UNITED STATES FOOD & DRUG ADMINISTRATION

Current Good Manufacturing Practice in Manufacturing,
Packaging, Labeling, or Holding Operations for Dietary Supplements

OMB Control No. 0910-0606 - Revision

SUPPORTING STATEMENT – **Part A: Justification**:

1. Circumstances Making the Collection of Information Necessary

The Dietary Supplement Health and Education Act (Pub. L. 103-417) added section 402(g) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 342(g)), which provides, in part, that the Secretary of Health and Human Services may, by regulation, prescribe good manufacturing practice 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*." Accordingly, we have promulgated regulations in part 111 (21 CFR part 111) establishing minimum CGMP requirements pertaining to the manufacturing, packaging, labeling, or holding of dietary supplements to ensure their quality. Part 111 establishes the minimum CGMP necessary for activities related to manufacturing, packaging, labeling, or holding dietary supplements to ensure the quality of the dietary supplement.

Subpart E of 21 CFR Part 111 (21 CFR 111.55-111.95) covers certain quality control specifications including component identity testing. Section 111.75(a)(1) provides for petitions to request an exemption from certain testing requirements under the regulation. According to § 111.75(a)(1)(ii), manufacturers may request an exemption when a dietary ingredient is obtained from one or more suppliers as identified in the petition. The regulation clarifies that we are willing to consider, on a case-by-case basis, a manufacturer's conclusion, supported by appropriate data and information in the petition submission, that it has developed a system that it would implement as a sound, consistent means of establishing, with no material diminution of assurance compared to the assurance provided by 100 percent identity testing, the identity of the dietary ingredient before use.

Part 111.75(a)(1) reflects FDA's determination that manufacturers that test or examine 100 percent of the incoming dietary ingredients for identity can be assured of the identity of the ingredient. However, we recognize that it may be possible for a manufacturer to demonstrate, through various methods and processes in use over time for its particular operation, that a system of less than 100 percent identity testing would result in no material diminution of assurance of the identity of the dietary ingredient as compared to the assurance provided by 100 percent identity testing. To provide an opportunity for a manufacturer to make such a showing and reduce the frequency of identity testing of components that are dietary ingredients from 100 percent to some lower frequency, we added to § 111.75(a)(1), an exemption from the

requirement of 100 percent identity testing when a manufacturer petitions the agency for such an exemption to 100 percent identity testing under 21 CFR 10.30 and the agency grants such exemption. Such a procedure would be consistent with FDA's stated goal, as described in the CGMP final rule, of providing flexibility in the CGMP requirements.

Part 111.75(a)(1)(ii) sets forth the information a manufacturer is required to submit in such a petition. The regulation also contains a requirement to ensure that the manufacturer keeps FDA's response to a petition submitted under § 111.75(a)(1)(ii) as a record under § 111.95.

To increase our operational efficiency we are consolidating burden approved under OMB control number 0910-0608, "Petition to Request an Exemption from 100 Percent Identity Testing of Dietary Ingredients: CGMP in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements," which covers related information collection..

We therefore request OMB approval of the information collection provisions found in 21 CFR part 111 and discussed in this supporting statement.

2. Purpose and Use of the Information Collection

Recordkeeping is 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 shows what is to be manufactured; what was manufactured; and whether the manufacturing controls ensure the identity, purity, strength, and composition of the product and effectively limit contaminants and prevent adulteration. Further, records 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, recordkeeping requirements helps to ensure industry adherence to CGMP. The regulations in part 111 establish what we believe are 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 provide for 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.

The reporting is used to show whether a particular manufacturer of dietary supplements has successfully, or unsuccessfully, petitioned FDA for an exemption from 100 percent identity testing for ingredients used in supplement manufacture.

Description of Respondents: Respondents to this collection of information include manufacturers, packagers and repackagers, labelers and re-labelers, holders, distributors, warehousers, exporters, importers, large businesses, and small businesses engaged in the dietary supplement industry. Respondents are from the private sector (for-profit businesses).

3. Use of Improved Information Technology and Burden Reduction

The regulations in part 111 do not specifically prescribe the use of automated, electronic, mechanical, or other technological techniques or other forms of information technology as necessary for use by firms. Companies are free to use whatever forms of information technology may best assist them in recordkeeping and reporting. We estimate that about seventy-five percent (75%) of this information collection will be done electronically.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection.

5. Impact on Small Businesses or Other Small Entities

We estimate that a substantial proportion (75%) of firms subject to the regulation are small businesses, however we believe the information collection requirements pose no undue burden on these entities. At the same time, we assist small businesses in complying with FDA regulatory requirements through our Regional Small Business Representatives and through the administrative and scientific staffs within the agency. We also provide a Small Business Guide on our website at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/small-entity-compliance-guide-current-good-manufacturing-practice-manufacturing-packaging-labeling

6. Consequences of Collecting the Information Less Frequently

Data collection is ongoing. We believe maintaining accurate records results from daily information collection activity. Less frequent information collection may reduce the reliability of documentation that is intended to ensure that dietary supplements are manufactured, packaged, labeled, and held in a manner that ensures the quality of the dietary supplement and that the dietary supplement is packaged and labeled as specified in the master manufacturing record.

