July 9, 2026
ELECTRONICALLY SUBMITTED

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Comment of the Collaborative for Evidence-Based Medicines on Bulk Drug Substances Nominated for Inclusion on the Section 503A Bulk Drug Substances List — BPC-157, KPV, TB-500, MOTs-C, Emideltide (DSIP), Semax, and Epitalon. Docket No. FDA-2025-N-6895; Pharmacy Compounding Advisory Committee Meeting of July 23–24, 2026.

To the Pharmacy Compounding Advisory Committee:

The Collaborative for Evidence-Based Medicines ("CEBM") is a national provider-led organization advancing evidence-backed medicines, safe compounding, and stronger oversight and accountability to protect patients. CEBM brings together providers, patient advocates, academics, consumer groups, manufacturers, and other stakeholders to advance our patient safety mission. The signatories to this letter are pharmacists, physicians, and regulatory professionals who sit on the CEBM Board or who are otherwise closely involved in CEBM's work to advance patient safety. As physicians and pharmacists who care for patients across a range of conditions, CEBM has a direct, professional interest in ensuring that any substance added to the 503A Bulks List is supported by rigorous evidence demonstrating that compounded drug products made from that substance can be used safely and effectively.

For the reasons set out below, CEBM does not support the inclusion of any of the nominated peptide substances on the 503A Bulks List.[1] As a threshold matter, CEBM urges FDA to ensure that any actual or potential conflicts of interest among Committee members are fully disclosed and addressed before the Committee makes any recommendation regarding the nominated peptide substances. First, the nominated peptide substances do not satisfy the evidentiary standard FDA has consistently applied to candidates for inclusion on the 503A Bulks List. Second, the Section 503A framework requires valid and reliable evidence demonstrating human safety and effectiveness, a standard none of the seven nominations meets. Third, broader public health considerations independently weigh against listing the nominated peptide substances on the 503A Bulks List. CEBM thus urges the Pharmacy Compounding Advisory Committee (the "Committee") to recommend to the U.S. Food and Drug Administration ("FDA") that the nominated peptide substances not be added to the 503A Bulks List.

[1] This letter will refer to the seven peptide substances under consideration by the Committee collectively as the "nominated peptide substances". These nominated peptide substances are BPC-157, KPV, TB-500, MOTs-C, emideltide (DSIP), semax, and epitalon, including both their free base and acetate forms.

I. The Committee's Assessment of the Nominated Peptide Substances Must Follow Applicable Conflict-of-Interest Requirements to Protect Patient Safety and Trust in FDA

CEBM respectfully raises, at the outset, a threshold concern regarding the integrity of the Committee's advisory process. The Committee is charged with reviewing and evaluating "scientific, technical, and medical issues concerning drug compounding."[2] The Committee's recommendation on whether to add substances to the 503A Bulks List must be made based solely on what is best for patients. Financial interests among Committee members, whether direct or indirect, have no place in that determination. The integrity of the Committee's process is itself a patient-safety issue because the Committee's advice informs FDA's ultimate decision whether unapproved substances may be used to compound drugs outside the ordinary safeguards of FDA approval or clinical trials.

CEBM is particularly concerned about both the reality and appearance of conflicts of interest in this proceeding. Those concerns include financial and professional interests associated with compounding pharmacies and other entities that market, dispense, supply, or otherwise stand to profit from compounded products made from the nominated peptide substances. Even when such interests do not mandate disqualification, they can compromise—or reasonably appear to compromise—the objectivity of recommendations that will affect whether patients are exposed to compounded drugs made from inadequately studied peptide substances.

Even the appearance of such conflicts is harmful. Prescribers, pharmacists, and most importantly, patients, must be able to trust that FDA's implementation of the Section 503A compounding framework is driven by science, law, and patient safety—not by financial interests. If the public reasonably perceives that recommendations for inclusion on the 503A Bulks List may be influenced by members with financial ties to the compounding or peptide marketplace, confidence in FDA's implementation of Section 503A will be undermined. That loss of confidence is not a procedural abstraction; it directly affects whether patients can trust that substances made available through compounding have been evaluated through an objective and credible process.

