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Dockets Management Staff (HFA–305)
Food and Drug Administration
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CITIZEN PETITION

The Partnership for Safe Medicines ("PSM") respectfully submits this citizen petition pursuant to 21 C.F.R. § 10.30 to request that the Commissioner of Food and Drugs refrain from taking the action set forth below with respect to allowing the compounding of drug products using any of the seven peptide products bulk drug substances recently considered at FDA's Pharmacy Compounding Advisory Committee ("PCAC" or "the Committee") on July 23-24, 2026.[1]

## Actions Requested

Reserving all other rights, through this petition, PSM respectfully requests that the U.S. Food and Drug Administration ("FDA" or "the Agency") refrain from taking action, whether through regulation, addition to "Category 1" under FDA's guidance on "Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug and Cosmetic Act"[2] ("503A Interim Policy") or otherwise through exercise of enforcement discretion or any other action, to allow for compounding of drug products using any of the seven peptide bulk drug substances. In addition, because the July 23-24, 2026 PCAC was constituted in violation of the Federal Advisory Committee Act ("FACA") and the Ethics in Government Act ("EIGA"), PSM further requests that FDA refrain from relying on it for purposes of meeting its statutory obligations under section 503A(c)(1) to convene and consult an advisory committee on compounding before issuing regulations to implement subsection (b)(1)(A)(i)(III).

## Statement of Grounds

### I. Executive Summary

FDA itself has stated that "American consumers benefit from having access to the safest and most advanced pharmaceutical system in the world."[3] The bedrock of this system is FDA's rigorous review and approval of new drugs before they can be sold to American patients.

[1] The peptide bulk drug substances are: BPC-157, KPV, TB-500, MOTS-c, emideltide, semax, and epitalon. We refer to these throughout as the "peptide bulk drug substances."
[2] *See* FDA, Guidance for Industry, Interim Policy on Compounding Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act (Jan. 2025).
[3] *See, e.g.*, FDA, Development & Approval Process | Drugs (Aug. 8, 2022), https://www.fda.gov/drugs/development-approval-process-drugs.

While federal law provides limited exceptions to the premarket approval requirements for prescription drugs, these exceptions are narrow. One such exception is for compounded drugs, including drugs compounded pursuant to Section 503A of the Federal Food, Drug and Cosmetic Act ("FDCA"). Among Section 503A's requirements is that the drug be compounded from a bulk drug substance that (1) complies with the standards of an applicable United States Pharmacopeia ("USP") or National Formulary ("NF") monograph, if a monograph exists, and the USP chapter on pharmacy compounding; (2) if such monograph does not exist, is a drug substance that is a component of a drug approved by FDA; or (3) if such monograph does not exist and the drug substance is not a component of a drug approved by FDA, the substance appears on a list developed by FDA through regulations (the "503A Bulks List").[4]

FDA regulations set forth clear and narrowly-prescribed criteria for substances to be added to the 503A Bulks List through notice-and-comment rulemaking. The seven peptide bulk drug substances here cannot be added to the 503A Bulks List as none come close to meeting the criteria set forth in regulations. Indeed, FDA itself concluded the same in briefing documents to the PCAC. Adding these substances to the 503A Bulks List would thus be arbitrary and capricious as a matter of law, bad public policy, and a danger to public health. Accordingly, FDA must refrain from adding these substances to the 503A Bulks List, adding them to "Category 1" under FDA's 503A Interim Policy,[5] or otherwise exercising "enforcement discretion" to permit compounding from such bulk drug substances.

## II. Legal and Regulatory Background

### A. Compounding Under Section 503A

American patients are protected by a drug regulatory system widely regarded as the most rigorous in the world. The bedrock of that system is FDA's review and approval of new drugs before they reach patients, reflected in Section 505 of the FDCA. This gold-standard framework requires drug developers to conduct extensive research to meet FDA's standards for safety, effectiveness, and quality before drugs are made available to the public.

There are, however, limited exceptions to the requirement that new drugs be reviewed and approved by FDA before being introduced into interstate commerce. Relevant here is Section 503A of the FDCA, which describes the conditions that must be satisfied for drug products compounded by a licensed pharmacist or licensed physician to be exempt from the following three sections of the FDCA: (1) section 501(a)(2)(B) (concerning current good manufacturing practice); (2) section 502(f)(1) (concerning the labeling of drugs with adequate

[4] *See* FDCA 503A(b)(1)(A).
[5] *See* FDA, Guidance for Industry, Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act (Jan. 2025) ("503A Interim Policy Guidance").

directions for use); and (3) section 505 (concerning the approval of drugs under new drug applications ("NDAs") or abbreviated new drug applications ("ANDAs")).[6]

One of the conditions set forth under Section 503A relates to the bulk drug substances that are appropriate to be compounded by 503A compounding pharmacies. As noted above, the bulk drug substance must: (1) comply with the standards of an applicable USP or NF monograph, if a monograph exists, and the USP chapter on pharmacy compounding; (2) if such monograph does not exist, is a drug substance that is a component of a drug approved by FDA; or (3) if such monograph does not exist and the drug substance is not a component of a drug approved by FDA, the substance is on the 503A Bulks List. Before issuing regulations to add a substance to the 503A Bulks List, the statute generally requires that FDA "convene and consult an advisory committee on compounding."[7] And the advisory committee "shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopoeia, pharmacy, physician, and consumer organizations, and other experts selected by the Secretary." FDA must also consult with USP in promulgating any such regulations.[8] Of note, the USP representative on the PCAC voted *against* recommending each of the seven peptide bulk substances for inclusion on the 503A Bulks List at the July 23-24 PCAC.

As noted, FDA must issue regulations to add a substance to the 503A Bulks List. The statute requires that FDA "include in the regulation the criteria for such substances, which shall include historical use, reports in peer reviewed medical literature, or other criteria [FDA] may identify."[9] FDA, as required by the statute, has issued regulations that set forth the following criteria the Agency considers when evaluating substances for inclusion on the 503A Bulks List:

> (1) The physical and chemical characterization of the substance;
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> (2) Any safety issues raised by the use of the substance in compounded drug products;
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> (3) The available evidence of the effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists; and
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> (4) 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.[10]

FDA's regulations contemplate that the Agency will conduct a holistic assessment of the nominated substance using each of these four criteria, and that FDA will "balanc[e] the criteria" before making a determination.[11] A holistic assessment is necessary, and FDA should consider all factors—particularly both whether any safety issues arise and whether there is available evidence

[6] FDCA 503A(a).
[7] FDCA 503A(c)(1).
[8] FDCA 503A(c)(2).
[9] FDCA 503A(c)(2).
[10] 21 C.F.R. § 216.23(c).
[11] *See id.* § 216.23(b).

of effectiveness or lack thereof—given the unique "risks and benefits that may be presented by a particular substance."[12] Moreover, when evaluating the safety and efficacy of the compounded drug product under the regulations, FDA also considers whether there is an FDA-approved drug or drug product that conforms to an over-the-counter monograph that may be available as an alternative therapy to treat a condition.[13]

