0.17 hours per week per recordkeeper = 0.51 hours per week; 0.51 hours per week × 52 weeks = 26.52 total annual hours, as presented in line 12 of Table 1.

This draft guidance recommends manufacturers of exempt infant formula to make and maintain records of controls to prevent adulteration during manufacturing, as specified in §§ 106.50 and 106.100(e). It is not possible to predict how often changes to the master

manufacturing order would be made or how often deviations from the master manufacturing order would occur. Based on expert opinion, FDA estimates that each year, three (at most) plants would change a master manufacturing order and that, on average, one senior validation engineer for each of the three (at most) plants would spend about 14 minutes per week on recordkeeping pertaining to the master manufacturing order. Thus, 3 recordkeepers × 0.23 hours per recordkeeper per week = 0.69 hours per week; 0.69 hours per week × 52 weeks = 35.88 hours as the total annual industry burden, as presented in line 13 of Table 1.

The draft guidance recommends manufacturers of exempt infant formula make and retain records of the testing of infant formula for microorganisms, as specified in §§ 106.55(d) and 106.100(e)(5)(ii) and (f)(7). We estimate that this recordkeeping represents a new collection of information for, at most, three plants (Ref. 1) and that one senior validation engineer per plant would spend 15 minutes per week on recordkeeping pertaining to microbiological testing. Thus, 3 recordkeepers × 0.25 hours per recordkeeper per week = 0.75 hours; 0.75 hours per week × 52 weeks 39 hours as the total annual industry burden, as presented in line 14 of Table 1.

The draft guidance recommends that exempt infant formula manufacturers make and maintain records consistent with the requirements for the labeling of mixed-lot packages of infant formula that apply to non-exempt infant formula manufacturers, as specified under § 106.60(c). We estimate that the draft guidance will result in infant formula diverters labeling 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 the Agency estimates that this burden would 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, for all plants combined, 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 hours per month × 12 months = 3 annual hours), as presented in line 15 of Table 1.

The draft guidance recommends nutrient testing for exempt infant formula manufacturers as specified in § 106.91(a)(1) through (4). It is estimated that the systems and processes of 100 percent of the exempt formula industry test in accordance with these provisions. Therefore, nutrient testing does not represent a new recordkeeping burden as nutrient testing is estimated to be common business practice in the exempt infant formula industry. Thus, no burden is estimated for these recommendations (Ref. 1).

The draft guidance also recommends on-going stability testing as specified under § 106.91(b)(1) through (3). It is estimated that the systems and processes of the infant formula industry partially adhere to this guidance in that 80 percent of infant formula plants (about 10 of 12 plants) conduct stability testing as recommended (Ref. 1). For the 20 percent of plants (2 of 12 plants) that do not conduct stability testing, 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 guidance represents a new information collection burden of 2 annual hours, per plant. Therefore, 2 hours per plant × 2 plants = 4 annual hours as shown in line 16 of Table 1.

The draft guidance recommends recordkeeping for test results as specified under §§ 106.91(d) and 106.100(e)(5)(i). This represents new information collections for the two

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 one senior validation engineer per plant would spend about 9 minutes per week maintaining records related to testing. Thus, 2 recordkeepers × 0.15 hours per recordkeeper per week = 0.3 hours per week × 52 weeks = 15.6 hours as the annual total industry burden, as presented in lines 17, 18, and 19 of Table 1.

The draft guidance recommends the creation of audit plans and procedures, as specified under § 106.94. FDA estimates that all exempt infant formula manufacturers currently conduct audits, but that 25 percent of infant formula plants (3 of 12 plants) do not conduct audits that include all elements specified in § 106.94 (Ref. 1). It is estimated that the ongoing review and updating of audit plans would require a senior validation engineer 8 hours per year, per plant. Therefore, 8 hours per year per plant × 3 plants = 24 annual hours to regularly review and update audit plans as shown in line 20 of Table 1.

The infant formula final rule does not mandate a frequency of auditing, therefore, one is not recommended in the draft guidance. For the purposes of this analysis, FDA estimates that a manufacturer would choose to audit once per week. Each weekly audit is estimated to require a senior validation engineer 4 hours, or 52 weeks × 4 hours = 208 hours per plant per year. Therefore, the total annual burden for the estimated three plants not currently acting in accordance to this guidance to update audit plans is 208 hours × 3 plants = 624 hours, as shown in line 21 of Table 1.

