

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

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

**January 2017
Compounding and Related Documents
Revision 1**

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

Guidance for Industry

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Contains Nonbinding Recommendations

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Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act Guidance for Industry¹

This guidance represents 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 office 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 the Agency) interim regulatory policy concerning compounding by outsourcing facilities registered under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act or Act)² using bulk drug substances. Section 503B of the FD&C Act includes certain restrictions on the bulk drug substances that outsourcing facilities can use in compounding and directs FDA to develop a list of bulk drug substances that can be used in compounding under that section. FDA is developing that list of bulk drug substances (the 503B bulks list), and this guidance describes FDA's interim regulatory policy regarding outsourcing facilities that compound human drug products using bulk drug substances while the list is being developed.^{3,4}

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.

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

² *Outsourcing facility* refers to a facility that meets the definition of an outsourcing facility under section 503B(d)(4) of the FD&C Act.

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

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II. BACKGROUND

A. Compounding From Bulk Drug Substances Under Section 503B

Section 503B of the FD&C Act 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 (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 582 (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 (a) it appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need, or (b) the drug compounded from such bulk drug substances appears on the drug shortage list in effect under section 506E of the FD&C Act at the time of compounding, distribution, and dispensing. Section 503B(a)(2)(A) of the FD&C Act.

A bulk drug substance is defined as meaning “the same as active pharmaceutical ingredient as defined in 21CFR 207.1(b).” See 21 CFR 207.3. Active pharmaceutical ingredient is defined as “any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body,” but the term “does not include intermediates used in the synthesis of the substance” (see section 503B(a)(2) and 21 CFR 207.3).^{5,6}

Bulk drug substances used in compounding under section 503B must also meet certain other requirements, including: (1) if an applicable monograph exists under the United States Pharmacopeia (USP), National Formulary (NF), or another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph, the bulk drug substance complies with the monograph; (2) the bulk drug substance must be manufactured by an establishment that is registered under section 510 of the FD&C Act; and (3) the bulk drug substance must be accompanied by a valid certificate of analysis (COA). Section 503B(a)(2) of the FD&C Act.

⁵ Section 503B references the definition of bulk drug substance in FDA’s drug establishment registration and listing regulations, which was codified at 21 CFR 207.3(a)(4) at the time section 503B was enacted. On August 31, 2016, FDA published a final rule in the Federal Register to update its registration and listing regulations in Part 207, which made minor changes to the definition of bulk drug substance and moved the definition to 21 CFR 207.3. The definition is also found in 207.1. See 81 FR 169 (August 31, 2016). Under the previous definition, bulk drug substance was defined to mean “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 a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances.”

⁶ Inactive ingredients are not subject to section 503B(a)(2) or the policies described in this guidance because they are not included within the definition of a bulk drug substance. See 21 CFR 207.3. Pursuant to section 503B(a)(3), inactive ingredients used in compounding must comply with the standards of an applicable United States Pharmacopeia or National Formulary monograph, if a monograph exists.

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B. Section 503B Bulks List

1. Section 503B Bulks List History

Section 503B, added to the FD&C Act by the Drug Quality and Security Act in 2013, requires that FDA create a list of bulk drug substances for which there is a clinical need by publishing a notice in the *Federal Register* proposing bulk drug substances for inclusion on the list, providing a public comment period of 60 calendar days, and then publishing a notice in the *Federal Register* designating bulk drug substances for inclusion on the list. See section 503B(a)(2)(A)(i) of the FD&C Act. In the December 4, 2013, *Federal Register* (78 FR 72838), FDA published a notice 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 503B of the FD&C Act.

