



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-N-1619]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements

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 (PRA).

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 oir_submission@omb.eop.gov. All comments should be identified with the OMB control number 0910-0606. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: JonnaLynn Capezzuto, Office of Operations, Food and Drug Administration, Three White Flint North, 10A63, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-3794.

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.

Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding
Operations for Dietary Supplements--21 CFR Part 111

OMB Control Number 0910-0606--Extension

On October 25, 1994, the Dietary Supplement Health and Education Act (DSHEA) (Pub. L. 103-417) was signed into law. DSHEA, among other things, amended the Federal Food, Drug, and Cosmetic Act (the FD&C Act) by adding section 402(g) of the FD&C Act (21 U.S.C. 342(g)). Section 402(g)(2) of the FD&C Act provides, in part, that the Secretary of Health and Human Services may, by regulation, prescribe good manufacturing practices for dietary supplements. Section 402(g) of the FD&C Act also stipulates that such regulations will be modeled after current good manufacturing practice (CGMP) regulations for food and may not impose standards for which there are no current, and generally available, analytical methodology. Section 402(g)(1) of the FD&C Act states that a dietary supplement is adulterated if “it has been prepared, packed, or held under conditions that do not meet current good manufacturing practice regulations.” Under section 701(a) of the FD&C Act (21 U.S.C. 371(a)), FDA may issue regulations necessary for the efficient enforcement of the FD&C Act. In the Federal Register of June 25, 2007 (72 FR 34752), (the June 25, 2007, final rule), FDA published a final rule that established, in part 111 (21 CFR part 111), the minimum CGMP necessary for activities related to manufacturing, packaging, labeling, or holding dietary supplements to ensure the quality of the dietary supplement.

Records are an indispensable component of CGMP. The records required by FDA’s regulations in part 111 provide the foundation for the planning, control, and improvement

processes that constitute a quality control system. Implementation of these processes in a manufacturing operation serves as the backbone to CGMP. The records show what is to be manufactured; what was, in fact, manufactured; and whether the controls that the manufacturer put in place to ensure the identity, purity, strength, and composition and limits on contaminants and to prevent adulteration were effective. Further, records will show whether and what deviations from control processes occurred, facilitate evaluation and corrective action concerning these deviations (including, where necessary, whether associated batches of product should be recalled from the marketplace), and enable a manufacturer to assure that the corrective action was effective. In addition, by establishing recordkeeping requirements, FDA can ensure that industry follows CGMP during manufacturing, packaging, labeling, or holding operations. The regulations in part 111 establish the minimum manufacturing practices necessary to ensure that dietary supplements are manufactured, packaged, labeled, or held in a manner that will ensure the quality of the dietary supplements during manufacturing, packaging, labeling or holding operations.

The recordkeeping requirements of the regulations include establishing written procedures and maintaining records pertaining to: (1) Personnel; (2) sanitation; (3) calibration of instruments and controls; (4) calibration, inspection, or checks of automated, mechanical, or electronic equipment; (5) maintaining, cleaning, and sanitizing equipment and utensils and other contact surfaces; (6) water used that may become a component of the dietary supplement; (7) production and process controls; (8) quality control; (9) components, packaging, labels and product received for packaging and labeling; (10) master manufacturing and batch production; (11) laboratory operations; (12) manufacturing operations; (13) packaging and labeling

operations; (14) holding and distributing operations; (15) returned dietary supplements; and (16) product complaints.

Description of Respondents: Manufacturers, dietary supplement manufacturers, packagers and repackagers, labelers and re-labelers, holders, distributors, warehousemen, exporters, importers, large businesses, and small businesses engaged in the dietary supplement industry.

The recordkeeping requirements of the regulations in part 111 are set forth in each subpart. In table 1, we list the annual burdens associated with recordkeeping, as described in the June 25, 2007, final rule. For some provisions listed in table 1, we did not estimate the number of records per recordkeeper because recordkeeping occasions consist of frequent brief entries of dates, temperatures, monitoring results, or documentation that specific actions were taken. Information might be recorded a few times a day, week, or month. When the records burden involves frequent brief entries, we entered 1 as the default for the number of records per recordkeeper. For example, many of the records listed under § 111.35 in table 1, such as § 111.35(b)(2) (documentation, in individual equipment logs, of the date of the use, maintenance, cleaning, and sanitizing of equipment), involve many short sporadic entries over the course of the year, varying across equipment and plants in the industry. We did not attempt to estimate the actual number of recordkeeping occasions for these provisions, but instead entered an estimate of the average number of hours per year. We entered the default value of 1 as the number of records per recordkeeper for these and similar provisions. For § 111.35, the entry for number of records is 1 as a default representing a large number of brief recordkeeping occasions.

In many rows of table 1, we list a burden under a single provision that covers the written procedures or records described in several provisions. For example, the burden of the batch

production records listed in table 1 under § 111.260 includes the burden for records listed under § 111.255 because the batch production records must include those records.

The number of records for batch production records (and other records kept on a batch basis in table 1) equals the annual number of batches. The estimated burden for records kept by batch includes both records kept for every batch and records kept for some but not all batches. We use the annual number of batches as the number of records that will not necessarily be kept for every batch, such as test results or material review and disposition records, because such records are part of records, if they are necessary, that will be kept for every batch.

