Guidance for Industry on Electronic Drug Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act

OMB Control No. 0910-[NEW]

Supporting Statement Part A

A. **Justification**

1. Circumstances Making the Collection of Information Necessary

On November 27, 2013, the President signed the Drug Quality and Security Act (DQSA) into law. The DQSA added a new section 503B to the Federal Food, Drug, and Cosmetic Act (FD&C Act) creating a category of entities called "outsourcing facilities." Outsourcing facilities, as defined in section 503B(d)(4) of the FD&C Act, are facilities that meet all of the requirements described in section 503B. These conditions include registering with FDA as an outsourcing facility and submitting regular reports identifying the drugs compounded by the outsourcing facility during the previous 6-month period.

The first of these reports must be submitted upon initial registration as an outsourcing facility. Thereafter, product reports must be submitted once during the month of June and once during the month of December each year, for as long as an establishment remains registered as an outsourcing facility.

Drug products compounded in an outsourcing facility can qualify for exemptions from the FDA approval requirements in section 505 of the FD&C Act (21 U.S.C. 355) and the requirement to label products with adequate directions for use under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)) if the requirements in section 503B are met.

The guidance is intended for entities that compound human drugs and elect to register as outsourcing facilities under section 503B of the FD&C Act. Once an entity has elected to register as an outsourcing facility, it must submit reports identifying the drugs compounded by the outsourcing facility. The guidance describes who must report, the format of the report, the content that should be included in each report, when to report, and how outsourcing facilities may submit reports to FDA.

The guidance contains the following collections of information, as specified by the DQSA:

Upon initial registration as an outsourcing facility, each outsourcing facility that registers shall submit a report identifying the drugs compounded by such outsourcing facility during the previous 6-month period, and, with respect to each drug reported, provide the active ingredient, the source of the active ingredient, the National Drug Code (NDC) number of the source drug or bulk drug ingredient, if available, the strength of the active ingredient per unit, the dosage form and route of administration, the package description, the number of individual units produced, and the NDC number of the final products, if assigned.

Once during the month of June each year and once during the month of December each year, each outsourcing facility shall submit a report identifying the drugs compounded by such outsourcing facility during the previous 6-month period, and, with respect to each drug reported, provide the active ingredient, the source of the active ingredient, the National Drug Code Number of the source drug or bulk drug ingredient, if available, the strength of the active ingredient per unit, the dosage form and route of administration, the package description, the number of individual units produced, and the NDC number of the final products, if assigned.

2. Purpose and Use of the Information Collection

After an entity has elected to register as an outsourcing facility, it must submit regular reports identifying the drugs compounded by the outsourcing facility during the previous 6-month period. The guidance describes who must report, the format of the report, the content that should be included in each report, when to report, and how outsourcing facilities may submit reports to FDA.

3. Use of Improved Information Technology and Burden Reduction

Section 503B(b)(3) of the FD&C Act requires outsourcing facilities to register and report by electronic means unless FDA grants a request for a waiver of this requirement because the use of electronic means is not reasonable for the person requesting the waiver. Compounded product information must be submitted to FDA electronically using the Structured Product Labeling (SPL) format and in accordance with section IV of the FDA guidance entitled "*Providing Regulatory Submissions in Electronic Format--Drug Establishment Registration and Drug Listing*" (available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm064994.htm)

4. Efforts to Identify Duplication and Use of Similar Information

The requirements do not duplicate nor are they similar to any current requirements for these outsourcing facilities.

5. Impact on Small Businesses or Other Small Entities

FDA estimates that approximately 32% of outsourcing facilities would be considered small businesses. The information being requested in the final guidance has been held to the absolute minimum required for the intended use of the data. Most of the information requested in this guidance is specifically required by section 503B of the FD&C Act.

6. Consequences of Collecting the Information Less Frequently

The frequencies related to the submission of drug product reports under this guidance are specified by the DQSA. Under section 503B(b)(2)(A) of the FD&C Act, facilities that elect to register with FDA must submit product reports upon registration and in June and December of each year. The drug reporting requirement and the frequency which reports shall be submitted is specified by statute; therefore, any less frequent collection of reports would be in conflict with the statutory requirements. In order to be recognized as an "outsourcing facility" as defined in the FD&C Act, an entity must report as specified; if an entity does not report, that entity is not eligible for the exemptions from the FDA approval requirements in section 505 of the FD&C Act (21 U.S.C. 355) and the requirement to label products with adequate directions for use under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)).

