Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document contact Sara Rothman, CDER Office of Compliance Office of Unapproved Drugs and Labeling Compliance (OUDLC) at 301-796-3110.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance/OUDLC

October 2015
Compounding and Related Documents

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Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION AND SCOPE

This guidance sets forth the Food and Drug Administration's (FDA or Agency) interim regulatory policy concerning compounding using bulk drug substances under section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act or Act). Section 503A of the FD&C Act includes certain restrictions on the bulk drug substances[2] that can be used in compounding and directs the FDA to develop a list of bulk drug substances that can be used in compounding under that section. FDA is developing this list of bulk drug substances (the 503A bulks list), and this guidance describes FDA's interim regulatory policy for licensed pharmacists in State-licensed pharmacies and Federal facilities, and for licensed physicians that compound human drug products using bulk drug substances while the list is being developed.[3] [4]

[1] This guidance has been prepared by multiple offices in the Center for Drug Evaluation and Research (CDER) and in consultation with the Office of Regulatory Affairs at the Food and Drug Administration.

[2] Section 503A references the definition of bulk drug substances in FDA regulations at 21 CFR 207.3(a)(4), which defines *bulk drug substance* as "any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances."

[3] This guidance does not apply to drugs compounded from bulk drug substances for use in animals. For proposed policies pertaining to compounding drug products from bulk drug substances for use in animals, see FDA's draft guidance, *Compounding Animal Drugs from Bulk Drug Substances*.

All FDA guidances are available on the FDA guidance web page. FDA updates guidances regularly. To make sure you have the most recent version of a guidance, always consult the guidance web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[4] FDA is developing a separate list of bulk drug substances that can be used in compounding under section 503B of the FD&C Act. Because section 503B contains different criteria for that list and provides for a different process for its development, the section 503B bulks list is covered under a separate guidance (see "Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act").

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. Compounding From Bulk Drug Substances Under Section 503A of the Act

Section 503A of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist in a State licensed pharmacy or Federal facility, or by a licensed physician, to be exempt from the following three sections of the FD&C Act: section 505 (concerning the approval of drugs under new drug applications or abbreviated new drug applications); section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and section 501(a)(2)(B) (concerning current good manufacturing practice requirements).

One of the conditions that must be met for a compounded drug product to qualify for these exemptions is that a licensed pharmacist or licensed physician compounds the drug product using bulk drug substances that:

(1) Comply with the standards of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph,[5] if a monograph exists, and the USP chapter on pharmacy compounding;
(2) If such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or
(3) If such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, appears on a list developed by the Secretary through regulations issued by the Secretary under subsection (c) of section 503A.
Section 503A(b)(1)(A)(i) of the FD&C Act.

Under section 503A(c)(1), before developing this list through regulation, FDA must also convene and consult an advisory committee on compounding unless FDA determines that the issuance of such regulation before consultation with the advisory committee is necessary to protect the public health.[6] The criteria for determining which bulk drug substances should appear on the section 503A bulks list "shall include historical use, reports in peer reviewed medical literature, or other criteria the Secretary may identify." Section 503A(c)(2) of the FD&C Act.

[5] A bulk drug substance is defined, in part, as a substance that "becomes an active ingredient or a finished dosage form of the drug, but does not include intermediates used in the synthesis of such substances" (see section 503A(b)(1)(A) and 21 CFR 207.3(4)). FDA has interpreted "an applicable USP or NF monograph" to mean an official USP or NF **drug substance** monograph. Accordingly, FDA does not consider USP monographs for dietary supplements to be "applicable" USP or NF monographs within the meaning of section 503A(b)(1)(A)(i)(I).

[6] Section 503A(c)(2) requires that FDA also consult with the USP in developing this list.

Bulk drug substances used in compounding under section 503A must also meet certain other requirements, including: (1) the bulk drug substance must be manufactured by an establishment registered under section 510 of the FD&C Act; and (2) the bulk drug substance must be accompanied by a valid certificate of analysis (COA). *See* 503A(b)(1)(A) of the FD&C Act.

In July 2014, FDA issued a guidance, *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*, that states:

> Until a bulk drug substances list is published in the *Federal Register* as a final rule, human drug products should be compounded using only bulk drug substances that are components of drugs approved under section 505 of the FD&C Act, or are the subject of USP or NF monographs[7].