Separate from the statutory requirement for adding bulk substances to the 503A Bulks List, FDA has articulated in guidance an "interim regulatory policy for licensed pharmacists in State-licensed pharmacies and Federal facilities and for licensed physicians who compound human drug products using bulk drug substances while the [503A Bulks List] is being developed."[14] First described in draft guidance in 2014, this so-called "interim policy" sets forth circumstances under which "FDA does not intend to take regulatory action for compounding drug products under section 503A using a bulk drug substance" that does not meet the requirements set forth in FDCA 503A(b)(1)(A)(i) (i.e., does not have a USP or NF monograph, is not a component of an FDA-approved drug, and is not on the 503A Bulks List). Under the "interim policy," FDA considers bulk drug substances nominated before January 7, 2025, and places such nominated substances into one of three categories:

> (1) Category 1: Substances Nominated for the Bulks List Currently Under Evaluation: These 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 on any other list.
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> (2) 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 503A 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.
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> (3) Category 3: Substances Nominated for the Bulks List Without Adequate Support: These substances may be eligible for inclusion on the 503A Bulks List but were nominated with insufficient supporting information for FDA to evaluate them.

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[12] List of Bulk Drug Substances That Can Be Used To Compound Drug Products in Accordance With Section 503A of the Federal Food, Drug, and Cosmetic Act, 84 Fed. Reg. 4696 (Feb. 19, 2019), https://www.federalregister.gov/documents/2019/02/19/2019-02367/list-of-bulk-drug-substances-that-can-be-used-to-compound-drug-products-in-accordance-with-section. For instance, where there is little or no evidence of effectiveness, PSM believes that FDA should have a correspondingly low tolerance for risk. For substances such as BPC-157, for which there is no adequate evidence establishing clinical benefit, even relatively modest safety concerns should weigh heavily against permitting its use in compounding because there is no demonstrated therapeutic benefit against which those risks can be balanced.

[13] *Id.*

[14] *See* 503A Interim Policy Guidance.

FDA, under its "interim policy," has permitted 503A compounding pharmacies to compound from bulk drug substances that have been placed in Category 1.[15]

### B. FDA Advisory Committees

As noted above, before issuing regulations to add a bulk substance to the 503A Bulks List, FDA generally must "convene and consult an advisory committee."[16] Here, FDA's PCAC is the relevant committee and, like other FDA advisory committees, is subject to applicable federal law governing advisory committees, notably the FACA and EIGA.

The FACA spells out the activities and operations of federal advisory committees.[17] Relevant here, the FACA requires that "the membership of the advisory committee be fairly balanced in terms of the points of view represented."[18] Further, FACA mandates that legislation authorizing advisory committees have "provisions to assure that the advice and recommendations of the advisory committee will not be inappropriately influenced by . . . any special interest."[19]

Members of advisory committees, including the PCAC, are also subject to the EIGA as "special government employees."[20] They are also subject to the prohibition in 18 U.S.C. § 208 on participating in "matters in which [they have] a personal financial interest, or in which certain persons or organizations with which [they are] affiliated have a financial interest."[21] While the statute does set forth a waiver process, PSM is not aware of any waiver issued here with respect to any individual member of the PCAC.

## III. Factual Background

It has never been lawful to compound these seven peptide bulk drug substances. With regards to 503A compounding, the peptide bulk drug substances have never been the subject of a USP or NF monograph, have never been a component of an FDA-approved drug, and have never been included on the 503A Bulks List. Despite this, some compounders have compounded products using these peptide bulk drug substances, initially taking the legally baseless position that mere nomination for FDA's consideration for the 503A Bulks List was sufficient. To address this baseless argument and to protect patient safety, in September 2023, FDA placed over a dozen peptide drug substances into Category 2 of the 503A Bulks List, reflecting the Agency's determination that such peptide drug substances presented "significant safety risks" for

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[15] *See* 503A Interim Policy Guidance.
[16] FDCA 503A(c)(1).
[17] *See* 5 U.S.C. Chapter 10.
[18] *See* 5 U.S.C. § 1004(b)(2).
[19] *Id* § 1004(b)(3).
[20] *See* https://www.fda.gov/advisory-committees/human-drug-advisory-committees/pharmacy-compounding-advisory-committee (noting that "almost all non-Federal members of [the PCAC] serve as Special Government Employees.").
[21] 18 U.S.C. § 208.

compounding, including risks related to immunogenicity, impurities, and availability of limited or no human clinical data.[22] The peptide drug substances placed in Category 2 at that time included six of the seven peptide bulk drug substances subject to this citizen petition.

During this period, inadequate enforcement of the FDCA allowed mass compounding to expand far beyond what the statute contemplated. This included not only mass compounding of glucagon-like-peptide-1 ("GLP-1"), erectile dysfunction, and hair loss drugs, but also mass compounding using the peptide bulk drug substances the Agency itself had previously identified as raising significant safety risks. This failure also permitted the proliferation of false and misleading advertising online, which generated substantial consumer demand for these unapproved and untested drugs. The enforcement failures are directly responsible for the situation FDA now confronts.

Subsequently, on April 16, 2026, FDA unexpectedly removed twelve peptide drug substances from Category 2, noting that the substances have been withdrawn by the nominators.[23] At the same time, FDA published a Federal Register notice announcing a PCAC meeting to consider seven peptide bulk drug substances for inclusion on the 503A Bulks List:

1) BPC-157 (free base), BPC-157 acetate for ulcerative colitis (UC)
2) KPV (free base), KPV acetate for wound healing and inflammatory conditions
3) TB-500 (free base), TB-500 acetate for wound healing
4) MOTS-c (free base), MOTS-c acetate for obesity and osteoporosis
5) Emideltide (free base), Emideltide acetate for opioid withdrawal, chronic insomnia, and narcolepsy
6) Semax (free base), Semax acetate for cerebral ischemia, migraine, and trigeminal neuralgia
7) Epitalon (free base), Epitalon acetate

In advance of the July 23-24 PCAC meeting, FDA announced the addition of several new members to the PCAC. Public reports suggested that many of these newly added PCAC members may have financial interests or affiliations with entities that could be directly affected by, and benefit from, recommendations made by the Committee in the upcoming PCAC meeting. Indeed, additional reporting suggested that FDA staff raised concerns with "appointing those who worked for peptide-related business and clients."[24] Notwithstanding these purported

[22] *See* FDA, Bulk Drug Substances Nominated for Use in Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic Act, https://web.archive.org/web/20241013110247/https://www.fda.gov/media/94155/download?attachment (Updated September 27, 2024).
[23] *See* https://web.archive.org/web/20260417111839/https://www.fda.gov/media/94155/download. In its briefing documents for the PCAC, FDA explained that while the nominators had withdrawn the nominations for each of the seven nominated peptide bulk drug substances, FDA was "evaluating the substances at its discretion." *See, e.g.,* Epitalon Briefing Materials at 8.
[24] *See* Rachel Roubein, FDA Raised Conflict of Interest Concerns Ahead of New Peptide Panel, Washington Post (Jul. 17, 2026).

conflicts, we are not aware of any waivers or other public documents addressing how the Agency considered and assessed any of these potential conflicts.

