



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-0329]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Guidance for Industry on Fees for Human Drug Compounding Outsourcing Facilities Under the Federal Food, Drug, and Cosmetic Act

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 (the 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 title. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Rd., COLE-14526, Silver Spring, MD 20993-0002, PRStaff@fda.hhs.gov.

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.

Guidance for Industry on Fees for Human Drug Compounding Outsourcing Facilities Under the
Federal Food, Drug, and Cosmetic Act

In the Federal Register of April 1, 2014 (79 FR 18297), FDA announced the availability of the draft guidance for industry entitled “Fees for Human Drug Compounding Outsourcing Facilities Under Sections 503B and 744K of the FD&C Act.” On November 27, 2013, President Obama signed the Drug Quality and Security Act (DQSA) (Pub. L. 113-54) into law. The DQSA added a new section 503B to the FD&C Act (21 U.S.C. 353B) that created 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 certain requirements described in section 503B, including, registering with FDA as an outsourcing facility and paying associated fees. 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 of the FD&C Act are met.

This guidance describes in detail the fee types and amounts an entity must pay to satisfy the fee requirements of sections 503B and 744K of the FD&C Act (21 U.S.C 379j-62) to be deemed an outsourcing facility and maintain its status as an outsourcing facility, the adjustments to the fees required by law, how to qualify as a small business to obtain a reduction of the annual establishment fee, how and when to submit payment to FDA, the effect of failure to pay fees, and fee-related dispute resolution.

In response to the April 1, 2014, Federal Register notice, FDA received one 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 1) The comment asserted that placement of facilities on a list of registered outsourcing facilities in fiscal year (FY) 2014 (before any registered outsourcing facilities had paid the required establishment fee) is contrary to the language of the DQSA, 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 DQSA to require that a facility be required to pay the establishment fee in full to be deemed a “registered outsourcing facility.”

(Response) 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 DQSA, 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 Web site in FY 2014. Accordingly,

FDA will not revise the proposed guidance to reflect the points addressed in the comment on issue one.

(Issue 2) 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.

(Response) 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 tables 1-3, FDA is estimating that approximately 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 3) 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.

(Response) 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 to 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 3. 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 DQSA 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 DQSA.

(Issue 4) The comment noted that FDA has not provided adequate guidance on the standards to which section 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 section 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 section 503B registration packets and instead identifying and operating as section 503A regulated pharmacies.

(Response) 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 of the FD&C Act. 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 37742, 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 section 503A or 503B of the

FD&C Act--focusing instead on sections 744J (21 U.S.C. 379j-61) and 744K of the FD&C Act--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 section 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 Web site make it clear that a facility has three choices: (1) Comply with the FDA approval requirements in section 505 of the FD&C Act, the requirement to label products with adequate directions for use under section 502(f)(1) of the FD&C Act, and the requirements for current good manufacturing practices under section 501(a)(2)(B)) of the FD&C Act; (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 of the FD&C Act; or (3) register as an outsourcing facility and meet the conditions under section 503B of the FD&C Act 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 section 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 of the FD&C Act. If they are not meeting the conditions necessary to qualify for the exemptions under either section 503A or 503B, they may be held to be in violation of any applicable provisions of the FD&C Act.

Burden estimates: As discussed previously, 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:

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).

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).

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 the 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 FY 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).

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).

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 1 hour to prepare and submit to FDA each request for reconsideration (“Average Burden Per Response” in table 2, row 2).

As described in section V.B of the guidance, an outsourcing facility may appeal, as set forth in § 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 § 10.75 (“Average Burden Per Response” in table 2, row 3).

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

Table 1.--Estimated Annual Reporting Burden--Establishment Fee¹

| 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 | 0.5 (30 min.) | 25 |
| Request for small business establishment fee reduction (FDA Form 3908) | 15 | 1 | 15 | 25 | 375 |
| Total | | | | | 400 |

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

Table 2.--Estimated Annual Reporting Burden--Reinspection Fee and Dispute Resolution Requests¹

| 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 | 0.5 (30 min.) | 7.50 |
| Reconsideration request | 6 | 1 | 6 | 1 | 6 |
| Appeal request | 3 | 1 | 3 | 1 | 3 |
| Total | | | | | 16.50 |

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

Table 3.--Estimated Annual Recordkeeping Burden¹

| 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 | 0.5 (30 min.) | 7.50 |

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

Dated: August 26, 2014.

Leslie Kux,

Assistant Commissioner for Policy.