FDA has received comments that this policy could be causing unnecessary and inappropriate disruptions in patient care because there are patients receiving drugs compounded with bulk drug substances that are not components of FDA-approved drugs, or the subject of an applicable USP or NF monograph, but that may ultimately be included on the 503A bulks list, and those patients' care should not be disrupted while the list is under development. After considering this issue, FDA has decided to use this guidance to describe its interim policy concerning compounding with bulk drug substances while the 503A bulks list is being developed. Once this guidance is finalized, FDA intends to revise the July 2014 guidance to state:

> FDA's interim policy concerning bulk drug substances that are not components of drugs approved under section 505 of the FD&C Act or that are not the subject of applicable USP or NF monographs can be found in the guidance, *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug and Cosmetic Act*.

FDA seeks to avoid unnecessary disruption to patient treatment while the Agency considers the bulk drug substances that were nominated with sufficient support to permit FDA to evaluate them and promulgates the regulations required under section 503A. Therefore, as described further below, FDA is issuing this interim guidance stating that it does not intend to take action for compounding of drug products under section 503A using a bulk drug substance if an applicable USP or NF monograph for the substance does not exist, and the substance is not a component of an FDA-approved product if, among other conditions, FDA has determined that the nomination for the bulk drug substance included adequate information for FDA to evaluate the substance and at this time, the substance does not appear to present safety concerns .

B. Efforts to Develop the List of Bulk Drug Substances under Section 503A

1. Section 503A Bulks List -- Early History

[7] See page 5.

Section 503A was enacted in 1997 as part of the Food and Drug Administration Modernization Act. In the *Federal Register* of April 7, 1998, (63 FR 17011), FDA invited all interested persons to nominate bulk drug substances for inclusion on the list of bulk drug substances that can be used in compounding under section 503A and received nominations for 41 different drug substances. In November 1998, FDA published a guidance for industry, *Enforcement Policy During Implementation of Section 503A of the Federal Food, Drug, and Cosmetic Act.* In this guidance, FDA announced that it would not normally take regulatory action relating to a drug product that had been compounded with a bulk drug substance that had been nominated for inclusion on the bulk drug substances list on or before November 21, 1999, while the substance was being evaluated, as long as the compounding complied with the other effective requirements in section 503A and did not appear to present a safety risk.[8]

In January 1999, after evaluating the nominated drug substances and consulting with the Pharmacy Compounding Advisory Committee (PCAC) as required by section 503A, FDA published a proposed rule listing 20 drug substances on the section 503A bulks list (64 FR 996, January 7, 1999). The preamble to the proposed rule indicated that 10 of the 41 nominated drug substances were the subject of a USP or NF monograph, or components of FDA approved drugs and did not need to be considered for inclusion on the list.[9] The proposed rule also described 10 nominated drug substances that were still under consideration for the bulk drug substances list and stated that one of the substances was withdrawn by its nominator at the first meeting of the PCAC. The PCAC reconvened in May 1999 to discuss drugs included in the proposed rule, in addition to other bulk drug substances (see 64 FR 19791 (April 22, 1999)).

However, after a 2002 U.S. Supreme Court decision holding that certain provisions of section 503A were unconstitutional,[10] FDA suspended its efforts to develop the bulk drugs list under section 503A.

Because of the amount of time that had passed between the publication of the proposed rule and the enactment of the 2013 Drug Quality and Security Act, which removed the provisions of the FD&C Act that the U.S. Supreme Court held to be unconstitutional in 2002, FDA felt it was necessary to begin again to develop the 503A bulk drug substance list. In the December 4, 2013, Federal Register (78 FR 72841), FDA published a notice withdrawing the 1999 proposed rule and inviting all interested persons to nominate bulk drug substances for inclusion on a list of bulk drug substances that can be used for compounding under section 503A of the FD&C Act.

2. Current Nominations for the 503A Bulks List

[8] The 1998 guidance was withdrawn in the *Federal Register* notice announcing the availability of the draft guidance *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*. See 78 FR 72901 (Dec. 4, 2013). The final guidance was published in July 2014. .

[9] See 64 FR 996, at 997 (January 7, 1999).

[10] For additional legal history of section 503A, see the guidance *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*.

In response to the December 2013, Federal Register notice, over 2,000 substances were nominated for the 503A bulks list. However, many of the substances nominated for the 503A list were for substances that can be compounded without being on the list because they are the subject of an applicable USP or NF monograph or are a component of an FDA-approved drug. In addition, many of the nominations were not for bulk drug substances used in compounding as active ingredients, or did not include sufficient information for FDA to evaluate the nominated substances for inclusion on the list. To improve the efficiency of the process for developing the 503A bulks list, FDA reopened the nomination process in July 2014 (79 FR 37742) and provided more detailed information on what it needs to evaluate nominations for the 503A bulks list. FDA stated that bulk drug substances that were previously nominated would not be considered further unless they were re-nominated with adequate support to permit a meaningful evaluation. Substances that were already eligible for use in compounding or that were not adequately supported would not be evaluated for placement on the 503A bulks list.

