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

0910-[NEW]

Supporting Statement

Terms of Clearance – None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

A facility that compounds drugs may elect to register with FDA as an outsourcing facility under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353b), as added by the Drug Quality and Security Act (DQSA). Products compounded in a registered 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 focuses on the electronic submission of establishment registration information. Each registered outsourcing facility would report to FDA certain information about the products it compounds. After the initial registration, under section 503B(b) of the FD&C Act, a facility that elects to register with FDA as an outsourcing facility must also do so annually between October 1 and December 31. Upon registration, the outsourcing facility must provide its name, place of business, a unique facility identifier, and a point of contact email address. The outsourcing facility must also indicate whether it intends to compound, within the next calendar year, a drug that appears on FDA's drug shortage list in effect under section 506E of the FD&C

Act (21 50 U.S.C. 356e), and whether it compounds from bulk drug substances, and, if so, whether it compounds sterile or non-sterile drugs from bulk drug substances.

2. Purpose and Use of the Information Collection

The guidance implements new provisions added to the FD&C Act in the DQSA in which Congress created a new statutory category of "outsourcing facilities" that compound human drugs. New section 503B of the FD&C Act (21 U.S.C. 353b) allows compounders to register with FDA as outsourcing facilities, and the draft guidance discusses the process for the registration of outsourcing facilities.

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 use of electronic means is not reasonable for the person requesting the waiver."

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 OPL's Economics Staff estimates that approximately 32% of outsourcing facilities would be considered small businesses. The information being requested in the final guidance, Registration of Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act, 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

After the initial registration, as required under section 503B(b) of the FD&C Act, a facility that elects to register with FDA as an outsourcing facility must also do so annually between October 1 and December 31. Thus, any less frequent collection of information would be in conflict with the statutory requirements.

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 accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of 12/4/2013 (78 FR 72899). FDA received 8 comments on the draft guidance, several of which raised issues pertaining to the information collection provisions in the draft guidance. The four issues raised are addressed below.

Issue One: Several commenters noted that the final guidance should clarify what product information will be included on the public list of registered outsourcing facilities required under section 503B(b)(1)(B)(ii) of the FD&C Act. Specifically, page 4, lines 133-134, of the Draft Guidance states that "information collected from the outsourcing facility registration, as well as certain product information, will be published in a list" authorized under section 503B(b)(1)(B)(ii) of the Act. The commenters requested assurances that confidential information submitted in product reports would remain confidential and not be posted on the Web. Other commenters requested clarification about how often the information will be updated.

FDA Response to Issue One: FDA has clarified the guidance. Specifically, the guidance now reads: “Section 503B(b)(1)(B)(ii) of the FD&C Act requires FDA to publish on the Internet

a list of registered outsourcing facilities that includes the name of each registered outsourcing facility, the state in which it is located, whether the facility compounds from bulk drug substances and whether such compounding from bulk drug substances is for sterile or non-sterile drugs. FDA will publish the information required, as well as the date of registration as an outsourcing facility and certain publicly disclosable information related to past FDA inspections and compliance actions. FDA intends to update the list of registered outsourcing facilities weekly."

Some of the commenters may have been confusing disclosure of registration information with disclosure of proprietary information required to be reported under section 503B(b)(2). That provision specifies that, upon initially registering as an outsourcing facility, once during the month of June of each year, and once during the month of December of each year, each facility that registers with the Secretary as an outsourcing facility shall submit to the Secretary a report providing certain information about the drugs that were compounded by the facility during the previous 6-month period. Unlike section 503B(b)(1), section 503B(b)(2) does not require that information reported be posted and specifies that reports submitted under the provision shall be exempt from inspection unless the Secretary finds that such an exemption would be inconsistent with the protection of the public health (section 503B(b)(2)(C)). FDA intends to address product reporting information in a separate guidance, "Electronic Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act." At this time, FDA does not intend to routinely disclose such information.

Issue Two: Another commenter noted that all registration information from the outsourcing facility should be made public using the Structured Product Labeling (SPL) format. The commenter suggested FDA obtain and make publicly available the following information:

Name/license number of supervising pharmacist(s), an indicator of compliance registration or date of first and last registration, and a link to FDA disciplinary actions and to a list of recalled products for that outsourcing facility.

FDA Response to Issue Two: The list of registered outsourcing facilities includes most of the information that the commenter suggested, including each facility's date of registration as an outsourcing facility and any action FDA has taken based on the most recent inspection. FDA publishes drug product recalls in its weekly Enforcement Report, which includes a description of the products subject to the recall. The commenter can check the Enforcement Report to view drug products that have been recalled. FDA does not include the name/license number of the supervising pharmacist because section 503B does not require facilities to provide this information to FDA when registering. This information is not in SPL format because FDA includes information in this list that is not captured in SPL, such as FDA regulatory actions.