At a minimum, FDA must ensure that any actual, potential, or apparent conflicts of interest are addressed under the statutory and regulatory procedures governing FDA advisory committees before the Committee votes or otherwise makes recommendations on the nominated peptide substances. FDA advisory committees must comply with applicable federal advisory committee and ethics requirements, including the Federal Advisory Committee Act's requirement that membership of a committee be fairly balanced in terms of points of view represented[3], FDA's

[2] U.S. Food and Drug Administration, "Pharmacy Compounding Advisory Committee Charter" current as of Apr. 25, 2026, *available at*: https://www.fda.gov/advisory-committees/pharmacy-compounding-advisory-committee/pharmacy-compounding-advisory-committee-charter (last accessed July 8, 2026).
[3] 5 U.S.C. § 1004(b)(2).

advisory committee regulations[4], and FDA's guidance documents.[5] Accordingly, FDA should ensure full disclosure of relevant interests and recusal or disqualification where required by applicable law, regulation, or FDA policy, so that the Committee's recommendation reflects independent scientific and regulatory judgment rather than financial or institutional interests.

This safeguard is especially important where, as here, the Committee's recommendation will address substances that FDA has already found raise serious concerns under the applicable criteria related to characterization, safety, effectiveness, and historical use. The more consequential the patient-safety stakes, the greater the need for a process that is—and is seen to be—free from inappropriate conflicts of interest.

II. The Evidence Must Demonstrate That Substances Nominated for Inclusion on the 503A Bulks List Satisfy the Regulatory Criteria for Listing

Because the Committee's recommendation will be the first application of the Section 503A framework to a cohort of peptide substances, it is important to ground this letter in the regulatory criteria that apply when FDA considers whether to add substances to the 503A Bulks List. The Section 503A framework that governs inclusion on the 503A Bulks List reflects a deliberate judgment that bulk drug substances used in compounding should satisfy threshold criteria before they are made broadly available outside the traditional new-drug approval pathway.

Section 503A of the Food, Drug, and Cosmetic Act ("FDCA") establishes the conditions under which a human compounded drug product may be exempt from three fundamental regulatory requirements: (1) current good manufacturing practice ("cGMP") requirements[6]; (2) labeling with adequate directions for use[7]; and (3) new drug application ("NDA") or abbreviated

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[4] 41 CFR 102-3.60(b) ("To comply with the Act's requirement for fairly balanced membership, during the Federal advisory committee member recruitment process agencies should consider the following: (1) The points of view required. During the formation of the advisory committee membership and as membership vacancies occur, agencies should ensure that they fully consider and understand the potential implications or anticipated impacts of the advisory committee's potential recommendations. This includes consideration of the groups and entities potentially affected or interested in such recommendations, as appropriate based on the nature and functions of the advisory committee, so that the agency can make informed decisions on the areas of expertise or perspectives that would advance the work of the advisory committee. Advisory committees requiring technical expertise should include persons with demonstrated professional or personal qualifications and experience relevant to the functions and tasks to be performed by the committee. (2) Outreach. Having identified the points of view that would promote a fairly balanced advisory committee membership, agencies should conduct broad outreach."); 5 CFR 2635.502; 21 CFR 14.80(a)(2) ("Members of a policy advisory committee…(2)Are subject to the conflict of interest laws and regulations either as special Government employees or as members of the uniformed services, including the Commissioned Corps of the Public Health Service").

[5] U.S. Food and Drug Administration, "Procedures for Evaluating Appearance Issues and Granting Authorizations for Participation in FDA Advisory Committees" June 2016, *available a*t: https://www.fda.gov/media/98852/download (last accessed July 8, 2026); U.S. Food and Drug Administration, "Guidance for the Public, FDA Advisory Committee Members, and FDA Staff: Public Availability of Advisory Committee Members' Financial Interest Information and Waivers" March 201*4*, *available* at: https://www.fda.gov/media/83188/download (last accessed July 8, 2026).

[6] 21 U.S.C. 351(a)(2)(B).

[7] 21 U.S.C. 352(f)(1).

new drug application approval.[8] In order to be exempt from these three core safety and effectiveness guardrails, there are three conditions under which pharmacies can compound from bulk drug substances: the bulk drug substance (1) complies with the standards of an applicable USP or NF monograph, if a monograph exists, and the USP chapter on pharmacy compounding; (2) if no such monograph exists, is a component of an FDA-approved drug; or (3) if no monograph exists and the substance is not a component of an approved drug, appears on a list of bulk drug substances developed by FDA through rulemaking, called the "503A Bulks List".[9] This third category—the 503A Bulks List—is the one at issue in these proceedings.