In response to this request for nominations, approximately 740 unique substances were nominated. Of the nominated substances:

- Approximately 275 substances are already eligible for use in compounding and do not need to appear on the 503A bulks list. They are components of an FDA-approved drug product or the subject of an applicable USP or NF monograph, which can be used in compounding pursuant to sections 503A(b)(1)(A)(i)(I) and (II) and, therefore, can be compounded without being included on the 503A bulks list. To determine if a bulk drug substance is the subject of an applicable USP or NF monograph, see the *USP-NF* available at www.USPNF.com. To determine if a bulk drug substance is a component of an FDA approved drug, see the FDA's *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, available at http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm.

- At least one[11] of the nominated substances is not a bulk drug substance. Rather, it is a finished drug product that was nominated by its brand name. Finished drug products are not eligible for the 503A bulks list because they do not meet the definition of a bulk drug substance in 21 CFR 207.3(4). Finished drug products can be used for compounding, provided that all of the other conditions of section 503A are met. *See* section 503A(b)(1)(B) of the FD&C Act.

- At least one of the substances is considered a biological product subject to approval in a biologics license application (BLA) under section 351 of the Public Health Service (PHS) Act when used for the indication proposed in the nomination. This substance is not eligible for the 503A bulks list because biological products subject to approval in a BLA under section 351 of the PHS Act are not eligible for the exemptions in section 503A of

[11] The over-the-counter finished drug product Maalox was nominated. Maalox is not a bulk drug substance.

the FD&C Act.[12] No biological products subject to approval in a BLA will be considered for the 503A bulks list.

- At least two of the substances are radiopharmaceuticals.[13] Section 503A does not apply to radiopharmaceuticals. Section 503A(d)(2) of the FD&C Act. Compounding of radiopharmaceuticals will be addressed in a separate guidance document, and no radiopharmaceuticals will be considered for the 503A bulks list.

- At least four of the nominated substances appear on the list published by FDA of substances that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective (withdrawn or removed list). Section 503A(b)(1)(C) of the FD&C Act.[14] Such substances cannot be used in compounding under section 503A of the FD&C Act and, therefore, are not eligible for inclusion on the 503A bulks list.

- One of the nominated substances has no currently accepted medical use and is included on Schedule I of the Controlled Substances Act (CSA) (21 U.S.C. § 812(c)).[15] The CSA does not allow possession or distribution of Schedule I substances (see 21 USC §§ 841(a)(1) and 829), except for research purposes (see 21 U.S.C. § 823(f)), and these substances will not be considered for the 503A bulk drug substances list at this time. Those desiring to do research on a Schedule I substance may apply to do so under an investigational new drug application (IND).

- Of the substances that are not components of an approved drug or the subject of an applicable USP or NF monograph and that are not biological products subject to licensure in a BLA or radiopharmaceuticals and do not appear on the withdrawn or removed list, approximately 390 substances were nominated without sufficient supporting evidence for FDA to evaluate them.

- The remaining substances may be eligible for inclusion on the 503A list and were nominated with sufficient supporting information for FDA to evaluate them. However, FDA has determined that some of these substances raise safety concerns.

FDA's website, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf contains the following lists of substances nominated for the 503A bulks list:

[12] The nominated substance is sodium hexachloroplatinate (IV) hexahydrate. See the draft guidance, *Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application (BLA)*.

[13] The two substances are GHRP-2 and GHRP-6.

[14] See 21 CFR 216.24. The four substances are: chloroform reagent, cobalt chloride hexahydrate, cobalt gluconate, and phenacetin.

[15] An extract of cannabidiol (CBD) and tetrahydrocannabinol (THC) derived from marijuana (marihuana) was nominated. Marijuana (marihuana) is a Schedule I substance.

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

503A List 2 – Bulk Drug Substances That Raise Safety Concerns: 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 503A bulks list. However, because FDA has identified safety concerns relating to the use of these bulk drug substances, FDA has placed them on a list on FDA's website of substances that may not be used in compounding under section 503A unless and until FDA publishes a final rule authorizing their use under section 503A.

503A List 3 – Bulk Drug Substances Nominated Without Adequate Support: These bulk drug substances may be eligible for inclusion on the 503A bulks list but were nominated with insufficient supporting information for FDA to evaluate them. These substances may be renominated with sufficient supporting information through a docket that FDA has established, as discussed below in section III.B.

