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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Chapter I

[Docket No. FDA-2015-D-3539]

Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing the availability of a guidance for industry entitled "Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act." The guidance describes FDA's interim regulatory policy regarding outsourcing facilities that compound human drug products using bulk drug substances while FDA develops the list of bulk drug substances that can be used in compounding under the Federal Food, Drug, and Cosmetic Act (the FD&C Act).

DATES: Submit electronic or written comments on Agency guidances at any time.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to http://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 http://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): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, 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-2015-D-3539 for "Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act". Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at

http://www.regulations.gov or at the Division of Dockets Management 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 http://www.regulations.gov. Submit both copies to the Division of Dockets Management. 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: http://www.fda.gov/regulatoryinformation/dockets/default.htm.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to http://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 Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Sara Rothman, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 5197, Silver Spring, MD 20993-0002, 301-796-3110.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act." A new section 503B (21 U.S.C. 353b), added to the FD&C Act by the Drug Quality and Security Act in 2013, describes the conditions that must be satisfied for human drug products compounded by an outsourcing facility to be exempt from the following three sections of the FD&C Act: Section 505 (21 U.S.C. 355) (concerning the approval of drugs under new drug applications or abbreviated new drug applications); section 502(f)(1) (21 U.S.C. 352(f)(1)) (concerning the labeling of drugs with adequate directions for use); and section 582 (21 U.S.C. 360eee-1) (concerning drug supply chain security requirements). One of the conditions that must be met for a drug product compounded by an outsourcing facility to qualify for these exemptions is that the outsourcing facility does not compound drug products using a bulk drug substance

unless: It appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need (see section 503B(a)(2)(A)(i) of the FD&C Act); or the drug compounded from such bulk drug substances appears on the drug shortage list in effect under section 506E of the FD&C Act (21 U.S.C. 356e) at the time of compounding, distribution, and dispensing (see section 503B(a)(2)(A)(ii) of the FD&C Act).

This guidance describes the conditions under which FDA does not intend to take action against an outsourcing facility for compounding a drug product from a bulk drug substance that does not appear on a list of bulk drug substances that can be used in compounding and is not used to compound a drug product that appears on the FDA drug shortage list at the time of compounding, distribution, and dispensing, while FDA develops the list of bulk drug substances that can be used in compounding pursuant to section 503B(a)(2)(A)(i) of the FD&C Act (503B bulks list).[1]

The guidance also describes FDA's process to establish the 503B bulks list, and it describes categories of substances that were nominated for inclusion on the 503B bulks list. These categories include:

- 503B Category 1--Bulk Drug Substances Under Evaluation: These bulk drug substances may be eligible for inclusion on the 503B bulks list, were nominated with sufficient supporting information for FDA to evaluate them, and do not appear on any other list.

[1] Elsewhere in this issue of the Federal Register, the Agency is making available a guidance entitled "Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act," which describes the conditions under which FDA does not intend to take action against a licensed pharmacist in a State-licensed pharmacy or Federal facility, or a licensed physician, for compounding a drug product from a bulk drug substance that cannot otherwise be used in compounding under section 503A of the FD&C Act while FDA develops the list of bulk drug substances that can be used in compounding under section 503A(b)(1)(A)(i)(III).

- 503B Category 2--Bulk Drug Substances That Raise Significant Safety Risks: These bulk drug substances were nominated with sufficient supporting information to permit FDA to evaluate them and they may be eligible for inclusion on the 503B bulks list. However, FDA has identified significant safety risks relating to the use of these bulk substances in compounding, and therefore does not intend to adopt the policy described for the bulk substances in Category 1.
- 503B Category 3--Bulk Drug Substances Nominated Without Adequate Support: These bulk drug substances may be eligible for inclusion on the 503B bulks list but were nominated with insufficient supporting information for FDA to evaluate them. These substances can be re-nominated with sufficient supporting information through a docket that FDA has established.

In the Federal Register of October 27, 2015 (80 FR 65768), FDA issued a notice announcing the availability of the draft version of this guidance. The comment period on the draft guidance ended on December 28, 2015. FDA received 11 comments on the draft guidance. In response to received comments or on its own initiative, FDA made several changes to the guidance to clarify particular points. In addition, FDA has made the following updates to the lists on its Web site of bulk drug substances that were nominated for inclusion on the 503A bulks list:[2]

- 503B Category 2: FDA has added one bulk drug substances to Category 2, germanium sesquioxide, because FDA identified significant safety risks relating to the use of this bulk drug substance in compounding.

[2] In the future, if FDA makes changes to the categories of bulk drug substances on its Web site, we intend to follow the procedure identified in the guidance.

- 503B Category 4: The draft interim guidance included a fourth category of bulk drug substances that would have identified substances that FDA evaluated for inclusion on the 503B bulks list but, after obtaining and considering public comments, decided not to place on the 503B bulks list. In the final interim guidance, FDA removed this fourth category because the Agency intends to identify the bulk drug substances that will not be placed on the 503B bulks list in the Federal Register notice that establishes the 503B bulks list. Therefore, we do not believe it is necessary to also include them in the categories identified in this guidance.

II. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or http://www.regulations.gov.

Dated: June 7, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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