



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-N-2973]

Agency Information Collection Activities; Proposed Collection; Comment Request; Obtaining Information for Evaluating Nominated Bulk Drug Substances for Use in Compounding Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (PRA), Federal Agencies are required to publish notice in the *Federal Register* concerning each proposed collection of information and to allow 60 days for public comment in response to the notice. This notice solicits comments on information collection associated with FDA research in obtaining information from medical specialty groups and/or medical experts regarding compounded drug products that contain certain bulk drug substances to support establishment of a list of bulk drug substances under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

DATES: Submit either electronic or written comments on the collection of information by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The <https://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2018-N-2973 for "Obtaining Information for Evaluating Nominated Bulk Drug Substances for Use in Compounding Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit

both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRASStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the *Federal Register* concerning each proposed collection of

information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Clinical Use of Bulk Drug Substances Nominated for Use in Compounding by Outsourcing
Facilities

OMB Control Number 0910-NEW

This information collection supports Agency-sponsored research. Section 503B of the FD&C Act requires FDA to develop a list of bulk drug substances that may be used in compounding under that section (503B bulks list). Compounding includes the combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug or bulk drug substance to create a drug. If certain conditions are met, drug products compounded by entities known as outsourcing facilities are exempt from the following requirements of the FD&C Act: requirements for FDA approval of drugs, labeling with adequate directions for use, and drug supply chain security requirements. Outsourcing facilities can only use a bulk drug substance to compound drugs if: (1) the substance appears on a list developed by FDA of bulk drug

substances for which there is a clinical need ("bulks list") or (2) the substance is used to compound a drug on FDA's drug shortage list at the time of compounding, distribution, and dispensing.

Many bulk drug substances have been nominated by the public for use in compounding by outsourcing facilities with adequate supporting information for FDA to evaluate them. The substances were nominated to treat a variety of conditions, ranging in degree of severity from treatment of warts to treatment of cancer. To inform our evaluation of bulk drug substances for inclusion on the 503B bulks list, we have proposed a research study with the University of Maryland (UMD) Center of Excellence in Regulatory Science and Innovation (CERSI) and the Johns Hopkins University (JHU) CERSI. We intend to seek input from the CERSI-UMD on the use of these bulk drug substances in clinical practice by examining their current and historical use in compounding. Information regarding the historical and current use of the substances in compounding obtained by this research will help inform our assessments as to the clinical need for outsourcing facilities to use the substance in compounding.

FDA's analysis concerning clinical need of nominated bulk drug substances consists of two parts. The collaboration with CERSI-UMD and CERSI-JHU pertains to part 2 of the analysis, which applies to bulk drug substances that are not components of FDA-approved drug products, as well as certain bulk drug substances that are components of FDA-approved drug products and have successfully completed part 1. One of the factors that FDA considers under part 2 is "current and historical use of the substance in compounded drug products, including information about the medical condition(s) that the substance has been used to treat and any references in peer-reviewed medical literature."

As needed, researchers will also engage outsourcing facilities that have compounded using the bulk drug substance. Researchers may use surveys, interviews, focus groups, and other information collect tools, as appropriate, to obtain information concerning the use of compounded product(s) from medical experts and outsourcing facilities. Within this context, the following questions may be posed:

1. What are the health conditions that the compounded drug is currently and has been historically used to treat? What is the patient population for which the compound drug has been used to treat?
2. What are the characteristics of the compounded drugs using the bulk drug substance (e.g., dosage form, strength, route of administration)?
3. Is the compounded drug considered standard therapy by healthcare practitioners, and is it recommended in clinical practice guidelines? If so, under what circumstances?
4. Does an approved drug exist for the health condition that the compounded drug product is used to treat? If so, what are the circumstances under which a compounded drug product using the bulk drug substance would be used in lieu of the approved drug product?
5. What is the historical use of the compounded drug to treat the health conditions identified, including the number of years during which the compounded drug has been prescribed for each use, and any change regarding its use over time?
6. To what extent do practitioners prescribe the compounded drug to treat each health condition identified? How many such prescriptions and/or orders have been written in the past 5 years? Have there been any notable changes in the number of prescriptions and/or orders written over this time?

7. How widespread is the use of the compounded drug product, including use in other countries?

8. Do practitioners order the compounded drug to maintain on hand before a patient presents with a need for the drug ("office stock"), or do practitioners typically write prescriptions for a patient after the patient presents with a need for the compounded drug? If the former, why (e.g., emergency situations, convenience)?

9. What, if any, information exists regarding the effectiveness of the compounded drug product in treating the specified health condition?

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

Table 1.--Estimated Annual Reporting Burden¹

Information Collection	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Focus groups and interviews	150	10	1,500	2	3,000

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

We base our estimate of the average burden per response on review activities familiar to the Agency. Noting that 2 hours per response is a significant amount of time, we are particularly interested in feedback regarding this estimate, including comments regarding how an alternative estimate might be derived.

Dated: September 11, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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