FDA published briefing materials for each of the seven nominated peptide bulk drug substances analyzing in detail the available evidence (or lack thereof) on the safety and effectiveness of drug products using the bulk drug substances, applying the regulatory evaluation criteria, and providing the Agency's recommendation to the PCAC. For each of the seven peptide bulk drug substances, FDA proposed not adding the substances to the 503A Bulks List. The concluding recommendation in the Agency's evaluation of BPC-157 is illustrative of FDA's recommendation for all seven of the peptide bulk drug substances:

> On balance, the physicochemical characterization, information on historical use, lack of evidence of effectiveness, and safety information identified for both BPC-157 (free base) and BPC-157 acetate weigh against them being added to the 503A Bulks List. In particular, FDA's proposal is based on the fact that BPC-157 (free base) and BPC-157 acetate are not well characterized from a physiochemical perspective, there is a lack of information on the safety profile and immunogenicity risks of BPC-157-related BDSs, there is insufficient evidence to make a conclusion on the effectiveness of BPC-157-related BDSs as a treatment for UC, and there are FDA-approved drug products that are indicated to treat UC, a serious chronic disease that may cause life-threatening complications. Accordingly, we propose not adding BPC-157 (free base) or BPC-157 acetate to the 503A Bulks List.[25]

At the PCAC meeting, FDA presented its recommendations to the PCAC that the seven peptide bulk drug substances not be added to the 503A Bulks List. Notwithstanding the Agency's recommendations, the PCAC voted in favor of recommending six of the seven peptides for inclusion on the 503A Bulks List.[26] The PCAC members voting in favor of adding the peptides to the 503A Bulks List were predominantly the newly added members, several of whom had the alleged conflicts of interest previously described.

## IV. FDA Must Refrain From Enabling Compounding of the Seven Peptide Bulk Drug Substances as a Matter of Law and Patient Safety

FDA must refrain from adding these seven peptide bulk drug substances to the 503A Bulks List, adding them to Category 1 of the 503A Interim Policy, or otherwise exercising enforcement discretion to enable compounding for several reasons. The evidence (including FDA's detailed analysis) is overwhelming that the peptide bulk drug substances do not meet the

[25] *See* FDA Briefing Document, PCAC Meeting July 23-24, BPC-157 – Related Bulk Drug Substances (BPC157 (free base) and BPC-157 acetate) at 47, https://www.fda.gov/media/193343/download ("BPC-157 Briefing Materials).

[26] The PCAC voted in favor of adding the following bulk substances to the 503A Bulks List: BPC-157, KPV, TB-500, Semax, MOTS-c, Epitalon. The PCAC voted against adding Emideltide to the 503A Bulks List.

criteria for addition to the 503A Bulks List; accordingly, any decision that departs from FDA's prior determination, the Agency's own career-staff analysis, and the otherwise available credible evidence on safety risks and lack of efficacy of compounding using these peptide bulk drug substances, would be arbitrary and capricious under the Administrative Procedures Act ("APA").[27] The vote of the PCAC should be afforded no weight in the Agency's analysis as the PCAC was not properly constituted, in violation of FACA and EIGA. We detail these points below.

### A. The Peptide Bulk Drug Substances Do Not Meet the Criteria For Inclusion On The 503A Bulks List

As FDA itself recommended in the briefing materials for the PCAC, the peptides do not meet the criteria for inclusion on the 503A Bulks List. FDA's expert staff conducted detailed analysis of the seven peptide bulk substances. In all cases, FDA proposed not adding the bulk substances to the 503A Bulks List. PSM includes below relevant excerpts from these briefing documents highlighting the Agency's thorough analysis and consideration of the relevant regulatory evaluation criteria:

- **BPC-157 (free base), BPC-157 acetate for ulcerative colitis (UC)**
  - *Evaluation Criteria #1: Physical and Chemical Characterization of the Substance.*
    - "From a chemical analysis standpoint, inconsistent naming conventions for BPC-157-related bulk drug substances also introduce risks because of the inability to determine which bulk drug substance a particular reference standard is referencing."[28]
  - *Evaluation Criteria #2: Safety Issues Raised by Use of Substance in Compounded Drug Products*
    - "Because there is lack of information regarding potential impurities that can be present in BPC157 (free base) and the lack of information on the potential of peptide aggregation, we cannot rule out the potential for immunogenicity associated with these impurities and peptide-related aggregates."[29]
  - *Evaluation Criteria #3: Available Evidence of the Effectiveness or Lack of Effectiveness.*
    - "There is a lack of evidence to support the effectiveness of BPC-157 (free base) and BPC-157 acetate as a treatment for UC.

[27] *See* 5 U.S.C. §§ 551–559.
[28] *See* BPC-157 Briefing Document at 9-10.
[29] *Id* at 15.

There has been a single, small trial evaluating BPC-157 in the treatment of UC, however, interpretation of the results is limited by the lack of details provided in the meeting abstract and the exploratory nature of the study."[30]

- *Evaluation Criteria #4: Historical Use of the Substance in Compounded Drug Products.*
  - "Although BPC-157 has been studied since at least 1993, there is insufficient information available to determine how long BPC-157-related BDSs have been used specifically in pharmacy compounding."[31]

- **KPV (free base), KPV acetate for wound healing and inflammatory conditions**
  - *Evaluation Criteria #1: Physical and Chemical Characterization of the Substance.*
    - "KPV (free base) is deemed to be not well-characterized from the physical and chemical characterization perspective because (1) inconsistent naming conventions that do not follow established chemical nomenclature standards (e.g., INN, IUPAC, USAN), and (2) BDS specific quality control attributes, including impurities, aggregates, and microbiological tests, were not found in the publicly available scientific literature and lack of a CoA in the nomination package which are offered as evidence to establishing identity, purity, and impurity profiles of the substance."[32]
  - *Evaluation Criteria #2: Safety Issues Raised by Use of Substance in Compounded Drug Products*
    - "There is lack of clinical and nonclinical safety information on the use of KPV (free base) and KPV acetate. FDA is particularly concerned about the lack of any human data on drug products containing these substances administered via any route of administration, including lack of information to assess immunogenicity or aggregation of KPV-related bulk drug substances."[33]

[30] *Id.* at 29.
[31] *Id*. at 22.
[32] *See* FDA Briefing Document, PCAC Meeting July 23-24, KPV–Related Bulk Drug Substances (KPV (Free Base) and KPV acetate) at 14, https://www.fda.gov/media/193346/download ("KPV Briefing Materials").
[33] *See id*. at 27.