Table 1.--Estimated Hourly Recordkeeping Burden

First Year Hourly Burden						
	21 CFR Section	No. of Recordkeepers	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 (3)	6	1	3	40	120
2	Controls to Prevent Adulteration Due to Automatic (Mechanical or Electronic) Equipment 106.35(c) and 106.100(f)(5)	30	1	3	6,400	19,200
	Total First Year Only Hourly Recordkeeping Burden					19,320
	Recurring Annual Hourly Burden					
	21 CFR Section	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Records	Hours per Record	Total Hours Annually
3	Controls to Prevent Adulteration Caused by Facilities--Testing for Radiological Contaminants[1]	12	1	12	1.5	4.5
	106.20(f)(3)					
4	Controls to Prevent Adulteration Caused by Facilities--Recordkeeping of Testing for	12	1	12	0.08	0.24

[1] As noted previously, the burden for making and maintaining such records is expected to occur once every 4 years. The total hours column reflects the total number of hours averaged over the 4 year period.

	Radiological Contaminants[2] 106.20(f)(4) and 106.100(f)(1)					
5	Controls to Prevent Adulteration Caused by Facilities--Testing for Bacteriological Contaminants 106.20(f)(3)	3	52	156	0.08	12.48
6	Controls to Prevent Adulteration Caused by Facilities--Recordkeeping of Testing for Bacteriological Contaminants 106.20(f)(4) and 106.100(f)(1)	3	52	156	0.08	12.48
7	Controls to Prevent Adulteration by Equipment or Utensils	3	52	156	0.21	32.76
	106.30(d)(1) and 106.100(f)(2)					
8	Controls to Prevent Adulteration by Equipment or Utensils	3	52	156	0.21	32.76
	106.30(e)(3)(iii) and 106.100(f)(3)					
9	Controls to Prevent Adulteration by Equipment or Utensils	3	52	156	0.19	29.64
	106.30(f)(2) and 106.100(f)(4)					
10	Controls to Prevent Adulteration Due to Automatic (Mechanical or Electronic)	3	52	3	520	1,560

[2] As noted previously, the burden for making and maintaining such records is expected to occur once every four years. The total hours column reflects the total number of hours averaged over the four-year period.

	Equipment					
	106.35(c) and 106.100(f)(5)					
11	Controls to Prevent Adulteration Due to Automatic (Mechanical or Electronic) Equipment 106.35(c) and 106.100(f)(5)	12	2	6	640	3,840
12	Controls to Prevent Adulteration Caused by Ingredients, Containers, and Closures	3	52	156	0.17	26.52
	106.40(g) and 106.100(f)(6)					
13	Controls to Prevent Adulteration During Manufacturing	3	52	156	0.23	35.88
	106.50 and 106.100(e)					
		3	52	156	0.25	39
14	Controls to Prevent Adulteration From Microorganisms					
	106.55(d), 106.100(e)(5)(ii), and 106.100(f)(7)					
15	Controls to Prevent Adulteration During Packaging and Labeling of Infant Formula 106.60(c)	1	12	12	0.25	3
16	General Quality Control-Testing 106.91(b)(1) through (3)	2	1	2	2	4
17	General Quality Control	2	52	104	0.15	15.6

	106.91(b)(1) and (d), and 106.100(e)(5)(i)					
	General Quality Control	2	52	104	0.15	15.6
18	106.91(b)(2) and (d), and 106.100(e)(5)(i)					
19	General Quality Control	2	52	104	0.15	15.6
	106.91(b)(3) and (d), and 106.100(e)(5)(i)					
20	Audit Plans and Procedures	3	1	3	8	24
	106.94--Ongoing Review and Updating of Audits					
21	Audit Plans and Procedures 106.94--Regular Audits	3	52	156	4	624
	Total Recurring Recordkeeping Burden					6,328.06
	Total Recordkeeping Burden					25,648.06

III. Reference

The following reference has been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 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.

1. Zink, Don. Statement of Donald L. Zink: Infant Formula Manufacturing Practices, 2013.

Dated: January 22, 2016.

Leslie Kux,

Associate Commissioner for Policy

[FR Doc. 2016-01690 Filed: 1/27/2016 8:45 am; Publication Date: 1/28/2016]