503A List 4 – Bulk Drug Substances That May Not Be Used to Compound Drug Products Under Section 503A (to be developed): These bulk drug substances were considered for inclusion on the 503A list, but after notice-and-comment rulemaking, FDA determined that they should not be used in compounding under section 503A.

3. Process for Developing the 503A List

FDA is currently evaluating the bulk drug substances that were nominated for the 503A bulks list with sufficient information to permit evaluation. FDA is considering a number of factors in prioritizing the order in which it reviews the nominated bulk drug substances, including but not limited to the following:

- Safety concerns about use of the bulk drug substance in compounding
- Whether the bulk drug substance was nominated by multiple parties or identified as necessary by medical professional organizations; and the
- The efficiency with which the evaluation can be completed, based on ease of acquiring the necessary information to conduct the review, available resources, and other logistical issues.

FDA may also group some nominated drug substances to facilitate efficient review and discussion. These include drugs that raise similar issues (such as vitamins or botanicals) or have been nominated for the treatment of the same condition (such as warts).

In conducting its evaluations, FDA reviews the information provided in support of the nomination and other available information to assess each bulk drug substance according to the following four criteria discussed at the PCAC meeting on February 23, 2015:

- The physical and chemical characterization of the substance;

- Any safety issues raised by the use of the substance in compounded drug products;
- Historical use of the substance in compounded drug products, including information about the medical condition(s) the substance has been used to treat and any references in peer-reviewed medical literature; and
- The available evidence of effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists.

In evaluating candidates for the 503A bulks list under these criteria, the Agency is using a balancing test. No single one of these criteria is dispositive. Rather, the Agency is considering each criterion in the context of the others and balancing them, on a substance-by-substance basis, to evaluate whether a particular substance is appropriate for inclusion on the list.

Once the evaluation of a substance is complete, FDA will present the results of its review to the PCAC to obtain its advice on whether to include the substance on the list. Section 503A(c)(1) of the FD&C Act.

Section 503A requires that FDA create the 503A bulks list by regulation. Section 503A(c) of the FD&C Act. After FDA has evaluated some substances and after it has consulted with the PCAC and USP and considered their input, FDA will publish a notice of proposed rulemaking (NPRM). The NPRM will propose to place some substances on the list and will also address the substances FDA has evaluated in consultation with the PCAC and USP, but is not proposing to include on the 503A bulks list. After publication of the NPRM, the public will have an opportunity to comment on the substances FDA has proposed for inclusion on the 503A bulks list as well as those FDA has proposed not to include on the list. FDA will then consider all comments submitted to the proposed rule and publish a final rule that establishes the 503A bulks list and identifies the substances that will not be placed on the list. FDA does not intend to evaluate all of the sufficiently supported nominations before publishing the NPRM. Rather, FDA intends to evaluate the substances and prepare the list on a rolling basis.

After FDA has made a determination on a group of substances (e.g., 10 substances), it will prepare an NPRM. The final rule will list the substances that can be used in compounding under section 503A and the preamble will identify those substances that have been evaluated and not placed on the list, if any. The substances that have been evaluated and that FDA will not place on the list will appear on 503A List 4 on FDA's web site.

After the final rule is published, drug products compounded using the substances on the 503A bulks list will be eligible for the section 503A exemptions provided the drug product is compounded in compliance with the other conditions of section 503A. Also, after the final rule is published, products compounded using the substances that have been evaluated and identified on 503A List 4 will remain ineligible for the exemptions under section 503A.

III. POLICY[16]

A. Compounding from Bulk Drug Substances under Section 503A

Under section 503A of the FD&C Act, a bulk drug substance that is not the subject of an applicable USP or NF monograph or is not a component of an FDA-approved drug cannot be used in compounding unless it appears on a list promulgated as a regulation pursuant to section 503A(b)(1)(A)(i)(III) of the FD&C Act. This list will be codified at 21 CFR part 216 subpart E.

However, until a substance has been considered and is identified in a final rule as being included or in the preamble of the final rule as not included on the 503A bulks list (and included on 503A list 4 as described in this guidance), FDA does not intend to take action against a State-licensed pharmacy, Federal facility, or licensed physician compounding a drug product using a bulk drug substance that is not a component of an FDA-approved drug product and that is not the subject of an applicable USP or NF monograph, provided that the following conditions are met:

1. The bulk drug substance appears on the 503A List 1 on FDA's website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf. The substance may be eligible for inclusion on the 503A bulks list, was nominated with sufficient supporting information for FDA to evaluate it, and has not been identified by FDA as a substance that appears to present safety concerns.