2. Nominations for the 503B Bulks List

In response to the December 2013 *Federal Register* notice, over 2,000 substances were nominated for the 503B bulks list. However, many of the nominations for the 503B bulks list were not for substances used in compounding as active ingredients, or they did not include sufficient information to allow FDA to evaluate the nominated substances for placement on the list. To improve the efficiency of the process for developing the 503B bulks list, FDA reopened the nomination process in July 2014 (79 FR 37747), and provided more detailed information on what it needs to evaluate nominations for the list. FDA stated that bulk drug substances that were previously nominated would not be further considered unless they were re-nominated and those nominations were adequately supported. Substances that were not adequately supported would not be evaluated by FDA to be placed on the 503B bulks list. The notice stated that the following information about clinical need is necessary to provide adequate support for nominations to the 503B bulks list:

- A statement describing the medical condition(s) that the drug product to be compounded with the nominated bulk drug substances is intended to treat;
- A list of FDA-approved drug products, if any, that address the same medical condition;
- If there are any FDA-approved drug products that address the same medical condition, an explanation of why a compounded drug product is necessary;
- If the approved drug product is not suitable for a particular patient population, an estimate of the size of the population that would need a compounded drug product;
- A bibliography of safety and efficacy data for the drug product compounded using the nominated substance, if available, including any relevant peer-reviewed medical literature; and
- If there is an FDA-approved drug product that includes the bulk drug substance nominated, an explanation of why the drug product proposed to be compounded must be compounded from bulk rather than with the FDA-approved drug product.

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In response to this request for nominations, approximately 2,590 unique substances were nominated. Of the nominated substances:

- Approximately 1,740 are biological products (all but one of these⁷ are individual allergenic extracts) subject to approval in a biologics license application (BLA) under section 351 of the Public Health Service (PHS) Act.

These products are not eligible for the 503B 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 503B.⁸ No biological products subject to approval in a BLA will be considered for the 503B bulks list.

- At least one⁹ of the nominated substances is not a bulk drug substance.

This is a finished drug product that was nominated by its brand name. Finished drug products are not eligible for the 503B bulks list because they do not meet the definition of a bulk drug substance in 21 CFR 207.3.

- At least one of the nominated substances is a radiopharmaceutical.¹⁰

Compounding of radiopharmaceutical products will be addressed in a separate guidance document.¹¹

- At least five of the nominated substances appear on the list of drugs 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)

Such substances cannot be used in compounding under section 503B of the FD&C Act, and therefore are not eligible for inclusion on the 503B bulks list.¹²

- 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)).¹³

⁷ The product is sodium hexachloroplatinate (IV) hexahydrate.

⁸ See the draft guidance, *Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application* for FDA's proposed policies regarding State-licensed pharmacies, Federal facilities, and outsourcing facilities that mix, dilute, or repackage biological products outside the scope of an approved BLA.

⁹ The over-the-counter finished drug product Maalox was nominated. Maalox is not a bulk drug substance.

¹⁰ The substance is sodium iodide I-131.

¹¹ FDA has published a draft guidance, "Compounding and Repackaging of Radiopharmaceuticals by Outsourcing Facilities," for public comment. That draft guidance proposes the Agency's policy regarding the use of bulk drug substances to compound radiopharmaceuticals under section 503B of the FD&C Act. Once that guidance is final, FDA intends to update this guidance to reflect the policies set forth therein.

¹² See section 503B(a)(4) of the FD&C Act. See also 21 CFR 216.24. The five substances are: chloroform reagent, cobalt chloride hexahydrate, cobalt gluconate, methapyrilene fumarate, and phenacetin.

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The CSA does not allow possession or distribution of Schedule I substances (see 21 U.S.C. §§ 841(a)(1) and 829), except for research purposes (21 U.S.C. § 823(f)), and these substances will not be considered for the 503B bulk drug substances list at this time. Those desiring to do research on a Schedule I substance can apply to do so under an investigational new drug application (IND).

- Of the substances that may be eligible for use in compounding under section 503B, approximately 650 substances were nominated without sufficient supporting evidence for FDA to evaluate them.
- The remaining substances that were nominated for inclusion on the 503B bulks list may be eligible for inclusion on the list and were nominated with sufficient supporting information for FDA to evaluate them. However, FDA has identified significant safety risks relating to the use in compounded drug products of some of these bulk drug substances.