- *Evaluation Criteria #3: Available Evidence of the Effectiveness or Lack of Effectiveness.*
    - "There is a lack of evidence to evaluate the effectiveness of KPV (free base) and KPV acetate products for the nominated uses of wound healing and inflammatory conditions. The nomination did not include, and FDA did not find any information on the use of KPV (free base) or KPV acetate administered in humans."[34]
- *Evaluation Criteria #4: Historical Use of the Substance in Compounded Drug Products.*
    - "Available literature indicates that the extent of KPV (free base) or KPV acetate use in compounding is unknown. Published literature did not reveal studies in which compounded drug products containing KPV (free base) or KPV acetate were used in humans."[35]

- **TB-500 (free base), TB-500 acetate for wound healing**
    - *Evaluation Criteria #1: Physical and Chemical Characterization of the Substance.*
        - "TB-500 (free base) is not physically and chemically well characterized based on (1) inconsistent naming conventions that do not follow established chemical nomenclature standards (e.g., INN, USAN, IUPAC), and (2) certain critical characterization data specific to TB-500 (free base), such as potential peptide impurities, were not found in publicly available scientific literature and CoA."[36]
    - *Evaluation Criteria #2: Safety Issues Raised by Use of Substance in Compounded Drug Products*
        - "FDA is concerned about the potential for immunogenicity of TB-500 (free base) when formulated in an injectable dosage form for SC/IM administrations due to the potential for aggregation as well as potential peptide-related impurities, as discussed in the impurities section. Injectable ROAs may present a particular risk for immunogenicity. We also note that the stability,

[34] *See id.* at 21.
[35] *See id*. at 19.
[36] *See* FDA Briefing Document, PCAC Meeting July 23-24, TB-500-Related Bulk Drug Substances (TB-500 (Free Base) and TB-500 acetate) at 16, https://www.fda.gov/media/193349/download ("TB-500 Briefing Materials).

pharmacological activity, and immunogenic properties of peptides are highly sensitive to the manufacturing process and quality attributes of the compounded/finished drug product."[37]

- *Evaluation Criteria #3: Available Evidence of the Effectiveness or Lack of Effectiveness.*
  - "There is a lack of evidence to evaluate the effectiveness of TB-500 (free base) and TB-500 acetate products for the nominated use of wound healing. The nomination did not include, and FDA did not find any information in the medical literature where, TB-500 was administered to patients to treat any disease or condition including its use in wound healing."[38]
- *Evaluation Criteria #4: Historical Use of the Substance in Compounded Drug Products.*
  - "At the time of this evaluation, currently available data and published literature are too limited for FDA to understand the historical use of TB-500-related BDSs in compounded drug products."[39]

- MOTS-c (free base), MOTS-c acetate for obesity and osteoporosis
  - *Evaluation Criteria #1: Physical and Chemical Characterization of the Substance.*
    - "MOTS-c acetate is considered not well-characterized from the physical and chemical characterization perspective because (1) inconsistent naming conventions that do not follow established chemical nomenclature standards (e.g., INN, IUPAC, USAN,), and (2) certain critical characterization data specific to MOTS-c acetate (including impurities, aggregates, microbial bioburden and/or bacterial endotoxin) were not found in the publicly available scientific literature, and the provided CoA, which was offered as evidence to establishing identity, purity, and impurity profiles of the substance."[40]
  - *Evaluation Criteria #2: Safety Issues Raised by Use of Substance in Compounded Drug Products*

[37] *Id*. at 16.
[38] *Id*. at 24.
[39] *Id*. at 23.
[40] *See* FDA Briefing Document, PCAC Meeting July 23-24, MOTS-c-Related Bulk Drug Substances (MOTS-c (free base) and MOTS-c acetate) at 19, https://www.fda.gov/media/193347/download ("MOTS-c Briefing Materials").

        - "There is a lack of clinical and nonclinical safety information on the use of MOTS-c. FDA is particularly concerned about the lack of human data on drug products containing this substance administered via any route of administration. MOTS-c is a peptide containing 16 amino acids for which there is a lack of information to assess its immunogenic safety risk. Therefore, potential safety risks associated with the use of MOTS-c in humans are unknown."[41]
    - *Evaluation Criteria #3: Available Evidence of the Effectiveness or Lack of Effectiveness.*
        - "There is a lack of evidence to evaluate the effectiveness of the MOTS-c-related BDSs for the nominated uses. The nomination did not include, and our evaluation did not identify, information on the use of MOTS-c-related BDSs administered in humans in order to evaluate whether MOTS-c-related BDSs are appropriate for the proposed uses in compounded drug products."[42]
    - *Evaluation Criteria #4: Historical Use of the Substance in Compounded Drug Products.*
        - "Published literature did not reveal studies in which compounded drug products containing MOTS-c or MOTS-c acetate were used in humans."[43]

- Emideltide (free base), Emideltide acetate for opioid withdrawal, chronic insomnia, and narcolepsy
    - *Evaluation Criteria #1: Physical and Chemical Characterization of the Substance.*
        - "Emideltide (free base) is considered not well-characterized from the physical and chemical characterization perspectives based on (1) inconsistent naming conventions that do not follow established chemical nomenclature standards (e.g., USAN, INN, IUPAC), and (2) certain critical characterization data specific to emideltide (free base), including specific tests for impurities, aggregates, and endotoxins, were not found in the publicly available scientific literature, and the nominations did not provide scientific literature

[41] *Id*. at 30.
[42] *Id*. at 31.
[43] *Id*. at 21.

or other information such as CoAs as evidence to establish identity, purity, and impurity profiles of the substance."[44]

- *Evaluation Criteria #2: Safety Issues Raised by Use of Substance in Compounded Drug Products*
  - "Considering that the context of use may be for chronic intermittent use, safety for emideltide-related products is insufficiently characterized."[45]
- *Evaluation Criteria #3: Available Evidence of the Effectiveness or Lack of Effectiveness.*
  - "Based on available clinical data, there is insufficient evidence concerning effectiveness to support the use of emideltide (free base) or emideltide acetate via the IV ROA for the treatment of chronic insomnia, narcolepsy, and opioid withdrawal. Clinical studies for chronic insomnia appear to be inconclusive and at best preliminary . . . FDA did not identify any data to support the effectiveness of emideltide (free base) or emideltide acetate for the treatment of chronic insomnia, narcolepsy, and opioid withdrawal via the nominated SC ROA."[46]
- *Evaluation Criteria #4: Historical Use of the Substance in Compounded Drug Products.*
  - "At the time of this evaluation, currently available data and published literature is too limited to inform the historical use of any form of emideltide compounded drug products."[47]

- **Semax (free base), Semax acetate for cerebral ischemia, migraine, and trigeminal neuralgia**
  - *Evaluation Criteria #1: Physical and Chemical Characterization of the Substance.*
    - "Semax (free base) is considered to be not well-characterized from the physical and chemical characterization perspective because (1) inconsistent naming conventions that do not follow established chemical nomenclature standards (e.g., INN, IUPAC, USAN), and

[44] *See* FDA Briefing Document, PCAC Meeting July 23-24, Emideltide-Related Bulk Drug Substances (Emideltide (free base) and Emideltide acetate) at 17, https://www.fda.gov/media/193344/download ("Emideltide Briefing Materials").
[45] *Id*. at 53.
[46] *Id*. at 41.
[47] *Id*. at 23.