2. The bulk drug substance:

    - Was originally manufactured by an establishment that is registered under section 510 (including a foreign establishment that is registered under section 510(i)) of the FD&C Act; and
    - Is accompanied by a valid COA from the original manufacturer.

"Original manufacturer" means the entity that originally produced the bulk drug substance and not a subsequent packer, repacker, labeler, or distributor.

3. The drug product compounded using the bulk drug substance is compounded in compliance with all other conditions of section 503A of the FD&C Act.

A drug product that is compounded by a licensed pharmacist in a State licensed pharmacy or Federal facility or by a licensed physician from a bulk drug substance that is not a component of an FDA-approved drug, is not the subject of an applicable USP or NF monograph, and/or that does not meet the three conditions described above is ***not*** eligible for the exemptions in section 503A and could be subject to regulatory action.

B. Bulk Drug Substances Not Nominated or Nominated Without Adequate Support

[16] See Appendix A for a chart summarizing FDA's interim policy.

As stated above, FDA is providing a list on its website of bulk drug substances that may be eligible for inclusion on the 503A bulks list but that FDA is unable to evaluate for inclusion on the list because the substances were nominated with insufficient supporting evidence for FDA to evaluate them (503A List 3). In the *Federal Register* of October 27, 2015, FDA has established a docket where these substances can be re-nominated with sufficient supporting information or to receive nominations for substances that were not previously nominated. FDA does not intend to evaluate these submissions until the Agency completes its review of the substances that were nominated for the 503A bulks list with adequate supporting information pursuant to the July 2, 2014, request for nominations (79 FR 37747).[17]

C. Comments about Nominated Bulk Drug Substances

If you feel that a substance that you nominated does not appear on the appropriate list or category as described in this guidance you can submit your comment to docket number FDA-2015-N-3534.

[17] Patients with medical conditions that need to be treated with drug products that are made from bulk drug substances that cannot be used in compounding may be able to obtain the drug products through FDA's Expanded Access programs. For information about these programs, visit FDA's website at http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm.

APPENDIX: SUMMARY OF POLICY

The following table summarizes the interim policy set forth in this guidance:

Category	FDA Policy
The bulk drug substance appears on 503A List 1 on FDA's website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf. Such substances may be eligible for inclusion on the 503A bulks list, were nominated with sufficient supporting information for FDA to evaluate them, and do not appear to present a safety concern.	FDA does not intend to take action for compounding a drug product from a bulk drug substance that does not meet the conditions of section 503A(b)(1)(A)(i) provided that the bulk drug substance was originally manufactured by an establishment registered with FDA under section 510 of the FD&C Act and is accompanied by a valid COA from the original manufacturer, and provided that the drug compounded from the bulk drug substance is compounded in compliance with the other conditions of section 503A.
The bulk drug substance is a component of an FDA-approved drug and/or the subject of an applicable USP or NF monograph.	The bulk drug substance can be used in compounding under section 503A of the FD&C Act provided it complies with the standards of the monograph (if one exists) and is compounded in compliance with the other conditions of section 503A.
The bulk drug substance appears on the withdrawn or removed list.	The bulk drug substance cannot be used in compounding under section 503A of the FD&C Act.
The bulk drug substance appears on 503A List 2 on FDA's website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf. The substance has been identified by FDA as presenting a safety concern.	The bulk drug substance cannot be used in compounding under section 503A of the FD&C Act unless and until FDA publishes a final rule authorizing its use under section 503A.
The bulk drug substance is a biological product subject to approval in a BLA.	The substance is not eligible for the 503A bulks list. FDA has issued a separate draft guidance document describing the Agency's proposed policies concerning mixing, diluting, and repackaging biological products subject to approval in a BLA.[18]
The bulk drug substance is a radiopharmaceutical product.	The substance is not eligible for the 503A bulks list. Compounding radiopharmaceuticals will be addressed in a separate guidance document.
The bulk drug substance appears on 503A List 3 on FDA's website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf. The substance may be eligible for inclusion on the 503A bulks list, but was nominated with insufficient supporting information for FDA to evaluate it.	The bulk drug substance cannot be used in compounding under section 503A of the FD&C Act. See section III.B of this guidance for information about re-nominating substances that were previously nominated with insufficient supporting information.
The bulk drug substance appears on 503A List 4 on FDA's website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf. The substance has been	The bulk drug substance cannot be used in compounding under section 503A of the FD&C Act.

[18] See FDA's draft guidance, *Mixing, Diluting, and Repackaging Biological Products Subject to Approval in a Biologics License Application (BLA)*.

identified by FDA after notice-and-comment rulemaking as a substance that should not be used in compounding under section 503A.	

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