FDA's website identifies the following categories of substances nominated for the 503B bulk drug substances list:¹⁴

503B Category 1 –Substances Nominated for the Bulks List Currently Under Evaluation: These 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.

503B Category 2 –Substances Nominated for the Bulks List That Raise Significant Safety Risks: These 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 substances in compounding pending further evaluation, and therefore does not intend to adopt the policy described for the substances in category 1. If FDA adds a substance to Category 2, it will publish a public communication (e.g. a safety alert) describing the safety risks and will post

¹³ An extract of cannabidiol (CBD) and tetrahydrocannabinol (THC) derived from marijuana (marihuana) was nominated. Marijuana (marihuana) is a Schedule I substance.

¹⁴ <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf>. As discussed in the July 2014 Federal Register notice requesting nominations for the 503B bulks list ((79 FR 37747), nominators were to confirm that all substances nominated for the list are active ingredients that meet the definition of a "bulk drug substance." Inclusion of a substance in any of these categories does not reflect a determination by FDA that the substance is a bulk drug substance. Whether a substance is a bulk drug substance subject to the conditions in section 503B(a)(2) depends on whether it meets the definition of a bulk drug substance in 21 CFR 207.3. If the substance is used in a compounded drug as an inactive ingredient, then it does not meet the definition of a bulk drug substance in 21 CFR 207.3, is not subject to the conditions in section 503B(a)(2), and need not appear on the 503B bulks list to be eligible for use in compounding. Instead, when used as an inactive ingredient, the substance is subject to the conditions in section 503B(a)(3), which applies to ingredients other than bulk drug substances used in compounded drugs

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the communication on FDA's human drug compounding website¹⁵ advising that the substance has been added to Category 2 and is no longer eligible for the policies that apply to substances in Category 1.

503B Category 3 –Substances Nominated for the Bulks List Without Adequate

Support: These 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, as discussed below in section III.B.

3. Process for Developing the 503B Bulks List

FDA is currently evaluating the bulk drug substances nominated for the 503B bulks list with sufficient supporting information for evaluation. FDA is considering a number of factors in prioritizing the order in which it reviews these 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
- 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 drug substances that raise similar issues (e.g., vitamins or botanicals) or that are nominated for the treatment of the same condition (e.g., warts).

FDA intends to publish a notice in the *Federal Register* that describes its proposed position on each substance it has evaluated along with the rationale for that proposal, for public comment. We note that there is no requirement in section 503B to consult the Pharmacy Compounding Advisory Committee (PCAC) before developing a 503B bulks list, as is required by section 503A(c)(1) for the 503A bulks list. However, after considering public comment on the nominated substances, FDA will determine whether PCAC input on any of the substances would be helpful to the Agency in making its determination, and if so, it will seek PCAC input. Once FDA makes a determination, it will publish in the *Federal Register* a list identifying the bulk drug substances for which it has determined there is a clinical need and FDA's rationale in making that determination. FDA will also publish in the *Federal Register* a list of those substances it considered but found that there is no clinical need to use in compounding and FDA's rationale in making this determination.

¹⁵ <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm>.

FDA also encourages compounding facilities to subscribe to FDA's list serve to receive updates at: http://service.govdelivery.com/service/subscribe.html?code=USFDA_429.

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Once FDA publishes a 503B bulks list in the *Federal Register* that reflects its determination regarding particular bulk drug substances, drug products compounded with substances on the 503B bulks list will be eligible for the 503B exemptions, provided the drug products are compounded in compliance with the other conditions of section 503B.¹⁶ Once FDA has published in the *Federal Register* its decision not to place a particular substance on the 503B bulks list, the policy described in section III of this guidance no longer applies.