The 503A Bulks List thus represents a critical regulatory gateway under which pharmacies are permitted to compound and dispense unapproved drugs. CEBM recognizes that compounding can serve an important role in patient care by meeting an individual patient's clinical need when a commercially available, FDA-approved product is unsuitable, such as because of a specific dosage requirement, an allergy to an inactive ingredient, or another patient-specific circumstance. However, precisely because bulk drug substances placed on the 503A Bulks List may be used in compounded drug products that are exempt from cGMP requirements, labeling requirements, and premarket approval requirements, FDA established four criteria to evaluate these substances under 21 C.F.R. § 216.23(c) to ensure that only substances with adequate characterization and evidence of safety and effectiveness can ultimately reach patients.[10] Those four criteria are:

1. the physical and chemical characterization of the substance;
2. any safety issues raised by the use of the substance in compounded drug products;
3. the available evidence of effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists; and
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.[11]

FDA has explained that it applies these criteria on a substance-by-substance basis, weighing them as appropriate based on the nature of the substance and its proposed use.[12] FDA applies these criteria within an assessment of whether the benefits of compounding with the nominated substances outweigh the risks.[13] Where a bulk drug substance is proposed to treat a serious or life-threatening condition, FDA weighs the effectiveness criterion more heavily given the serious consequences of ineffective therapy; conversely, the safety criterion receives greater weight where the substance is proposed for treatment of less serious illness.[14] FDA's application of the criteria to particular substances is subject to discussion with the Committee and the United States Pharmacopeia ("USP"). To add a substance to the 503A Bulks List, FDA must engage in notice-and-comment rulemaking.

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[8] 21 U.S.C. 355.
[9] 21 U.S.C. 353a.
[10] 84 Fed. Reg. 4697 (Feb. 19, 2019).
[11] 21 C.F.R 216.23(c).
[12] 84 Fed. Reg. 4699 (Feb. 19, 2019).
[13] *Id* at 4700. (acknowledging that the regulatory criteria will be "applied on a substance-by-substance basis, given the risks and benefits that may be presented by a particular substance.").
[14] *Id*.

III. FDA's Preliminary Assessment that the Nominated Peptide Substances Should Not Be Added to the 503A Bulks List at This Time Is Sound

We agree with FDA's preliminary assessment that the nominated peptide substances are not suitable for use in compounding under the applicable regulatory criteria and should not be included on the 503A Bulks List at this time.[15] FDA's preliminary assessment is consistent with, and reinforced by, how FDA has applied these regulatory criteria in the past. In 2019, when FDA declined to add several substances to the 503A Bulks List, each refusal traced directly to the regulatory criteria in 21 C.F.R. § 216.23(c). As an illustrative example, silver protein mild failed across nearly every criterion. FDA found it was not well-characterized at all—the very name could denote a range of different products—going to the first criterion.[16] On safety, FDA was troubled regarding its side effects such as permanent discoloration of the skin, conjunctiva, and internal organs.[17] On effectiveness, the controlled evidence was poor. For instance, in one study the silver protein mild was numerically inferior to no treatment, and in another it was inferior to an approved product, povidone iodine.[18] And although silver protein mild had been used since the early 1900s, FDA found that its use had collapsed once approved ocular anti-infectives became available.[19] The FDA also declined to add oxitriptan, piracetam, and tranilast to the 503A Bulks List after balancing the same regulatory criteria.[20]

The main lesson from FDA's 2019 decisions is that when evaluating substances for inclusion on the 503A Bulks List, FDA looks for credible, reliable evidence including adequate characterization, an absence of unresolved safety signals, and sufficient evidence of effectiveness for the specific proposed use and route of administration. FDA is not persuaded merely by a record of historical use. As described in Section IV, none of the nominated peptide substances are currently supported by sufficient evidence to justify adding these substances to the 503A Bulks List. This assessment is supported by FDA's initial evaluation of the nominated peptide substances and decision that none of the substances should be listed on the 503A Bulks List.[21]

As further historical evidence, in September 2023, after reviewing nominations for other bulk drug substances proposed to be included on the 503A Bulks List, FDA categorized the nominated peptide substances under Category 2 as described in the "Interim Policy on Compounding Bulk Drug Substances Under 503A and 503B of the FDCA" ("Interim Policy").[22] According to the Interim Policy, a bulk drug substance is listed under Category 2 if FDA