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

There are no special circumstances relating to this information collection. (The submission of proprietary, trade secret, or other confidential information is addressed under section 10 below).

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

In response to the November 24, 2014, Federal Register (81 FR 69857) notice, FDA received 3 comments on the revised draft guidance that raised issues pertaining to the information collection. The issues raised are addressed below.

Issue One: Several comments said that the guidance should clarify FDA's definition of the source of the active ingredient used to compound the final product and the information the outsourcing facility should submit to FDA. One commenter requested clarification with regard to the source of active ingredient and whether the Agency will require solely the name of the registered supplier for the bulk and finished drug product or will outsourcing facilities be expected to provide other information.

FDA Response to Issue One: FDA thanks the commenter for raising this issue, which is beyond the scope of the present guidance. FDA intends to address this issue in future guidance or regulations.

Issue Two: One commenter expressed concern about being unable to submit a product report within the required 30-day reporting period because of the extensive amount of time to create a product report, especially for facilities with large product portfolios. The comment noted that FDA failed to recognize that each outsourcing facility will have numerous SPL entries into the electronic reporting system to make up a product report.

FDA Response to Issue Two: FDA agrees that the estimated total burden hours in the tables should be increased, and we have changed our estimate below. A facility's product report

is comprised of individual product SPL submissions, identified as responses in the table. FDA has also clarified in the final guidance, however, that there are ways to simplify the submission of product reporting information and reduce the number of responses and total burden of submitting product reporting information. Initially, the creation of product report submissions can be time consuming, but submissions can be saved, updated, and resubmitted for subsequent reporting periods instead of creating a new submission each time. In addition, multiple strengths of the same drug, package sizes, and source NDC numbers can be consolidated into a single product submission in SPL. FDA has changed the estimates that were provided in the November 24, 2014, Federal Register notice to account for the fact that each product report will consist of multiple SPL responses per facility.

9. Explanation of Any Payment or Gift to Respondents

There is no payment or gift to respondents associated with this guidance.

10. Assurance of Confidentiality Provided to Respondents

Information submitted to the FDA under these requirements will be handled consistent with applicable disclosure laws and regulations, including but not limited to the Freedom of Information Act (5 U.S.C. 552) and FDA's disclosure regulations in 21 CFR part 20.

As explained in the guidance, FDA intends to make proactive disclosures of some of the information provided by respondents. Section 503B(b)(1)(B)(i) provides that outsourcing facility registrations are available for inspection to any person so requesting and section 503B(b)(2)(C) specifies that product reports are exempt from inspection under section 503B(b)(1)(B)(i) unless the Secretary finds that such an exemption would be inconsistent with the protection of the public health. FDA finds that exempting from disclosure some of the information submitted in product reports would be inconsistent with the protection of the public health, specifically, for each marketed product: the name of the outsourcing facility, address of the outsourcing facility, name of the active ingredient, strength of the active ingredient per unit, dosage form, package description, and NDC of the final product (if assigned). This information is generally required on product labels or publicly available, but publication of this information will facilitate product recalls when they are necessary, and assist the public in finding outsourcing facilities that have compounded certain drug products, particularly drugs in shortage. FDA intends to publish this information on our Web site. FDA does not intend to publish information about a drug submitted in a product report if an outsourcing facility notes in the report that it has not distributed the drug and has not advised any person of its intent or ability to compound the drug.

11. Justification for Sensitive Questions

There are no sensitive questions associated with this guidance.

12. Estimates of Annualized Hour Burden and Costs

12a. Annualized Hour Burden Estimate

Based on current data for outsourcing facilities, we estimate a total of approximately 55 outsourcing facilities ("Number of Respondents" in table 1, row 1) will submit to FDA an initial report identifying all drugs compounded in the facility in the previous 6 months. For the purposes of this calculation, each product's SPL submission is considered a separate response, and therefore each facility's product report will include multiple responses.