FDA intends to evaluate the substances nominated for the 503B list on a rolling basis. FDA will begin by publishing a *Federal Register* notice identifying a group of substances (e.g., 10 substances) that it has considered and whether it proposes the substances for inclusion on the list. Under section 503B, an outsourcing facility may only compound using bulk drug substances that are on FDA's 503B bulks list or that are used to compound drugs that appear on the shortage list in effect under section 506E of the FD&C Act at the time of compounding, distribution, and dispensing. To avoid unnecessary disruption to patient treatment while FDA considers the substances that were nominated with sufficient support to permit FDA to evaluate them, FDA is issuing this guidance stating that at this time it does not intend to take action against an outsourcing facility for failing to compound in accordance with section 503B(a)(2) if certain conditions are met. Those conditions include that the nomination for the relevant bulk drug substance was submitted with adequate information for FDA to evaluate the substance and that FDA has not identified significant safety risks about its use in compounding prior to publication of the *Federal Register* notice identifying those substances FDA has determined will or will not be placed on the 503B bulks list.

III. POLICY¹⁷

A. Compounding from Bulk Drug Substances Under Section 503B

Under section 503B of the FD&C Act, a bulk drug substance cannot be used in compounding unless it is used to compound a drug that appears on the FDA drug shortage list at the time of compounding, distribution, and dispensing, or it appears on the 503B bulks list.

FDA does not intend to take action against an outsourcing facility for compounding a drug product using a bulk drug substance that is not on the 503B bulks list if the drug compounded from the bulk drug substance: (i) appeared on FDA's drug shortage list within 60 days of distribution and dispensing, and (ii) was to fill an order that the outsourcing facility received for the drug while it was on FDA's drug shortage list.¹⁸

¹⁶ See section 503B(a)(11) of the FD&C Act.

¹⁷ See Appendix A for a summary of FDA's interim policy.

¹⁸ An outsourcing facility may not be able to predict when a drug shortage will be resolved, and the facility may have orders for a compounded drug in-house that were in progress when the drug was removed from FDA's drug shortage list (e.g., the outsourcing facility may have compounded a drug while it was in shortage, but the shortage ended while the outsourcing facility awaits the results of sterility testing before release.) This policy provides some regulatory flexibility where an outsourcing facility fills orders that it received while a drug was in shortage. However, this policy does not apply if an outsourcing facility continues to fill orders received after the shortage

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In addition, at this time FDA does not intend to take action against an outsourcing facility for compounding a drug using a bulk drug substance that does not appear on the 503B bulks list and that is not used to compound a drug that appears on the FDA drug shortage list at the time of compounding, distribution, and dispensing, provided that the following conditions are met:

1. The bulk drug substance appears on 503B Category 1 on FDA's website at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf>. A Category 1 substance may be eligible for inclusion on the 503B bulks list, was nominated for inclusion on the 503B bulks list with adequate supporting information for FDA to evaluate it, and has not been identified by FDA as a substance that appears to present a significant safety risk in compounding before a determination as to whether to place it on the 503B bulks list has been made.
2. The original manufacturer and all subsequent manufacturers of the bulk drug substance are establishments that are registered under section 510 (including foreign establishments that are registered under section 510(i)) of the FD&C Act;
3. The bulk drug substance is accompanied by a valid COA;
4. If the bulk drug substance is the subject of an applicable USP or NF monograph, the bulk drug substance complies with the monograph; and
5. The drug product compounded using the bulk drug substance is compounded in compliance with all other provisions of section 503B of the FD&C Act.

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

This policy does not apply to an outsourcing facility that compounds a drug using a bulk drug substance that does not meet each of the above conditions and where the bulk drug substance was not used to compound a drug that appears on the FDA drug shortage list at the time of compounding, distribution, and dispensing, or that appeared on the FDA drug shortage list within 60 days of distribution and dispensing.

B. Substances Not Nominated or Nominated Without Adequate Support

As stated above, FDA is providing a list on its website of substances nominated for the 503B bulks list that may be eligible for inclusion on the list, but that FDA is unable to evaluate for inclusion on the list at this time because the substances were nominated with insufficient supporting evidence for FDA to evaluate them (503B Category 3). In the *Federal Register* of October 27, 2015, FDA established a docket (October docket) where these substances can be re-

ends, or if the outsourcing facility continues to fill orders more than 60 days after the drug was removed from FDA's drug shortage list.

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nominated with sufficient supporting information or where nominations for substances that were not previously nominated can be submitted.