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[15] U.S. Food and Drug Administration, "FDA Briefing Document Pharmacy Compounding Advisory Committee (PCAC) Meeting July 23-24, 2026" *available at*: https://www.fda.gov/media/193342/download (last accessed July 1, 2026).
[16] 84 Fed. Reg. 4704 (Feb. 19, 2019).
[17] *Id.*
[18] *Id.*
[19] *Id.*
[20] 84 Fed. Reg. 4703 (Feb. 19, 2019).
[21] U.S. Food and Drug Administration, "FDA Briefing Document Pharmacy Compounding Advisory Committee (PCAC) Meeting July 23-24, 2026" *available at*: https://www.fda.gov/media/193342/download (last accessed July 1, 2026).
[22] U.S. Food and Drug Administration, "Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act" Jan. 2025, *available at*: https://www.fda.gov/media/174456/download (last visited June 24, 2026).

determines that it presents significant safety risks. FDA determined that compounded drugs produced from the seven nominated substances may pose increased risks of immunogenicity, may include peptide-related impurities, and present complexities in properly characterizing their active pharmaceutical ingredients ("APIs").[23] For many, FDA found that a lack of "sufficient information to know whether the [compounded] drug would cause harm" was enough to warrant inclusion in Category 2.[24] Designation as a Category 2 substance means that the substance is not permitted for use in compounding by 503A entities. By placing all the nominated peptide substances in Category 2, FDA has already determined, after reviewing the evidence, that the nominated peptide substances present significant safety risks in compounding and that, for several, the record was too thin even to evaluate whether the resulting compounded drug would cause patient harm. FDA's current preliminary assessment builds upon that earlier determination to confirm the significant safety risks presented by the nominated peptide substances.

FDA's confirmation of unresolved safety concerns, coupled with the absence of reliable evidence of effectiveness for the proposed uses (as described in Section IV), support the conclusion that the nominated peptide substances do not satisfy the safety and effectiveness criteria of 21 C.F.R. § 216.23(c). To add the nominated peptide substances to the 503A Bulks List would establish an inconsistent legal precedent by suggesting that substances unable to satisfy the criteria of 21 C.F.R. § 216.23(c) may nonetheless be listed for broad compounding, destabilizing the Section 503A framework that depends on FDA applying its regulatory criteria consistently and through a reasoned evaluation of the record.

IV. The Section 503A Framework Requires Sufficient Evidence of Human Safety and Effectiveness—A Standard None of These Nominated Peptide Substances Currently Meet

As providers responsible for the patients who will likely receive compounded drugs made from the nominated peptide substances (if added to the 503A Bulks List), CEBM begins from a straightforward premise: a substance should not be made available for compounding drugs for patients until its record is sufficient to satisfy the § 216.23(c) criteria—characterization, safety, effectiveness, and historical use—to demonstrate that the benefits from compounding from such substance would outweigh the risk it would expose patients to. To be clear, the evidence required to support a nomination to the 503A Bulks List is not the same as that required to support an NDA—substances do not have to be supported by "substantial evidence" from adequate and controlled trials to support effectiveness.[25] Nonetheless, nominated substances must meet a baseline requirement that the balance of the four regulatory criteria supports that benefits of compounding with a nominated substance would outweigh the risks.

The nominated peptide substances cannot clear even that minimum bar. The evidence for each rests overwhelmingly on in vitro experiments and animal models, with little-to-no

[23] U.S. Food and Drug Administration, "Certain Bulk Drug Substances for Use in Compounding that May Present Significant Safety Risks" current as of Apr. 22, 2026, *available at*: https://www.fda.gov/drugs/human-drug-compounding/certain-bulk-drug-substances-use-compounding-may-present-significant-safety-risks (last visited June 24, 2026)
[24] *Id*.
[25] 21 U.S.C. 355(d).

methodologically adequate human clinical data (especially *validated* human data) to support conclusions about safety or effectiveness for the nominated uses. Even where limited human data exists, those data generally do not evaluate the same route of administration, formulation, dose range, duration of exposure, patient population, or intended real-world use proposed for compounded products. These flaws are magnified by the immunogenicity risks that FDA has identified for the majority of these peptides, as well as the elevated risks from sterile injectable drugs, the route by which most are administered. These deficiencies are for the nominators to answer. As the parties seeking to have nominated peptide substances added to the 503A Bulks List, the nominators bear the obligation to provide sufficient evidence demonstrating that each substance satisfies the applicable criteria. They have failed to do so here. CEBM agrees with the FDA's assessment of each peptide substance and its determination that none should be listed on the 503A Bulks List.

