Guidance for Industry on Fees for Human Drug Compounding Outsourcing Facilities Under Sections 503B and 744K 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

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, including registering with FDA as an outsourcing facility and paying an annual establishment fee. 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 pay certain fees to be registered as an outsourcing facility. The guidance describes the types and amounts of fees that outsourcing facilities must pay, the adjustments to fees required by law, how outsourcing facilities may submit payment to

FDA, the consequences of outsourcing facilities' failure to pay fees, and how an outsourcing facility may qualify as a small business to obtain a reduction in fees.

The guidance contains the following collections of information:

1. Upon receiving registration information from a facility seeking to register as an outsourcing facility, FDA will send an invoice for an establishment fee to the outsourcing facility. The invoice contains instructions for paying the establishment fee, as discussed in section III.E of the guidance. This process would be repeated annually under the timeframes described in the guidance. An outsourcing facility is not considered registered until the required establishment fee is paid for that fiscal year. (Section III.A of the guidance).

2. Outsourcing facilities that are reinspected will be assessed a reinspection fee for each reinspection. The reinspection fee is designed to reimburse FDA when it must visit a particular outsourcing facility more than once because of noncompliance identified during a previous inspection. A reinspection fee will be incurred for each reinspection that occurs, until FDA finds that the noncompliant conditions have been adequately addressed. After FDA conducts a reinspection, we will send an invoice to the email address indicated in the facility's registration file. The invoice contains instructions for paying the reinspection fee, as discussed in section III.E of the guidance. (Section III.C of the guidance).

3. Certain outsourcing facilities may qualify for a small business reduction in the amount of the annual establishment fee. To qualify for this reduction, an outsourcing facility must submit to FDA a written request and a certification that the entity meets the requirements for the reduction. For every fiscal year that the firm seeks to qualify as a small business and receive the fee reduction, the written request must be submitted to FDA by April 30 of the preceding fiscal

year. For example, an outsourcing facility must submit a written request for the small business reduction by April 30, 2014, to qualify for a reduction in the fiscal year 2015 annual establishment fee. As described in the guidance, section 744K of the FD&C Act also requires an outsourcing facility to submit its written request for a small business reduction in a format specified by FDA in the guidance. The guidance specifies that Form FDA 3908 is the format for submitting requests for a small business fee reduction. (Section III.D of the guidance).

4. Those outsourcing facilities that request a small business reduction in the amount of the annual establishment fee will receive a small business designation letter notifying the facility of FDA's decision. Outsourcing facilities eligible to pay a reduced fee should maintain a copy of the small business designation letter applicable to that fiscal year for their records. (Section III.D of the guidance).

5. An outsourcing facility may request a reconsideration under 21 CFR 10.75 of an FDA decision related to the fee provisions of section 744K of the FD&C Act. As explained in the guidance, the request should state the facility's rationale for its position that the decision was in error and include any additional information that is relevant to the outsourcing facility's argument. (Section V.B of the guidance).

6. An outsourcing facility may appeal, as set forth in 21 CFR 10.75, an FDA denial of a request for reconsideration of an FDA decision related to the fee provisions of section 744K of the FD&C Act. (Section V.B of the guidance).

2. Purpose and Use of the Information Collection

Once an entity has elected to register as an outsourcing facility, it must pay certain fees to be registered as an outsourcing facility. The guidance describes the types and amounts of fees

that outsourcing facilities must pay, the adjustments to fees required by law, how outsourcing facilities may submit payment to FDA, the consequences of outsourcing facilities' failure to pay fees, and how an outsourcing facility may qualify as a small business to obtain a reduction in fees.

3. Use of Improved Information Technology and Burden Reduction

The guidance encourages outsourcing facilities to make all submissions electronically. For example, to qualify for a small business reduction of the annual establishment fee, an entity must submit Form FDA 3908 certifying that the entity meets the requirements for the reduction. The guidance states that the completed form should be submitted via email to CDERCollections@FDA.HHS.gov, with the subject line containing "Outsourcing Facility Small Business Reduction request." When disputes arise between an outsourcing facility and FDA about an FDA decision related to the fee provisions of sections 503B and 744K of the FD&C Act, the outsourcing facility may request a reconsideration of that decision. The guidance states that all requests for reconsideration should be submitted via email to the Director of the Division of User Fee Management and Budget Formulation at CDERCollections@FDA.HHS.gov, with the subject title "Request for Reconsideration of Agency Decision – Outsourcing Facility Fee Determination." If a request is denied upon reconsideration, the outsourcing facility may choose to appeal the denial. The guidance states that all requests for appeals should be submitted to the Director of CDER's Office of Management at CDERCollections@FDA.HHS.gov with the subject title "Appeal of Agency's Decision at Reconsideration – Outsourcing Facility Fee Determination."