Taking into account that a particular product that is compounded into different strengths from different sources of active ingredient can be reported in a single SPL response, we estimate that the number of products reported per facility will average 220 products per facility ("Number of responses per respondent" in tables 1 and 2, row 1). This estimate is based on current data in product reports.

Concerning the comment that each outsourcing facility will have numerous SPL entries, FDA agrees and has changed the estimates that were provided in the November 24, 2014, Federal Register notice to account for the fact that each product report will consist of multiple SPL responses per facility. We estimate that preparing and submitting this information electronically could take up to approximately 2 hours for each initial SPL response ("Average burden per response" in table 1, row 1).

We also estimate that a total of approximately 55 outsourcing facilities ("Number of Respondents" in table 2, rows 1 and 2) will submit to FDA a report twice each year identifying all drugs compounded at the facility in the previous six months. As described above, we estimate on average 220 SPL responses per facility. We estimate that preparing and submitting this information electronically will take approximately .5 hours per response ("Average burden per response" in table 2, rows 1 and 2). We have reduced the burden for semiannual product submissions due to the fact that outsourcing facilities can save each SPL response once initially created and submitted. For subsequent reports, an outsourcing facility may resubmit the same file(s) after changing only the following data elements to appropriate values for the reporting period (along with other data as appropriate): RootID and version number (both SPL metadata); effective date (to identify the reporting period); and the number of units produced. Furthermore, if a product was not compounded during a particular reporting period, no SPL response needs be sent for that product during that reporting period.

We expect to receive no more than one waiver request from the electronic submission process for initial product reports and semi-annual reports, and each request should take approximately 1 hour to prepare and submit to FDA.

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

Table 1.—Estimated Initial Reporting Burden[1]

Product Reporting for Compounding Outsourcing Facilities	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Average burden per response (hours)	Total Hours
Submission of Initial Product Report	55	220	12,100	2	24,200
Waiver Request From Electronic Submission of Initial Product Report	1	1	1	1	1
Total					24,201

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

Table 2 - Estimated Annual Reporting Burden[1]

Product Reporting for Compounding Outsourcing Facilities	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Average burden per response (hours)	Total Hours
Submission for June Product Report	55	220	12,100	.5	6,050
Submission for December Product Report	55	220	12,100	.5	6,050
Waiver Request From Electronic Submission of Product Reports	1	1	1	1	1
Total					12,101

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

12b. Annualized Cost Burden Estimate

The industry burden estimate calculated above would result in labor costs. FDA estimates that registrations are generally submitted by a regulatory affairs manager, and that labor hours are valued using the mean hourly wage of $63.89 as reported by the U.S. Department of Labor, Bureau of Labor Statistics, 2013 Employment Occupational Statistics for Management Occupations (SOC 11-0000) in Pharmaceutical and Medicine Manufacturing (North American Industry Notification, NAICS, code 325400). Wages are further adjusted for benefits and overhead, for an average hourly labor cost of $127.78 ($63.89 x 2). Using this wage rate, times 36,302 hours calculated above for this information collection, equals approximately $4,638,541.78 in labor costs.

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

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

14. Annualized Cost to the Federal Government.

We estimate approximately 0.5 FTE ($142,500; each FTE equals $285,000) annually to do the following: Receive, review, acknowledge, and confirm outsourcing facility product reporting submissions; respond to inquiries regarding outsourcing facility product reporting, including interpretation of section 503B product reporting provisions. This does not include IT development and maintenance costs. Development of IT solution cost is $107,000 via the Drug Quality Compliance Portal contract. Annual maintenance costs are included in the Operations and Maintenance portion of that contract.

15. Explanation for Program Changes or Adjustments

Because human drug compounders have not been required to register and list under section 510 of the FD&C Act and 21 CFR 207, it has been difficult to anticipate the number of outsourcing facilities that will participate in the process and the burden hours that they will incur. Consequently, we estimated a total of 302 hours in the PRA section of the November 24, 2014, Federal Register notice. As a result of the public comments, we have re-evaluated and increased the total burden hours to 36,302.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no plans for tabulation and publication and project time scheduling.

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

The OMB expiration data will be displayed where required.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.