Adding the nominated peptide substances to the 503A Bulks List despite these evidentiary gaps would shift unresolved questions of safety, dosing, effectiveness, and product quality from controlled research settings into routine patient care, thus turning patients into test subjects. When the evidence base of a substance consists predominantly of animal studies, inadequate human studies and in vitro research, the administration of a compounded drug with these peptide substances to a person becomes the first meaningful test of whether the substance is safe. Patients should not bear that risk for substances that have never been adequately studied in humans.

a. The Safety of the Nominated Peptide Substances Has Not Been Established in Humans, and Compounding Magnifies the Resulting Risks

Across the nominated peptide substances, the claimed safety data rest largely on non-human evidence—in vitro assays, rodent pharmacology studies, and, in a minority of cases, small and methodologically deficient human reports. For four of the seven substances—MOTS-C, KPV, TB-500, and epitalon—there are no known clinical studies assessing safety via any route of administration, and accordingly the potential safety risks in humans are unknown. In the FDA briefing documents, the nominators did not submit any nonclinical toxicity studies for MOTs-C, KPV, and TB-500, leaving even the animal safety record incomplete.[26]

For the three substances with some human data—BPC-157, emideltide, and semax—the studies share similar disqualifying weaknesses.

- **BPC-157**: As of 2025, only three peer-reviewed human pilot studies have been published, evaluating intra-articular treatment for chronic knee pain, intravesical treatment for interstitial cystitis, and intravenous safety/pharmacokinetics in healthy volunteers.[27] All these studies were small (the largest involving 16 patients) and for a

[26] U.S. Food and Drug Administration, "FDA Briefing Document Pharmacy Compounding Advisory Committee (PCAC) Meeting July 23-24, 2026" *available at*: https://www.fda.gov/media/193342/download (last accessed July 1, 2026).

[27] McGuire, FP, R Martinez, A Lenz, L Skinner and DM Cushman, 2025, Regeneration or Risk? A Narrative Review of Bpc-157 for Musculoskeletal Healing, Curr Rev Musculoskelet Med 18:611. ("Only three pilot studies have examined BPC-157 in humans, including its use for intraarticular knee pain, interstitial cystitis, and intravenous safety/pharmacokinetics. No adverse effects were reported, but rigorous, large-scale trials are

different indication than the nomination here. FDA only identified two limited human studies that have been conducted to treat ulcerative colitis.[28] These studies are small, short-duration studies (the largest involving roughly two dozen subjects) that evaluated exploratory doses, supplied limited safety data and unclear safety monitoring. Further, the available human studies do not establish safety for the nominated oral, subcutaneous, nasal, or transdermal routes, and they do not address the dosing, duration, formulation, or patient populations likely to be encountered in compounded use.

- **Emideltide (DSIP)**: Human studies of emideltide have been published since at least 1981, but the body of clinical evidence remains small, dated, and methodologically limited. The published studies fall into three treatment categories: chronic insomnia[29], narcolepsy[30], and opioid/alcohol withdrawal.[31] These studies were uniformly small and were limited by methodological concerns, including a lack of or poor selection of control groups, intra-subject (rather than parallel placebo-arm) comparisons, heterogeneous dosing regimens, and unknown long-term benefit.
- **Semax**: The human evidence for semax is sparse, methodologically limited, and altogether absent for the nominated subcutaneous route. FDA identified only two English-language clinical references that studied semax for the indicated uses and both are small, uncontrolled, open-label studies.[32] The remaining human data come from studies in healthy adults and are uniformly small and limited by a lack of blinding, the absence of a control group, a failure to report actual scores or standard deviations, and insufficient detail on study design and endpoints.[33]

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lacking…This review highlights that given the robust preclinical evidence and high public interest, there is a critical need for well-designed human trials to assess the safety, efficacy, and clinical utility of BPC-157 in musculoskeletal medicine.").

[28] Ruenzi, M, M Stolte, M Veljaca, K Oreskovic, J Peterson and UCS Group, 2005, A Multicenter, Randomized, Double Blind, Placebo-Controlled Phase II Study of Pl 14736 Enema in the Treatment of Mild-to-Moderate Ulcerative Colitis, Gastroenterology 128:A584; Veljaca, M, D Pavic Sladoljev, B Mildner, K Brajsa, M Bubenik, S Stipanicic, M Tabak-Slosic, L Brnic, M Khan, Z Krznaric, A Bischoff, A Schroeder, W Van Dongen and F Van Schaik, 2003, Safety, Tolerability and Pharmacokinetics of Pl 14736, a Novel Agent for Treatment of Ulcerative Colitis, in Healthy Male Volunteers, Gut 2003;51:A309.