Issue Three: One commenter requested insight on how FDA intends to communicate with industry those facilities that had previously registered as human drug compounders before the implementation of section 503B and those who are now registering under section 503B.

FDA Response to Issue Three: The FDA has made available on the public Internet a list of the facilities that have registered under section 503B as outsourcing facilities. FDA does not have a list of facilities that had previously registered as human drug compounders before section 503B was enacted as there was no category of registered human drug compounder before this. Some human drug compounding facilities may have registered prior to the enactment of section 503B as human drug manufacturers under section 510 of the FD&C Act. A list of all firms that are registered as manufacturers under section 510 is available to the public on FDA's Drug

Establishments Current Registration Site (DECRS), which is separate from the list of outsourcing facilities that have registered under section 503B.

Issue Four: Another commenter noted that FDA should define what would constitute an undue burden justifying the granting of a waiver from the submission of registration information electronically.

FDA Response to Issue Four: Section 503B(b)(3) of the FD&C Act specifies the standard FDA is to use to determine whether a waiver should be granted. FDA may grant a waiver if it finds that "use of electronic means is not reasonable for the person requesting the waiver." FDA does not anticipate many instances in which electronic submission of registration information will not be reasonable for the person requesting the waiver, because the information requested is minimal, and the electronic system for submitting the information is an Internet based system accessible to all firms seeking to register. Because human drug compounders are not currently required to register and report as outsourcing facilities, it is difficult to anticipate the number of outsourcing facilities that will participate in the process.

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

Confidentiality of the information submitted under these requirements is protected under 21 CFR part 20. The unauthorized use or disclosure of trade secrets is specifically prohibited under Section 310(j) of the FD&C Act. Most of the information requested in this guidance is required by law to be made public (see section 503B(b)(1) regarding the list that the Secretary shall make available on the public Internet Web site of the FDA, including a list of the name of each registered facility and certain information about the drug products they compound). FDA

will not disclose any information that is considered a trade secret and prohibited under section 310(j) of the FD&C Act, and such information is not requested in this guidance.

11. Justification for Sensitive Questions

There are no sensitive questions associated with this guidance.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

Under the guidance, outsourcing facilities that elect to register should submit the following registration information to FDA for each facility:

-- Name of the facility;

-- Place of business;

-- Unique facility identifier;

-- Point of contact email address and phone number;

-- Whether the facility intends to compound drugs that appear on FDA's drug shortage list in effect under section 506E of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 356e); and

-- An indication of whether the facility compounds from bulk drug substances, and if so, whether it compounds sterile or nonsterile drugs from bulk drug substances. After initial registration, outsourcing facilities should register annually between October 1and December 31of each year.

Registration information should 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." In the draft guidance that issued on December 4, 2013, FDA provided an alternative interim registration mechanism for use after initial passage of the DQSA and until

September 30, 2014. The final guidance specifies the use of the SPL format for all registrations. Under the final guidance, outsourcing facilities may request a waiver from the SPL electronic submission process by submitting a written request to FDA explaining why the use of electronic means is not reasonable.

We estimate that approximately 50 outsourcing facilities ("number of respondents" and "total annual responses" in table 1, row 1) will annually submit to FDA registration information using the SPL format as specified in the guidance, and that preparing and submitting this information will take approximately 4.5 hours per registrant ("average burden per response" in table 1, row 1). We expect to receive no more than one waiver request from the electronic submission process annually ("number of respondents" and "total annual responses" in table 1, row 2), and that each request should take approximately 1 hour to prepare and submit to us ("average burden per response" in table 1, row 2).

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

Table 1.—Estimated Annual Reporting Burden

Compounding Outsourcing Facility	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Electronic Submission of Registration Information Using SPL Format	50	1	50	4.50	225
Waiver Request From Electronic Submission of Registration Information	1	1	1	1	1
Total					226

12b. Annualized Cost Burden Estimate

The industry burden estimate calculated above would result in labor costs. FDA OPL's Economics Staff 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 226 hours calculated above for this information collection, equals approximately $28,878.28 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) to do the following: Receive, review, acknowledge, and confirm outsourcing facility registration submissions; respond to inquiries regarding outsourcing facility registration, including interpretation of section 503B registration provisions; and update and submit a weekly list of new 503B registrants to be published on FDA's website.

15. Explanation for Program Changes or Adjustments

This is a new data collection.

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.