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's OPL Economics Staff estimates that 32% of outsourcing facilities would be considered small businesses. The guidance states that certain small businesses can qualify for a reduction of the annual establishment fee (a small business reduction). Entities that qualify as small businesses under section 744K(c)(4) of the FD&C Act are required to pay only one-third of the annual establishment fee. An entity with worldwide gross annual sales, including the sales of all affiliates, totaling $1,000,000 or less in the 12 months ending on April 1 of the FY immediately preceding the FY in which the annual establishment fee is assessed may qualify for a small business reduction. To qualify, an entity must submit to FDA a written request for such a reduction, certifying that the entity meets the requirements for the reduction. The request must be submitted electronically on Form FDA 3908, which is attached to the guidance.

In an effort to minimize the burden on small business and simplify the process for receiving the benefit of a small business reduction, FDA developed Form FDA 3908 for use by small businesses, and the information requested in the form has been held to the minimum necessary to process a small business reduction request.

6. Consequences of Collecting the Information Less Frequently

The frequencies related to the payment of fees under this guidance are specified by the DQSA. For example, under section 744K(a)(1) of the FD&C Act, facilities that elect to register with FDA must pay an annual establishment fee. The annual registration period, when to pay the establishment fee, and the small business reduction request deadline are all specified by statute.

Thus, any less frequent collection of the payment of fees 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 the Federal Register of April 1, 2014 (79 FR 18297), FDA announced the availability of the draft version of this guidance that addressed new provisions in the FD&C Act, as amended by the Compounding Quality Act (CQA), and set forth its interpretation of fees for human drug compounding pharmacies that choose to register as outsourcing facilities. FDA received 1 comment on the draft guidance, which raised several issues pertaining to the information collection provisions in the draft guidance. These issues are discussed below.

Issue One: The comment asserted that placement of facilities on a list of registered outsourcing facilities in fiscal year 2014 (before any registered outsourcing facilities had paid the required establishment fee) is contrary to the language of the CQA, because those entities had not yet paid the requisite establishment fee and, therefore, could not qualify as outsourcing facilities. The comment recommended that FDA interpret the CQA to require that a facility be required to pay the establishment fee in full to be deemed a "registered outsourcing facility".

FDA Response to Issue One: As the comment points out, section 744K(g)(3)(A) of the FD&C Act provides that "[a]n outsourcing facility shall not be considered registered under section 503B(b) in a fiscal year until the date that the outsourcing facility remits the

establishment fee under this subsection for such fiscal year." Section 744K(a)(1), however, provides that "[f]or fiscal year 2015 and each subsequent fiscal year, the Secretary shall, in accordance with this subsection, assess and collect—(A) an annual establishment fee from each outsourcing facility." The plain language of the statute makes clear that FDA is not to assess and collect the annual establishment fee for human drug outsourcing facilities until FY 2015. Because the fee provisions of the CQA, under section 744K, do not become effective until FY 2015, no fees are due in 2014, and payment of the establishment fee is not a prerequisite to registration in FY 2014. Therefore, failure to pay a fee was not a bar to registration as an outsourcing facility or to FDA placing such facilities on its list of registered outsourcing facilities on its website in FY 2014. Accordingly, FDA will not revise the proposed guidance to reflect the points addressed in the comment on issue one.

Issue Two: The comment expressed concern regarding FDA's estimation in the notice accompanying the guidance that only 20 of the current [at the time the notice was published] 43 facilities that registered in FY 2014 will pay the required establishment fee and be deemed registered outsourcing facilities for FY 2015.