In the Federal Register of September 29, 2016 (81 FR 66967), FDA published a 60-day notice requesting public comment on the proposed collection of information. FDA received comments from two commenters.

(Comment 1) One commenter had concerns about whether the processes being used to assess the contents of supplements are genuine and accurate and how this is regulated; whether records regarding labeling indicate what is actually contained in a supplement; and whether these records will be available to the public.

These comments appear to address PRA issues of practical utility and ways to enhance the quality, utility, and clarity of the information to be collected.

(Response 1) In this collection of information, FDA is evaluating the burden of retaining records and making them available to regulatory officials, but not the burden for proactively submitting them to FDA. FDA reviews the records maintained while conducting an investigation (e.g., during a facility inspection and during the followup communication until a particular investigation is closed out). The investigation of a particular firm by FDA is exempt from the PRA and is not included as part of the burden estimate. The required elements of

labeling are part of different regulations and do not apply to this collection of information. The commenter also discussed the safety of a particular product but CGMP regulations deal with establishing a quality product, not necessarily a safe product. Finally, the commenter discussed allowing the records maintained to be made public. These records are required to be maintained by the firm and are not proactively submitted to FDA, but they are required to be made available to FDA during inspections. If FDA obtains these records during the investigation of a firm, the public can submit a Freedom of Information Act request but the document they would typically receive would be redacted because the records are the property of the firm.

(Comment 2) The second commenter stated that the labeling on dietary supplement products should be consistent and FDA regulated, the term “healthy” should be required to have a standard meaning, and “healthy” should not be allowed to be used unless it meets FDA requirements of the term.

(Response 2) The recordkeeping for CGMPs has nothing to do with the required elements of food and dietary supplement labeling, which are covered under FDA’s labeling regulations. FDA recently published, on May 27, 2016, a final rule for Nutrition (and Supplement) Facts Labels (81 FR 33741), and is currently reviewing new requirements for labeling your food “healthy”. This information collection for CGMP addresses recordkeeping for specifications for a label and labeling operations.

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

Table 1.--Estimated Annual Recordkeeping Burden¹

21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
111.14, Records of personnel practices, including documentation of training	15,000	4	60,000	1	60,000
111.23, Records of physical plant sanitation practices, including pest control and water quality	15,000	1	15,000	0.2 (12 minutes)	3,000
111.35, Records of equipment and utensils calibration and sanitation practices	400	1	400	12.5	5,000
111.95, Records of production and process control systems	250	1	250	45	11,250
111.140, Records that quality control personnel must make and keep	240	1,163	279,120	1	279,120
111.180, Records associated with components, packaging, labels, and product received for packaging and labeling as a dietary supplement	240	1,163	279,120	1	279,120
111.210, Requirements for what the master manufacturing record must include	240	1	240	2.5	600
111.260, Requirements for what the batch record must include	145	1,408	204,160	1	204,160
111.325, Records that quality control personnel must make and keep for laboratory operations	120	1	120	15	1,800
111.375, Records of the written procedures established for manufacturing operations	260	1	260	2	520
111.430, Records of the written procedures for packaging and labeling operations	50	1	50	12.6	630
111.475, Records of product distribution and procedures for holding and distributing operations	15,000	1	15,000	0.4 (24 minutes)	6,000
111.535, Records for returned dietary supplements	110	4	440	13.5	5,940
111.570, Records regarding product complaints	240	600	144,000	0.5 (30 minutes)	72,000
Total					929,140

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

The average burden per recordkeeping estimates in table 1 are based on those in the June 25, 2007, final rule, which were based on our institutional experience with other CGMP requirements and on data provided by Research Triangle Institute in the “Survey of Manufacturing Practices in the Dietary Supplement Industry” cited in that rule.

The estimates in table 1 of the number of firms affected by each provision of part 111 are based on the percentage of manufacturers, packagers, labelers, holders, distributors, and warehouseers that reported in the survey that they have not established written SOPs or do not maintain records that were later required by the June 25, 2007, final rule. Because we do not have survey results for general warehouses, we entered the approximate number of facilities in that category for those provisions covering general facilities. For the dietary supplement industry, the survey estimated that 1,460 firms would be covered by the final rule, including manufacturers, packagers, labelers, holders, distributors, and warehouseers. The time estimates include the burden involved in documenting that certain requirements are performed and in recordkeeping. We used an estimated annual batch production of 1,408 batches per year to estimate the burden of requirements that are related to the number of batches produced annually, such as § 111.260, “What must the batch production record include?” The estimate of 1,408 batches per year is near the midpoint of the number of annual batches reported by survey firms.

The length of time that CGMP records must be maintained is set forth in § 111.605. Table 1 reflects the estimated burdens for written procedures, record maintenance, periodically reviewing records to determine if they may be discarded, and for any associated documentation for that activity for records that are required under part 111. We have not included a separate estimate of burden for those sections that require maintaining records in accordance with § 111.605, but have included those burdens under specific provisions for keeping records. For example, § 111.255(a) requires that the batch production records be prepared every time a batch is manufactured, and § 111.255(d) requires that batch production records be kept in accordance with § 111.605. The estimated burdens for both § 111.255(a) and (d) are included under § 111.260, what the batch record must include.

Dated: April 14, 2017.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2017-07965 Filed: 4/19/2017 8:45 am; Publication Date: 4/20/2017]