(2) BDS-specific quality control attributes, including impurities, aggregates, bacterial endotoxins, and microbial bioburden testing, were not found in the publicly available scientific literature and lack of CoA in the nomination which are offered as evidence to establishing identity, purity, and impurity profiles of the substance of semax (free base) delivered via the subcutaneous (SC) and intranasal spray routes of administration (ROAs)."[48]

- *Evaluation Criteria #2: Safety Issues Raised by Use of Substance in Compounded Drug Products*
  - "It is concerning, however, that, in mice, semax also potentiated amphetamine-induced dopamine release in the striatum because increased dopaminergic tone in the striatum is a response typically induced by drugs of abuse such as cocaine."[49]
  - "Based on available clinical information for semax (free base) and semax acetate, the use of semax-related bulk drug substances in compounding may raise safety concerns. Most of the references did not discuss safety. One reference (Cherkasova et al. 2002) discussed possible antithrombotic properties of semax and this raises concern about the risk of bleeding, particularly in certain populations at risk for bleeding or if combined with other medications that increase bleeding risk."[50]
- *Evaluation Criteria #3: Available Evidence of the Effectiveness or Lack of Effectiveness.*
  - "There is insufficient evidence of effectiveness to support use of semax (free base) or semax acetate for cerebral ischemia. The only available information was in the form of a meeting abstract that lacked information about relevant clinical endpoints."[51]
  - "There is insufficient evidence of effectiveness to support use of semax (free base) or semax acetate for headache pain (analgesia) in subjects with migraine headache. The results from only one small, uncontrolled, open label study showed that semax was not

[48] *See* FDA Briefing Document, PCAC Meeting July 23-24, Semax – Related Bulk Drug Substances (Semax (free base) and Semax acetate) at 15, https://www.fda.gov/media/193348/download ("Semax Briefing Materials").
[49] *Id*. at 37.
[50] *Id*. at 43.
[51] *Id*. at 25.

effective in resolving headache pain for the majority of subjects with migraine."[52]

- "There is insufficient evidence of effectiveness to support use of semax (free base) or semax acetate for analgesia in patients with trigeminal neuralgia pain that is severe and distressing. The results from only one small, uncontrolled, open-label study showed that semax was not effective in resolving pain for the majority of subjects with trigeminal neuralgia in the study."[53]

- *Evaluation Criteria #4: Historical Use of the Substance in Compounded Drug Products.*
  - "The extent to which semax has been used in compounding is unclear."[54]

- **Epitalon (free base), Epitalon acetate**
  - *Evaluation Criteria #1: Physical and Chemical Characterization of the Substance.*
    - "Epitalon (free base) is considered not well-characterized from the physical and chemical characterization perspective based on (1) inconsistent naming conventions that do not follow established chemical nomenclature standards (e.g., INN, USAN, IUPAC), and (2) data/information relevant to certain critical quality attributes for establishing its identity, purity, and quality for its intended use in the proposed dosage form (injection) were either lacking or deemed to be inadequate in the nomination packages or not found in the publicly available scientific literature."[55]
  - *Evaluation Criteria #2: Safety Issues Raised by Use of Substance in Compounded Drug Products*
    - "Based on available information, we conclude that there are no clinical data to support the safety of epitalon (free base) or epitalon acetate when used in humans. Therefore, there is a lack of important information regarding the use of these substances

[52] *Id*. at 26-27.
[53] *Id*. at 28.
[54] *Id*. at 20.
[55] FDA Briefing Document, PCAC Meeting July 23-24, Epitalon-Related Bulk Drug Substances (Epitalon (Free Base) and Epitalon Acetate) at 16, https://www.fda.gov/media/193345/download ("Epitalon Briefing Materials").

administered subcutaneously, including whether the drug would cause harm if administered to humans."[56]

- *Evaluation Criteria #3: Available Evidence of the Effectiveness or Lack of Effectiveness.*
    - "Based on available information, we conclude that there is a lack of evidence to support the effectiveness of epitalon (free base) or epitalon acetate for the proposed use of insomnia, a disorder which increases the risk for serious conditions. Available clinical information discusses the effects of epitalon-related BDSs on melatonin or melatonin metabolite levels. However, we did not identify studies evaluating the use of these substances in patients with insomnia, particularly when administered via the proposed SC ROA."[57]
- *Evaluation Criteria #4: Historical Use of the Substance in Compounded Drug Products.*
    - "The extent to which any form of epitalon has been used in compounding is unclear. . . . At the time of this evaluation, currently available data and published literature is too limited for FDA to understand the historical use of any form of epitalon in compounded drug products."[58]

To summarize FDA's findings, with which PSM strongly agrees and emphasizes the robust detail and analysis contained within, FDA found for all of the seven peptide bulk drug substances that:

1. The bulk drug substances are not physically and chemically well-characterized. In other words, based on current scientific understanding, there is no consensus agreement on what the peptide bulk drug substances *actually are*. Permitting compounding using bulk drug substances without clearly defined chemical and physical structures presents significant risks to patients and strongly weighs against inclusion on the 503A Bulks List.
2. There are significant safety issues associated with compounding from the peptide bulk drug substances, most notably immunogenicity-related safety risks. While FDA identified safety concerns with all of the bulk drug substances, the Agency's finding with respect to BPC-157 is instructive and reflective broadly of the safety issues identified: "The consequences of triggering an immune response may range from antibody responses with no apparent clinical manifestations to life-threatening and catastrophic reactions. Such

[56] *Id*. at 38.
[57] *Id*. at 28.
[58] *Id*. at 23.

outcomes are often unpredictable in patients administered therapeutic protein or peptide products. One possible consequence of the development of an immune response is the development of neutralizing antibody activity that may lead to loss of efficacy or even result in the neutralization of the activity of the endogenous peptide counterpart."[59]

3. There are extremely limited human clinical data to assess the purported effectiveness of the seven peptide bulk drug substances. Indeed, for several of the peptide bulk drug substances, FDA emphasized that there are *no* human clinical data available to assess purported effectiveness. This factor again weighs strongly against including the substances on the 503A Bulks List.
4. There are extremely limited data, if any, on historical use of the bulk drug substances in compounding.

In conclusion, FDA found, for each of the seven peptide bulk drug substances, that all four of the regulatory criteria weighed against adding the substances to the 503A Bulks List. This was not – and is not – a close call. A determination by FDA to add these substances to the 503A Bulks List would go flatly against the robust evidentiary record and would be inconsistent with FDA's regulations. A decision to include these peptide bulk drug substances on the 503A Bulks List would thus be arbitrary and capricious and, accordingly, FDA cannot take such action. Indeed, in other similar circumstances where FDA found that the evaluation criteria weighed against inclusion on the 503A Bulks List, the Agency proceeded to issue regulations codifying such determination that such bulk drug substances will not be included on such list.[60]

Arguments offered by proponents of adding the peptide bulk drug substances to the 503A Bulks List are not persuasive. In particular, we note the following "arguments" proffered by these proponents and explain why such arguments are both not persuasive to establish that the bulk drug substances should be included on the 503A Bulks List.