FDA Response on Issue Two: FDA's estimates at the time the guidance was published, just a few months after the legislation was enacted, were its best estimates of how many firms were likely to register as outsourcing facilities. Registration as an outsourcing facility is a voluntary process, and FDA cannot predict with any certainty how many firms will register. As of July 18, 2014, 51 firms were registered. However, since registration began in December 2013, some firms have registered and then de-registered. Estimates of how many facilities will register in FY 2015 and beyond when establishment fees take effect are highly uncertain. Thus,

for purposes of calculating the information collection burden in the final guidance, in the tables below, FDA is estimating that 50 outsourcing facilities will register and pay establishment fees, and we have adjusted the other estimates (except for the "average burden per response") accordingly.

Issue Three: The comment noted that FDA failed to correlate the deadline to submit a request for a small business fee reduction with the deadline to comment on the small business reduction program in general. The comment noted that the deadline to submit a request for a small business reduction preceded the deadline for submitting comments to the public docket on the draft guidance. The comment suggested that this failure preempted stakeholders from submitting comments on the small business reduction program prior to the deadline for submitting their request to receive the small business reduction. The commenter expressed concern that FDA is not soliciting adequate input from interested parties. The commenter recommended that FDA provide more opportunities for stakeholder input. Moreover, the comment suggested that FDA extend the deadline for submitting small business reduction requests to such time as FDA has reviewed all comments.

FDA Response to Issue Three: FDA notes that section 744K(c)(4)(B) states that "[t]o qualify for the exception under this paragraph, a small business shall submit to the Secretary a written request for such exception . . . to the Secretary not later than April 30 of such immediately preceding fiscal year." The annual April 30 deadline for requesting a small business reduction is not a creation of FDA and the draft guidance; it is a statutory requirement mandated by Congress. FDA cannot revise the deadline enacted by Congress. Accordingly, FDA will not revise the draft guidance to permit entities to submit FY 2015 small business

reduction requests after April 30, 2014. In addition, notwithstanding the fact that the deadline to submit a small business reduction request preceded the deadline to submit comments on the draft guidance, the public had a full and meaningful opportunity to submit comments on the draft guidance. The draft guidance was made available on April 1, 2014, and the period to provide comments lasted 60 days, closing on June 2, 2014. FDA reviewed all comments submitted, and considered each of them carefully. Having considered all comments received, FDA will not revise the draft guidance in response to comments on issue three. Furthermore, FDA has recently held a series of meetings with stakeholders to hear their views and concerns on any aspects of FDA's implementation of the Compounding Quality Act they wanted to discuss. Over 40 organizations participated, including the commenter, and there was a robust discussion of the issues and concerns associated with many aspects of the implementation effort. FDA will consider the input provided during these meetings as it moves forward to implement the Act.

Issue 4: The comment noted that FDA has not provided adequate guidance on the standards to which 503B and 503A facilities will be held. This lack of guidance, the comment argues, creates uncertainty and confusion in the compounding industry about standards of practice expected by FDA. The comment further noted that notwithstanding the lack of guidance and the confusion within the industry, FDA has not provided an opportunity for facilities to decline to operate as outsourcing facilities under section 503B and instead identify themselves as 503A pharmacies. Instead, the comment notes, FDA has dictated that all of these facilities will be deemed in violation of the new drug requirements of the FD&C Act and in possession of misbranded drugs until they pay the establishment fee. The comment recommends that FDA

outline a clear process for outsourcing facilities interested in withdrawing their 503B registration packets and instead identifying and operating as 503A regulated pharmacies.

FDA Response to Issue 4: FDA notes that the comments focus primarily on matters not covered by the draft guidance, i.e., the standards for satisfying the conditions necessary to qualify for the exemptions under sections 503A and 503B. These standards will be addressed in other guidance and regulations, such as the recently issued final guidance entitled "Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act," (79 FR 3774; July 2, 2014) and the draft guidance entitled, "Current Good Manufacturing Practice – Interim Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act." (79 FR 37743; July 2, 2014). Because the draft fees guidance does not discuss the substantive provisions of 503A or 503B—focusing instead on 744J and 744K—the response to this issue cannot be addressed in the context of this draft guidance. Accordingly, FDA will not incorporate the recommendations suggested in the comments on this issue into the final version of this draft guidance.