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

There are no special circumstances associated with this collection of information.

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

In accordance with 5 CFR 1320.8(d), we published a 60-day notice for public comment in the *Federal Register* of December 5, 2019 (84 FR 66658). No comments were received.

9. Explanation of Any Payment or Gift to Respondents

We do not provide any payment or gift to respondents.

10. Assurance of Confidentiality Provided to Respondents

Company records describing manufacturing procedures, which may be consulted during FDA plant inspections, and records that the agency may copy or take possession of, often contain trade secret and commercial confidential information. Confidential commercial information is protected from disclosure under the Freedom of Information Act (FOIA) under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)), by Section 301(j) of the FD&C Act, and by part 20 of the Agency's regulations (21 CFR part 20).

Privacy Act

This information collection request (ICR) is collecting personally identifiable information (PII) or other data of a personal nature. Recordkeeping requirements pertaining to quality control operations require the signatures of quality control personnel when certain specified, quality control procedures are performed or when certain information is provided. *See* 21 CFR 111.140(b)(2)(ii) and (b)(3)(vii). The recordkeeping requirements pertaining to training require documentation of training, including the person(s) trained. *See* 21 CFR 111.14(b)(2). The complaints recordkeeping requirements require a written record of every product complaint that is related to good manufacturing practice. This written record must include the name, address, or telephone number of the complainant, if available. *See* 21 CFR 111.570(b)(2)(ii)(C). This collection of information asks the respondents to maintain records at their site. Therefore, no records are stored with FDA.

In preparing this supporting statement our Privacy Office was consulted to ensure appropriate handling of information collected. We determined that although PII is collected, the collection is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Act do not apply. Specifically, we do not use name or any other personal identifier to routinely retrieve records from the information collected.

11. Justification for Sensitive Questions

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

12. Estimates of Annualized Burden Hours and Cost

12a. Annualized Hour Burden Estimate

The recordkeeping and reporting requirements of the regulations in part 111 are set forth in each subpart. In Table 1, we list the annual burdens associated with recordkeeping. 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 one 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 many 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.

We estimate the burden of this collection of information as follows:

Table 1 – Estimated Annual Recordkeeping Burden[1]

21 CFR Section; Activity	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 mins.)	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 mins.)	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 mins.)	72,000
TOTAL					929,140

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

The burden estimates in Table 1 are based on the agency's institutional experience and other CGMP requirements.

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 (e.g., what the batch record must include).

Table 2 – Estimated Annual Reporting Burden[1]

21 CFR Section; Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
111.75; petition for exemption from 100 percent identity testing	1	1	1	8	8

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

In the last 3 years, we have received one new petition to request an exemption from 100 percent identity testing of dietary ingredients; therefore, the agency estimates that one or fewer petitions will be submitted annually. Based on our experience with petition processes, we estimate that the assembly of information in support of the petition required by § 111.75(a)(1)(ii) will take about 8 hours.

12b. Annualized Cost Burden Estimate

We estimate that the average hourly wage for respondents' workers involved in recordkeeping is equivalent to a GS-5-1 level in the locality pay area of Washington- Baltimore in 2020, approximately $18.83/hour. Doubling this wage to account for overhead costs, we estimate the

average hourly cost to respondents to be $37.66/hour. Therefore, the overall estimated cost incurred by the respondents is $34,991,713.68 (929,148 burden hours x $37.66/hour = $34,991,713.68).

Table 3.--Estimate of Annualized Cost Burden

Activity	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Recordkeeping	929,148	$37.66	$34,991,713.68

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

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

14. Annualized Cost to the Federal Government

FDA's review of the retained records would generally occur as part of its routine or for cause establishment inspection activities. We estimate that review of the retained records would take five hours per inspection. We estimate the hourly cost for review and evaluation to be $49.19 per hour, the GS-13/Step-1 rate for the Washington-Baltimore locality pay area for the year 2020. To account for overhead, this cost is increased by 100 percent, making the total cost $98.38 per hour. We estimate the cost to the Federal Government for the review of records to be $491.90 per review ($98.38/hour x 5 hours) and that we review records for an average of 100 inspections per year. Thus, we estimate the total annual cost to the Federal Government to be $49,190 ($491.90 x 100 inspections).

15. Explanation for Program Changes or Adjustments

We have made no changes to our estimate of the information collection based on our most recent review. However, in consolidating burden from OMB control number 0910-0608, the information collection reflects an increase of 8 hours and one response annually applicable to petitions under 21 CFR 111.75. We have also consolidated previously itemized elements found at *Question 12* of this supporting statement into a single, cumulative estimate we attribute to the recordkeeping requirements found in 21 CFR part 111.

16. Plans for Tabulation and Publication and Project Time Schedule

The results of this information collection will not be published.

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

There are no reasons why display of the expiration date for OMB approval of the information collection would be inappropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.