- Several public commenters at the PCAC meeting argued that, because people are obtaining these substances illegally, FDA should add them to the 503A Bulks List to bring them into a "regulated" space.[61] As an initial matter, whether a substance is being used illegally is not one of the regulatory criteria for evaluation. So this argument must be dismissed outright as a matter of law. Even setting aside the fact that this is not an appropriate regulatory evaluation criteria, accepting this rationale would set a dangerous policy precedent. The appropriate solution to addressing illegal distribution of bulk

[59] *See* BPC-157 Briefing Materials at 43.
[60] *See, e.g.,* 84 Fed. Reg. 4703-04 (concluding that silver protein mild would not be added to the 503A Bulks List and observing that, like for all the substances here, "silver protein mild is not well-characterized, and the term ''silver protein mild'' can refer to a variety of different drug products," that silver protein mild presented safety concerns, and that there is "no reliable evidence that silver protein mild would be effective for the proposed use).
[61] *See, e.g.,* Hims & Hers Comments to Docket No. FDA-2025-N-6895, at 2 https://www.regulations.gov/comment/FDA-2025-N-6895-1727 ("[T]hese therapies must be brought out of the gray market and into trusted channels overseen by vetted healthcare professionals.").

substances is enforcement—not legalization.[62] Indeed, if FDA were to add these substances to the 503A Bulks List or otherwise permit compounding of such substances, this would create an incentive for unscrupulous actors to create an illegal market for additional substances and, later, use that as leverage to argue for such substances to be added to the 503A Bulk List. This is simply not tenable. It is also bad policy and contrary to the law.

- Other stakeholders argued that FDA should permit compounding of these substances to enable the generation of real world data ("RWD") that could help inform an assessment of whether the substances are safe and effective. Again, as a matter of law, this is not a criteria for evaluation set forth in FDA's regulations. And, again, as a matter of policy, accepting such an argument would be unwise. Indeed, this would invert the bedrock principle underlying the FDCA that drugs must be demonstrated safe and effective before introduction into interstate commerce, would undermine FDA's regulatory framework, and render effectively moot the criteria for evaluating the substances for inclusion on the 503A Bulks List. Furthermore, the investigational new drug ("IND") application process is the appropriate pathway to generate clinical evidence to support drug approval – not conducting observational studies of a substance that is mass marketed to patients without first being assessed for safety and effectiveness.

- Proponents of adding these substances to the 503A Bulks List argued that FDA could impose "guardrails" on compounding once the substances were added to the 503A Bulks List.[63] For example, one PCAC voting member, in explaining her vote to include BPC-157 on the 503A Bulks List, stated that she would "like to see some tighter restrictions with APIs [active pharmaceutical ingredients] from U.S.-based pharmacies only, patient registries, mandatory side effects reporting."[64] Again, as an initial matter, whether or not there are guardrails on compounding is not a relevant regulatory factor FDA must consider in evaluating a substance for inclusion on the 503A Bulks List. Moreover, the statute does not allow for FDA to impose additional "guardrails" on compounding that are not set forth in law. As FDA staff noted at the PCAC, the Agency "do[esn't] have a lot of regulatory authority" to add guardrails once a substance is added to the list; indeed, "once [a peptide] is on a list, any bulk drug manufacturer can make it

[62] Appropriate enforcement mechanisms include, but are not limited to, FDA coordination with other agencies and regulators (e.g., Customs and Border Patrol, state boards of pharmacy) as well as working with the Department of Justice to prosecute in certain circumstances. Recent FDA warning letters are instructive of at least some of the avenues available for FDA enforcement. *See, e.g.,* FDA, Warning Letter to TXP Innovations LLC dba Tex Peptides (Aug. 24, 2026).
[63] Hims and Hers Comments at 4. ("Regulated access, done properly, with the right guardrails, education, and transparency, is the answer that actually serves patient safety and builds the knowledge base that better care requires.").
[64] *See* July 23, 2026 Meeting of the PCAC at 4:46:46, https://www.youtube.com/watch?v=DhDC0DAYdBI.

any way they want and test it to any standard they want."[65] Accordingly, any argument that FDA can simply add "guardrails" when adding substances to the 503A Bulks List is simply a self-serving talking point that has no basis in law.

- Other stakeholders pointed to the lack of adverse event reports associated with use of the nominated substances. This is a red herring. Because these substances are not currently permitted to be compounded or otherwise legally marketed for human use in the United States, adverse event reporting is limited. Moreover, because marketing these substances is presently unlawful, the entities that are marketing these peptides are not going to report adverse events to FDA. Thus, it stands to reason that there would be extremely limited adverse event reporting for these substances.

- Finally, several stakeholders argued that because, for certain peptide bulk drug substances, there was no clinical evidence of safety issues, the Agency should add the substances to the 503A Bulks List. This, again, inverts the regulatory evaluation criteria and suggests that lack of data is a factor that, bizarrely, counsels in favor of adding a substance to the 503A Bulks List. Moreover, this argument is nonsensical. Simply because there are no safety data does not mean that the substance is safe. Indeed, if lack of safety data is a compelling factor for adding a substance to the 503A Bulks List, there would be no incentive for manufacturers to garner the necessary safety data to secure drug approval. And FDA, in the federal register notice announcing the PCAC, has helpfully already cut off this argument, observing that "[t]he absence of information does not mean that safety risks do not exist."[66]

PSM strongly agrees with FDA's detailed analysis and evaluation of these substances and the Agency's finding, in the PCAC briefing materials, that these substances should not be added to the 503A Bulks List. Proponents of adding the substances to the list have offered arguments that are sorely lacking as a matter of law and policy. Accordingly, as FDA has recommended, the Agency must refrain from adding these substances to the 503A Bulks List. A determination otherwise would go flatly against the Agency's own assessment without any reasoned basis, in contravention to the requirements for reasoned decision-making under the APA.

### B. The PCAC Was Not Properly Constituted and Does Not Satisfy the Section 503A(c)(1) Requirement of Convening and Consulting an Advisory Committee on Compounding Prior to Promulgating Regulations

The PCAC was not properly constituted according to applicable statutory requirements because of the clear conflicts of interest with several members of the Committee. According to public reports, several of the PCAC members appear to have conflicts of interest directly related

[65] *See id* at 6:23:21.
[66] *See* 84 Fed. Reg. 4696 at 4699.

to the peptide bulk drug substances under consideration. Reporting from STAT[67] highlighted the following potential conflicts of interest:

- "Gabriel Alizaidy is the scientific director of Maximus, an online wellness clinic that prescribes … peptides …. The FDA issued a warning letter to Maximus earlier this month for marketing compounded GLP-1 products tirzepatide and semaglutide."
- "Asare B. Christian is a sports medicine physician and founder of Philadelphia-based Aether Medicine …. Aether's website points to peptides as one of its preferred treatments ….";
- "Melissa Loseke … is osteopathic physician and owner of the Re-New Institute in Omaha, Neb., which … offers peptides ….";
- "Gerald E. Morris …, the medical director at AMG Center for Regenerative Medicine & Aesthetics in Tucson, Ariz., offers peptide therapies ….";
- "Joshua Starbuck is the founder and medical director of Hawaii-based Makena Health …. Makena's website lists peptides as one of its key therapies."