With regard to providing a process for registered outsourcing facilities to de-register and identify themselves as 503A pharmacies, the final guidance describes how a registered outsourcing facility can de-register. With regard to the substantive effect of de-registering, the law, the guidance, and information on FDA's website make it clear that a facility has three choices: (1) Comply with the FDA approval requirements in section 505 of the FDCA [21 U.S.C. § 355], the requirement to label products with adequate directions for use under section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)], and the requirements for current good manufacturing practices (CGMP) under section 501(a)(2)(B)); (2) meet the conditions to qualify

for the exemptions from these three requirements by meeting the conditions to qualify for the exemptions under section 503A; or (3) register as an outsourcing facility and meet the conditions under section 503B to qualify for the exemptions from the FDA approval requirements and adequate directions for use. A firm's compliance status will be determined by whether they have registered as an outsourcing facility and are meeting the conditions of 503B (including payment of the required fee if they register on or after October 1, 2014), or if they have not registered, whether they are meeting the conditions of section 503A. If they are not meeting the conditions necessary to qualify for the exemptions under either 503A or 503B, they may be held to be in violation of any applicable provisions of the FDCA.

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. Small business reduction request forms submitted to FDA are handled exclusively by FDA employees. All forms received are uploaded into an internal Access database. Original documents will be destroyed after the information has been converted into an electronic format. The electronic files will be maintained according to FDA document retention schedules and destroyed when no longer needed for administrative, legal, or audit purposes.

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

The guidance pertains to entities that compound human drugs and elect to register as outsourcing facilities. These outsourcing facilities must pay certain fees to FDA. The guidance describes the fee types and amounts, the adjustments to fees required by law, how to submit payment, the effect of failure to pay fees, and how to qualify as a small business to obtain a reduction of the annual establishment fee. The guidance contains the following collections of information:

1. As described in section III.A of the guidance, upon receiving registration information from a facility seeking to register as an outsourcing facility, FDA will send an invoice for an establishment fee to the outsourcing facility. The invoice contains instructions for paying the establishment fee, as discussed in section III.E of the guidance. This process would be repeated annually under the timeframes described in the guidance. An outsourcing facility is not considered registered until the required establishment fee is paid for that fiscal year.

We estimate that annually a total of 50 outsourcing facilities ("no. of respondents" in table 1, row 1) will pay to FDA 50 establishment fees ("total annual responses" in table 1, row 1) as described in the guidance. We also estimate that it will take an outsourcing facility 0.50 hours to prepare and submit to FDA each establishment fee ("average burden per response" in table 1, row 1).

2. As described in section III.C of the guidance, outsourcing facilities that are reinspected will be assessed a reinspection fee for each reinspection. The reinspection fee is designed to reimburse FDA when it must visit a particular outsourcing facility more than once because of

noncompliance identified during a previous inspection. A reinspection fee will be incurred for each reinspection that occurs. After FDA conducts a reinspection, we will send an invoice to the email address indicated in the facility's registration file. The invoice contains instructions for paying the reinspection fee, as discussed in section III.E of the guidance.

We estimate that annually a total of 15 outsourcing facilities ("no. of respondents" in table 2, row 1) will pay to FDA 15 reinspection fees ("total annual responses" in table 2, row 1) as described in the guidance. We also estimate that it will take an outsourcing facility 0.50 hours to prepare and submit to FDA each reinspection fee ("average burden per response" in table 2, row 1).

3. As described in section III.D of the guidance, certain outsourcing facilities may qualify for a small business reduction in the amount of the annual establishment fee. To qualify for this reduction, an outsourcing facility must submit to FDA a written request certifying that the entity meets the requirements for the reduction. For every fiscal year that the firm seeks to qualify as a small business and receive the fee reduction, the written request must be submitted to FDA by April 30 of the preceding fiscal year. For example, an outsourcing facility must submit a written request for the small business reduction by April 30, 2015, to qualify for a reduction in the fiscal year 2016 annual establishment fee. As described in the guidance, section 744K of the FD&C Act also requires an outsourcing facility to submit its written request for a small business reduction in a format specified by FDA in the guidance. The guidance specifies that Form FDA 3908 is the format for submitting requests for a small business fee reduction.