[29] Schneider-Helmert, D, 1986, Efficacy of DSIP to Normalize Sleep in Middle-Aged and Elderly Chronic Insomniacs, Eur Neurol, 25(6):448-453; Schneider-Helmert, D, 1987, Effects of Delta-Sleep-Inducing Peptide on 24-Hour Sleep-Wake Behaviour in Severe Chronic Insomnia, Eur Neurol, 27(2):120-129; Schneider-Helmert, D, F Gnirss, M Monnier, J Schenker and GA Schoenenberger, 1981, Acute and Delayed Effects of DSIP (Delta Sleep-Inducing Peptide) on Human Sleep Behavior, Int J Clin Pharmacol Ther Toxicol, 19(8):341-5; Schneider-Helmert, D and GA Schoenenberger, 1981, The Influence of Synthetic DSIP (DeltaSleep-Inducing-Peptide) on Disturbed Human Sleep, Experientia, 37(9):913-917; Schneider-Helmert, D and GA Schoenenberger, 1983, Effects of DSIP in Man. Multifunctional Psychophysiological Properties Besides Induction of Natural Sleep, Neuropsychobiol, 9(4):197- 206.

[30] Schneider-Helmert, D, 1984, Effects of DSIP on Narcolepsy, Eur Neurol, 23(5):353-357.

[31] Dick, P, C Costa, K Fayolle, ME Grandjean, A Khoshbeen and R Tissot, 1984, DSIP in the Treatment of Withdrawal Syndromes From Alcohol and Opiates, Eur Neurol, 23(5):364-371; Backmund, M, K Meyer, HB Rothenhaeusler and M Soyka, 1998, Opioid Detoxification With Delta Sleep-inducing Peptide: Results of an Open Clinical Trial, J Clin Psychopharmacol, 18(3):257-258.

[32] U.S. Food and Drug Administration, "FDA Briefing Document Pharmacy Compounding Advisory Committee (PCAC) Meeting July 23-24, 2026," *available at*: https://www.fda.gov/media/193348/download (last accessed June 30, 2026).

[33] *Id.*

The overarching trend is unmistakable. Whether a nomination offered no human data or only fragmentary human data, none of the nominated peptide substances are supported by the controlled, adequately powered, peer-reviewed human clinical evidence necessary to characterize a safety profile sufficient for therapeutic use in compounded form. CEBM agrees with FDA's evaluation that none of the nominated peptide substances should be placed on the 503A Bulks List because none of them have been proven to be safe for use in humans.

b. The Evidentiary Record for the Nominated Peptides Is Predominantly Preclinical and Does Not Establish Effectiveness in Humans

The effectiveness record exhibits the same structural deficiency as the safety records: limited human evidence, frequent reliance on preclinical or mechanistic data, and a lack of adequate route-specific and indication-specific clinical evidence. For every nominated peptide substance, there is a lack of sufficient evidence of effectiveness for the nominated uses. MOTs-C, KPV, and TB-500 offered no human efficacy data whatsoever. Where human efficacy studies do exist, they are uniformly preliminary and inconclusive—emideltide's insomnia studies were small, poorly controlled, and contradictory across investigators[34]; semax's effectiveness rested on small, uncontrolled, open-label studies that failed to demonstrate benefit[35]; and the single BPC-157 ulcerative colitis abstract that FDA identified showed no statistically significant difference from placebo and omitted essential trial details.[36]

The recurring lesson is that therapeutic benefit cannot be extrapolated from animal or cell-based data to human patients. Mechanistic plausibility in a rodent model or a culture dish does not establish that a substance will be effective—or safe—in a human. Absent adequate human clinical evidence, the efficacy claims advanced for the nominated peptide substances remain speculative. And for conditions ranging from obesity and osteoporosis to ulcerative colitis, insomnia, and cerebral ischemia, FDA-approved therapies with established efficacy already exist, further weakening claims that patients need access to compounded drugs made from these inadequately supported substances.

c. FDA Must Evaluate These Substances Against Their Predictable Real-World Uses, Not Only the Narrow Uses Nominated for Review

In assessing these substances, FDA and the Committee should evaluate the safety of the nominated peptide substances in light of their foreseeable real-world use, because route, dose, duration, patient population, concomitant therapies, and indication may differ substantially from the narrow uses presented for review. Practically, the nominated peptide substances are and would continue to be used by consumers far beyond the narrow uses presented for review. It is appropriate—and indeed necessary—for FDA to weigh the foreseeable real-world uses of the nominated peptide substances and FDA has expressly recognized that "when FDA is aware of another use that may be relevant to its evaluation of a substance for the 503A Bulks List, such as