Despite these clear conflicts of interest—or, at minimum, the appearance of conflicts—FDA issued no waivers for these members. Indeed, it has been reported that despite concerns being raised within FDA relating to potential conflicts of interest, the Department of Health and Human Services ("HHS") directed FDA to add these members without assessing the purported conflicts.[68]

The conflicts of interest and absence of any waivers violates both the FACA and EIGA. Accordingly, FDA cannot add any of these peptides to the 503A Bulks List because the PCAC – which is generally required to be consulted before adding any substance to the list—was not properly constituted.

*First*, with respect to FACA, the PCAC was not "fairly balanced in terms of the points of view represented and the functions" the members perform.[69] The points of view of at least five of the PCAC members, as noted above, appear to have been informed by their interests in business that promote and sell peptide products – products using the very types of bulk drug substances that the PCAC was considering. Accordingly, the FACA was not "fairly balanced" and, in fact, was biased by potential conflicts of interest, in violation of FACA.[70]

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[67] Lizzy Lawrence and Sarah Todd, *Longevity, Wellness Physicians Named to Panel Advising FDA on Peptides—New Panelists Could Benefit From Rule Changes, raising ethics concerns*, STAT (June 29, 2026), https://www.statnews.com/2026/06/29/new-fda-peptide-advisers-compounding-committee-conflicts/

[68] Roubein, supra note 24.

[69] 5 U.S.C. § 1004(b)(2), (c).

[70] FACA is applicable here. FACA "shall apply to each advisory committee except to the extent that the Act establishing the advisory committee specifically provides otherwise." 5 U.S.C. § 1003(a). Section 503A of the FDCA does not "specifically provide[] otherwise," rather, it simply provides that FDA shall "convene and consult an advisory committee on compounding . . . . The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopoeia, pharmacy, physician, and consumer organizations, and other experts selected by the Secretary." 21 U.S.C. § 353a(c)(1). And such a committee is plainly an "advisory committee" under FACA, which is broadly defined as relevant here as "a committee, board,

The imbalance is confirmed by how the Committee's statutorily specified members voted. For instance, the USP representative voted against recommending the peptides to be added to the 503A Bulks List. Once the newly added members with alleged conflicts are set aside, the Committee's own mandated experts did not support adding these substances to the list.

*Second,* the PCAC members appointed by HHS did not comply with the conflict-of-interest requirements applicable to Special Government Employees under 18 U.S.C. § 208 (implemented at 5 C.F.R. part 2640), nor with the financial-disclosure requirements of EIGA. FDA notes that "almost all non-Federal members of [the PCAC] serve as Special Government Employees."[71] Special Government Employees are subject to EIGA requirements and must file financial disclosure statements with their agencies and negotiate conflict-of-interest remediation. Unless an employee obtains a waiver, the employee must be disqualified from any matter in which the employee, or others whose interests are imputed to the employee, has a financial interest.[72] FDA's decision not to require a waiver, even though several PCAC members had clear financial interests in the matter, was contrary to law and arbitrary and capricious under the Administrative Procedure Act. Given these flaws in the PCAC's composition, and the statutory requirement that FDA generally convene the PCAC before issuing regulations to add substances to the 503A Bulks List, the Agency cannot lawfully take action to add any of the seven peptide bulk drug substances to the 503A Bulks List. Taking such action would be arbitrary and capricious under the APA.

### C. Adding the Peptide Bulk Drug Substances Would Reverse FDA's Own 2023 Category 2 Determination Without a Reasoned Basis

Adding these peptide bulk drug substances to the 503A Bulks List would not merely lack record support — it would reverse a determination FDA made only recently. In September 2023, FDA placed these very peptide bulk drug substances in Category 2 of its 503A Interim Policy, reflecting the Agency's express finding that they present "significant safety risks" for compounding, including risks relating to immunogenicity, impurities, and the availability of limited or no human clinical data. FDA's 2026 briefing materials confirm that these same deficiencies persist: the substances remain poorly characterized, their safety profiles remain unestablished, and human clinical data remain absent.

An agency that reverses a prior position must display awareness that it is changing course and must supply a reasoned explanation that confronts the factual findings underlying its earlier decision. FDA can offer no such explanation here, because nothing in the scientific record has

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commission, council, conference, panel, task force, or other similar group, or any subcommittee or other subgroup thereof . . . that is established or utilized to obtain advice or recommendations for the President or one or more agencies or officers of the Federal Government and that is— (i) established by statute . . . or (iii) established or utilized by one or more agencies." 5 U.S.C. § 1001(2).

[71] *See* https://www.fda.gov/advisory-committees/human-drug-advisory-committees/pharmacy-compounding-advisory-committee.

[72] 5 CFR § 2640.103(d).

changed since 2023 to move these substances from posing "significant safety risks" to affirmatively suitable for compounding; to the contrary, the Agency's career reviewers reaffirmed the 2023 concerns. Listing these substances would therefore be arbitrary and capricious as an unexplained reversal of FDA's own findings.

### D. Listing Would Authorize Uncontrolled Bulk-Substance Sourcing With No Enforceable Quality Standard

The safety risks associated with compounding with these peptide bulk drug substances are exacerbated by how the bulk material is sourced. Once a substance is placed on the 503A Bulks List, this creates the risk that any bulk drug manufacturer may produce it by any method and test it to any standard of its choosing. For these peptide bulk drug substances, which have no USP or NF monograph and no established reference standard, there is no enforceable specification against which identity, purity, or potency can be verified. In practice, the material is sourced predominantly from unregistered foreign suppliers, much of it labeled "for research use only" and "not for human use." Placing these substances on the list would enable compounding and widespread distribution of these peptides without the supply-chain safeguards Congress mandated for approved drugs under the Drug Supply Chain Security Act — precisely the exposure to unsuitable bulk drug substances that the 503A Bulks List framework exists to prevent. This concern was voiced directly by the USP representative at the PCAC meeting, and FDA should heed these concerns and not add the substances to the 503A Bulks List.

### E. Adding These Peptide Bulk Drug Substances To The 503A Bulks List Would Pose Significant Safety Risks and Weaken Incentives for Drug Development

Adding these peptide bulk drug substances to the 503A Bulks List, placing the peptide bulk drug substances into Category 1 of the 503A Interim Policy, or taking any other action to authorize compounding of products using these peptide bulk drug substances will pose significant patient safety risks and weaken incentives for drug development.

The 503A Bulks List, FDA's 503A Interim Policy, or any other action of purported "enforcement discretion" should not be used to circumvent the drug approval process. Section 503A authorizes pharmacies to compound a drug product when it is clinically necessary for an individual, identified patient, not to provide a pathway for mass-compounded products that have not satisfied FDA's review for safety and effectiveness. The appropriate pathway for evaluating unapproved substances is the IND process.[73]

Adding these substances to the 503A Bulks List, including them on "Category 1" of FDA's 503A Interim Policy, or otherwise allowing compounding using these substances would

[73] Of interest, an analog of one of the seven peptide bulk substances under consideration was studied in a clinical trial under an IND and is considered a failed drug candidate. The sponsor of the MOTs-C analog CB4211 paused development after concluding that the formulation of CB4211 used in the Phase 1b stage of the trial is not suitable for further development, and that efforts to produce an improved formulation "have not been successful to date. *See* CohBar, Inc., Form 10-K at F-6, https://www.sec.gov/ix?doc=/Archives/edgar/data/1522602/000121390023018882/f10k2022_cohbarinc.htm.

result in uncontrolled and unconsented human experimentation with drug products that lack evidence of safety and efficacy and FDA approval. Patients treated with compounded drugs made from such substances are not protected by the robust regulatory guardrails provided by the IND framework, including informed consent requirements, institutional review board review, adverse event reporting, and FDA oversight. Allowing compounding of these substances not only endangers patients, but it also weakens the incentives for manufacturers to invest in costly and time-intensive research and clinical trials, ultimately discouraging innovation that leads to new medicines for patients.