We estimate that annually a total of 15 outsourcing facilities ("no. of respondents" in table 1, row 2) will submit to FDA a request for a small business reduction in the amount of the

annual establishment fee. We estimate that 15 outsourcing facilities will submit Form FDA 3908 ("total annual responses" in table 1, row 2) to FDA annually, as described in the guidance, and that it will take an outsourcing facility 25 hours to prepare and submit to FDA each Form FDA 3908 ("average burden per response" in table 1, row 2).

4. As described in section III.D of the guidance, those outsourcing facilities that request a small business reduction in the amount of the annual establishment fee will receive a small business designation letter notifying the facility of FDA's decision. Outsourcing facilities eligible to pay a reduced fee should maintain a copy of the small business designation letter applicable to that fiscal year for their records.

We estimate that annually a total of 15 outsourcing facilities ("no. of recordkeepers" in table 3) will keep a copy of their small business designation letter ("total annual records" in table 3), and that maintaining each record will take 0.5 hours ("average burden per recordkeeping" in table 3).

5. As described in section V.B of the guidance, an outsourcing facility may request a reconsideration under 21 CFR 10.75 of an FDA decision related to the fee provisions of section 744K of the FD&C Act. As explained in the guidance, the request should state the facility's rationale for its position that the decision was in error and include any additional information that is relevant to the outsourcing facility's argument.

We estimate that a total of 6 outsourcing facilities ("no. of respondents" in table 2, row 2) annually will submit to FDA a request for reconsideration as described in the guidance. We estimate that it will take an outsourcing facility approximately 1 hour to prepare and submit to FDA each request for reconsideration ("average burden per response" in table 2, row 2).

6. As described in section V.B of the guidance, an outsourcing facility may appeal, as set forth in 21 CFR 10.75, an FDA denial of a request for reconsideration of an FDA decision related to the fee provisions of section 744K of the FD&C Act.

We estimate that a total of 3 outsourcing facilities ("no. of respondents" in table 2, row 3) annually will submit an appeal of an FDA denial of a request for reconsideration. We estimate that it will take an outsourcing facility 1 hour to prepare and submit each appeal under 21 CFR 10.75 ("average burden per response" in table 2, row 3).

In the Federal Register of August 22, 2014 (79 FR 51176), FDA announced that it is submitting to OMB the PRA burden for submitting outsourcing facility registration information to FDA as specified in the guidance for industry entitled "Registration for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act."

The estimated reporting and recordkeeping burdens for this collection of information are as follows:

Table 1.-- Estimated Annual Reporting Burden – Establishment Fee

Type of Reporting	No. of Respondents	No of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Payment of annual establishment fee	50	1	50	0.50 (30 min.)	25
Request for Small Business Establishment Fee Reduction (FDA Form 3908)	15	1	15	25	375
Total					400

Table 2 -- Estimated Annual Reporting Burden - Reinspection Fee and Dispute Resolution Requests

Type of Reporting	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Payment of re-inspection fee	15	1	15	0.50 (30 min.)	7.50
Reconsideration request	6	1	6	1	6
Appeal request	3	1	3	1	3
Total					16.50

Table 3 -- Estimated Annual Recordkeeping Burden

Type of Recordkeeping	No. of Recordkeepers	No. of Records Per Recordkeeper	Total Annual Records	Average Burden per Record	Total Hours
Copy of small business designation letter	15	1	15	0.50 (30 min.)	7.50

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 424 hours calculated above for this information collection, equals approximately $54,178.72 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

Type of Activity	Est. No. Hours	Hourly Rate	Total Cost
Drafting regulations, Federal Register notices, and so forth	380	$ 137	$ 52,060
Evaluating small business exemption requests	52	$ 137	$ 7,124
Processing annual fee payments (including reinspections)	972	$ 137	$ 133,164
Undertaking communications and outreach efforts	115	$137	$ 15,755
Totals	1,519		$ 208,103

Notes:

1. The hourly rate is determined by dividing the Agency's fully-loaded cost of $285,000 per FTE by the number of hours per FTE per year (2,080) to arrive at $137 per hour.

2. The annual FTE impact is (1,519 / 2,080 hours per year) = 0.73 FTE.

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.