After a substance is nominated to the October docket,¹⁹ FDA will determine whether the nomination is supported with sufficient information to allow FDA to evaluate it. After FDA makes that determination, the nominated substance will be placed in one of the three categories described in section II.B.2 above, and the categorization will be published on the FDA website. Once the category of a substance is published, FDA intends to apply the policy described in section III.A. of this guidance to that substance. FDA generally expects to categorize bulk drug substances nominated to the October docket and to publish updated categories on its website on the first business day of each month. Please note that until substances nominated for the October docket have been categorized, the policy does *not* apply to those substances.

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-3469. If you have new information on a previously-nominated substance that was placed in Category 3, the substance can be re-nominated with the additional information.

A nominator may also submit a comment to the docket requesting withdrawal of any of its nominations. If the party nominating the substance was the sole nominator, FDA will update the categories described in this guidance to reflect the withdrawn nomination.²⁰ FDA intends to provide notice to the public before removing any nominated substances from Category 1 or Category 2.

Withdrawal of a nomination upon the nominator's request, and resulting updates to the categories described in this guidance, do not reflect a determination by FDA regarding the validity of the nomination or of any reasons given by the nominator for requesting withdrawal. In addition, FDA may continue to evaluate a substance at its discretion even if the nominator submits a comment requesting withdrawal of the nomination.

¹⁹ This includes re-nominations of substances with sufficient supporting information.

²⁰ If multiple parties nominated the same substance, each party that nominated the substance must withdraw its nomination for the nominated substance to be considered withdrawn and for the categories to be updated to reflect that withdrawal.

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APPENDIX: SUMMARY OF POLICY

The following table summarizes the interim policy for bulk drug substances set forth in this guidance:

Category	FDA Policy
<p>The bulk drug substance is in 503B Category 1 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf.</p> <p>Such substances may be eligible for inclusion on the 503B bulks list, were nominated with adequate supporting information for FDA to evaluate them, and have not been identified by FDA as presenting significant safety risks.</p>	<p>The bulk drug substance is not on the 503B bulks list. However, pending a determination about whether to put the bulk drug substance on the 503B bulks list, FDA does not intend to take action against an outsourcing facility for compounding a drug product from a bulk drug substance that does not meet the conditions of section 503B(a)(2) provided that the bulk drug substance is manufactured by an establishment registered with FDA under section 510 of the FD&C Act, is accompanied by a valid COA, complies with an applicable USP monograph, if one exists, and provided that the drug compounded from the bulk drug substance is compounded in compliance with the other conditions of section 503B.</p>
<p>The bulk drug substance appears on the withdrawn or removed list.</p>	<p>The bulk drug substance cannot be used in compounding under section 503B of the FD&C Act.</p>
<p>The bulk drug substance is in 503B Category 2 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf. The substance has been identified by FDA as presenting a significant safety risk in compounding pending further evaluation.</p>	<p>The bulk drug substance is not on the 503B bulks list, and cannot be used for compounding consistent with section 503B(a)(2) unless it is used to compound a drug that appears on FDA’s drug shortage list.</p>
<p>The bulk drug substance is a biological product subject to approval in a BLA.</p>	<p>The bulk drug substance is not eligible for the 503B 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.²¹</p>
<p>The bulk drug substance is a radiopharmaceutical product.</p>	<p>Compounding radiopharmaceuticals will be addressed in a separate guidance document.</p>
<p>The bulk drug substance is in 503B Category 3 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf. The substance may be eligible for inclusion on the 503B bulks list but was nominated with insufficient supporting information for FDA to evaluate it.</p>	<p>The bulk drug substance is not on the 503B bulks list, and cannot be used for compounding consistent with section 503B(a)(2) unless the bulk drug substance is used to compound a drug that appears on FDA’s drug shortage list. See section III.B of this guidance for information about supplementing inadequately supported nominations.</p>

²¹ See FDA’s revised draft guidance, *Mixing, Diluting, and Repackaging Biological Products Subject to Approval in a Biologics License Application*.