### F. Adding these to Category 1 Would be Contrary to Law and FDA's Own Interim Policy

Some stakeholders have suggested that, in lieu or in advance of adding the substances to the 503A Bulks List – which by law requires rulemaking – FDA should add the peptide bulk drug substances to "Category 1" under its 503A Interim Policy, effectively enabling 503A compounding.[74] FDA cannot do this. First, FDA's 503A Interim Policy is contrary to law. Second, and setting aside that FDA's 503A Interim Policy is unlawful, placing the substances in Category 1 would be inconsistent with the 503A Interim Policy itself. We describe these arguments in turn.

As stakeholders have previously noted, FDA's 503A Interim Policy is unlawful and must be rescinded.[75] The FDCA is clear in setting forth when bulk substances may be compounded under Section 503A: the bulk substance must either have a USP/NF monograph, be a component of an FDA-approved drug, or appear on a list "developed by [FDA] through regulations."[76] FDA's "interim" policy—which is effectively over 25 years old—contravenes the critical statutory requirements by permitting compounding with bulk drug substances that have not been placed on the 503A Bulks List.

Indeed, FDA itself has noted that building the 503A Bulks List is part of the Agency's "statutory mandate" that seeks to "protect the public from exposure to bulk drug substances that are not suitable for use in compounded drug products," and "prevent the use of drug products for which there is insufficient evidence that benefits to the patient might outweigh possible risks."[77] The 503A Interim Policy does not provide any of these assurances. The current interim policy places patients at risk of receiving compounded drugs that may pose safety, efficacy, and quality risks. And, as such, the 503A Interim Policy should be rescinded as a matter of law and policy. Accordingly, FDA cannot add the seven peptide bulk drug substances to "Category 1."

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[74] *See, e.g.,* Letter from Scott Brunner, CEO, Alliance for Pharmacy Compounding, to Acting Commissioner Kyle Diamantas (Aug. 25, 2026) (APC Letter).
[75] *See, e.g.,* PhRMA, Comments to Docket No. FDA-2015-D-3517 (Jan. 8, 2024).
[76] FDCA 503A(b)(1)(A)(i).
[77] See FDA, List of Bulk Drug Substances That Can Be Used To Compound Drug Products in Accordance With Section 503A of the Federal Food, Drug, and Cosmetic Act, 84 Fed. Reg. 4696, 4708 (Feb. 19, 2019).

Even if FDA's 503A Interim Policy were lawful, adding the seven peptide bulk drug substances to Category 1 would be inconsistent with such Interim Policy. Specifically, the 503A Interim Policy does not apply to "substances nominated on or after . . . January 7, 2025."[78] Because the seven peptide bulk substances have had their nominations withdrawn, and any subsequent nomination would be after January 7, 2025, they therefore fall outside the scope of FDA's Interim Policy.

Putting aside that the Interim Policy itself is legally flawed, even the purported rationale of the interim policy would not be served by addition of these peptides. Specifically, the 503A Interim Policy was intended to avoid "inappropriate disruptions in patient care."[79] In other words, the 503A Interim Policy was intended to preserve compounding practices that pre-dated the relevant enactment and amendments to FDCA Section 503A. None of the peptide bulk drug substances here reflect compounding practices that predate either the initial 1997 enactment of section 503A or the amendments made by the Drug Quality and Security Act in 2013. Accordingly, from a pure policy perspective, utilizing the 503A Interim Policy to enable compounding using these peptide bulk drug substances would be inconsistent with the underlying policy aims of such Interim Policy.

### G. Other Efforts to Expand Compounding of Peptide Bulk Drug Substances Risks Patient Safety and Undermines the Incentives for Seeking FDA Approval of Safe and Effective Medicines

PSM notes that at least one commenter has proposed a "regulatory framework for the approval of peptide therapeutics."[80] Setting aside the fact that any such pathway would require legislation, this proposed "framework" rests on dubious scientific assertions, including erroneously suggesting that peptide drug substances that mimic naturally occurring molecules or hormones in the body do not pose safety risks. More fundamentally, however, PSM emphasizes that such a pathway would be contrary to public health and, in effect, would take us back to a pre-1962 FDA when substantial evidence of effectiveness was not required for a drug to receive FDA approval. The Kefauver-Harris Amendments of 1962 added the substantial evidence of effectiveness requirement for approval, and were a direct response to the thalidomide tragedy, which demonstrated the risks of unsafe and ineffective medicines. The mere existence of policy proposals to create an "approval lite" pathway for peptides simply reinforces the fact that there is not sufficient evidence that these peptides are safe and effective for use in humans, and that the proponents of expanded use of peptides, in fact, know this.

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[78] *See* 503A Interim Policy Guidance at 10.
[79] *See id* at 7.
[80] *See* American Academy of Peptide Medicine, "A Regulatory Framework for the Approval of Peptide Therapeutics Under Strict Manufacturing, Safety, and Clinical Oversight," https://www.pepmed.org/downloads/AAPM-Regulatory-Framework-2026.pdf ("AAPM White Paper").

While PSM is not aware of any active efforts within FDA or elsewhere to implement any sort of separate peptide "framework," we highlight here significant concerns should any such policymaking be pursued.

More broadly, concerted efforts of the compounding industry to subvert FDA authority, disrupt the regulatory framework, and put patients at risk should not be rewarded through permission to expand compounding. Rather, FDA must utilize its existing authorities to take enforcement action against unlawful compounding and help the Agency's mission to protect the public health.

## V. Conclusion

FDA's mission is to "protect the public health by ensuring the safety, efficacy, and security of human drugs" and to "advance[e] the public health by helping to speed innovations."[81] Allowing compounding using these seven peptide bulk drug substances would be directly contrary to FDA's mission. Moreover, and as detailed in this petition, allowing compounding using these substances either through adding them to the 503A Bulks List, including them on "Category 1" of FDA's 503A Interim Policy, or otherwise through purported "enforcement discretion," would be contrary to law, policy, and the public health. Accordingly, FDA must refrain from taking such action for these reasons set forth in this petition.

## VI. Environmental Impact

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.30.

## VII. Economic Impact

Petitioner will submit economic information upon request of the Commissioner.

## VIII. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Signature: Shabbir Imber Safdar

Name of petitioner: Shabbir Imber Safdar, CFE, Executive Director, Partnership for Safe Medicines

[81] *See* FDA, What We Do: FDA Mission, https://www.fda.gov/about-fda/what-we-do.

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