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[34] Schneider-Helmert, *supr*a note 29; Schneider-Helmert, *su*pra note 30; *Dick* supra no*t*e 31.
[35] U.S. Food and Drug Administration, *supra* note 32.
[36] U.S. Food and Drug Administration, "FDA Briefing Document Pharmacy Compounding Advisory Committee (PCAC) Meeting July 23-24, 2026" *available at*: https://www.fda.gov/media/193343/download (last accessed June 30, 2026).

when a use other than that for which it was nominated is widespread, FDA may consider that use in its discretion."[37] A listing decision premised solely on the nominated indication, without accounting for predictable prescribing and marketing outside of the nominated use, would fail to protect patients from foreseeable harm.

Listing a substance on the 503A Bulks List would not restrict compounding to the indications described in the notice. Once a substance is listed, it may be compounded for any use a prescriber is willing to support. This gap matters because the scientific literature gives providers no reliable basis to counsel patients about the risks of these compounded products. With no established clinical guidelines and an evidentiary record too sparse to characterize safety, dosing, pharmacokinetics, durability of effect, or contraindications, prescribers must weigh benefits against risks without the information needed to determine whether a compounded drug can be expected to treat the illness it is being prescribed to address. Given the aggressive marketing already surrounding these peptides and the absence of any mechanism to restrict compounding to the nominated indications once a substance is listed, widespread compounding for uses that have never been evaluated is not a possibility but a certainty.

Consider the nominated substance BPC-157. This peptide substance is presented for the 503A Bulks List for an indication of ulcerative colitis. However, this substance is aggressively marketed by online vendors as a treatment for repairing tendons, ligaments, and muscles and reducing inflammation, nearly always alongside claims about athletic performance, recovery, and anti-aging.[38] The submitted nominations do not address the uses that will predominate in the real world for each peptide substance. And if, as described above, the safety evidence cannot even support the nominated uses, it certainly cannot protect patients who will be exposed to the nominated peptide substances for purposes unsupported by the evidence.

d. Risk of Immunogenicity Supports Not Including the Nominated Substances on the 503A Bulks List

Immunogenicity presents a direct and serious threat to patient safety, and FDA has identified a risk of immunogenicity in the majority of the nominated peptide substances.[39]

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[37] 84 Fed. Reg. 4701 (Feb. 19, 2019).

[38] Prohealth Longevity, "Pure BPC-157-500 mcg, 60 capsules" *available at*: https://www.prohealth.com/products/prohealth-bpc-157-500-mcg-60-capsules-ph703?srsltid=AfmBOoq93sQ2IHlrGK0cp72clboEZNdhtW4RHhttU_sERFb-GlpRI7cl (last accessed June 25, 2026) (advertising BPC 157 for "gut health", "healthy aging", "joint health" and "muscle health"); DesertMobileMedical, "BPC-157 Peptide" *available at*: https://desertmobilemedical.com/product/bpc-157-peptide/?srsltid=AfmBOop4Tfc1E1ueUFdZpMcdAKHxIIJsYZrsWM8OwhKghL22YROujOte (last accessed June 25, 2026) ("Body Protection Compound-157 is a powerful regenerative peptide known for its ability to accelerate healing, reduce inflammation, and support recovery across the entire body. Originally derived from gastric proteins, BPC-157 works systemically to promote blood flow, tissue repair, and cellular regeneration—making it highly valuable for patients dealing with injuries, chronic inflammation, gastrointestinal dysfunction, or delayed recovery. It's one of the most popular peptides in performance medicine, longevity therapy, and musculoskeletal regeneration.").

[39] U.S. Food and Drug Administration, "Certain Bulk Drug Substances for Use in Compounding that May Present Significant Safety Risks" current as of Apr. 22, 2026, *available at*: https://www.fda.gov/drugs/human-drug-compounding/certain-bulk-drug-substances-use-compounding-may-present-significant-safety-risks (last accessed June 30, 2026).

Immunogenicity is the unwanted development of an immune response usually marked by development of antibodies to a therapeutic product.[40] The clinical consequences of immunogenicity for a patient can span a wide spectrum. Some patients develop antibodies with no apparent effect. Others experience altered pharmacokinetics, loss of efficacy, or toxicity from drug accumulation. Still others suffer severe harm, including hypersensitivity or anaphylaxis, immune-complex disease, or neutralizing antibodies that cross-react with the patient's own endogenous peptide and cause a deficiency syndrome. Whether a patient mounts such a response depends on patient-specific factors such as genetics, immune competence, and underlying disease, and critically on the product itself, including both the active ingredient and the impurities that accompany it. Sequence variants and peptide-related impurities can create new epitopes that the immune system treats as foreign, while aggregates, process-related impurities, contaminants, excipients, and leachates act as adjuvants that inflame the administration site, activate antigen-presenting cells, and drive antibody production.[41]

Patients receiving compounded peptide products may be especially exposed to this harm because the analytical methods needed to detect and control peptide-related impurities, sequence variants, degradation products, and aggregates may exceed the routine capabilities of many traditional compounding settings. FDA has emphasized that the concern for peptides is different in kind from small molecules, that injectable routes such as subcutaneous, intravenous, intramuscular, and intradermal carry greater immunogenic risk than oral administration, and that peptide-related impurities are difficult to detect because they can share the peptide's own amino acid sequence, requiring advanced techniques such as liquid chromatography and high-resolution mass spectrometry.[42] Impurities and contaminants can activate immune cells at trace levels measured in picograms and nanograms. Thus, mitigating the risk demands sophisticated manufacturing and testing strategies of the kind a compounding facility does not employ. FDA's own laboratory testing has identified concerns relevant to innate immune activation in compounded peptide products, including findings suggesting that routine sterilizing filtration may not fully mitigate immune activation in all samples.[43] FDA concluded that product immunogenicity constitutes a real risk for compounded peptides that may result in significant harm to patients, including life-threatening reactions such as anaphylaxis.

This patient-safety risk is neither theoretical nor speculative. FDA's published Category 2 list expressly identifies immunogenicity as a significant safety risk for six of the seven nominated peptides: BPC-157, MOTs-C, emideltide, epitalon, semax, and TB-500.[44] Because no nominator supplied the data needed to characterize or exclude this FDA-identified hazard, patients cannot be assured these products are safe, and the risk cannot be resolved on the present record. Consistent with CEBM's patient-safety mission, these substances should not be listed on

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[40] U.S. Food and Drug Administration, "Food and Drug Administration Center For Drug Evaluation And Research Pharmacy Compounding Advisory Committee (PCAC), December 4th, 2024, FDA Presentation" *available at*: https://www.fda.gov/media/185641/download (last accessed June 30, 2026).
[41] *Id.*
[42] *Id.*
[43] *Id.*
[44] U.S. Food and Drug Administration, "Certain Bulk Drug Substances for Use in Compounding that May Present Significant Safety Risks" current as of Apr. 22, 2026, *available at*: https://www.fda.gov/drugs/human-drug-compounding/certain-bulk-drug-substances-use-compounding-may-present-significant-safety-risks (last accessed June 30, 2026).

the 503A Bulks List unless and until adequate immunogenicity and safety data demonstrate that patients will not be exposed to unacceptable harm.

e. Risks Associated with Injectable Route of Administration Further Support Not Including the Nominated Substances on the 503A Bulks List

Finally, the route of administration significantly increases the risk profile of the nominated peptide substances. Six of the seven substances are proposed predominantly or exclusively for injection. KPV is nominated for topical use, yet FDA observed that techniques used to enhance skin penetration could increase systemic absorption, and no human data exist to characterize the resulting exposure or risk.

Compounded sterile injectable drugs inherently carry heightened risks. Sterility, purity, potency, and stability must each be rigorously maintained, and any failure is delivered directly into the body, bypassing the protective barriers that mitigate the consequences of contamination by other routes. Dosing variability, systemic exposure, and the absence of adequate human pharmacokinetic and safety data compound these hazards because there is no reliable basis to define a safe dose, treatment duration, or monitoring strategy.

This distinction is significant because the majority of substances currently on the 503A Bulks List are topical products, whose risk profile differs fundamentally from that of peptides delivered via injection. Adding the nominated peptide substances would therefore mark a notable departure from the character of the existing list, extending it to substances whose injectable route, immunogenic potential, and absent human safety data categorize these substances as high-risk relative to the current substances on the 503A Bulks List. That atypical and elevated risk profile reinforces the conclusion that the nominated peptides do not belong on the 503A Bulks List.

V. Broader Public Health Consequences Confirm That the Nominated Substances Should Not Be Listed

a. Marketing-Driven Patient Demand for the Nominated Peptide Substances Does Not Justify Listing Substances That Cannot Satisfy the Regulatory Criteria

Some proponents contend that patient demand supports adding the nominated peptide substances to the 503A Bulks List. This faulty argument is based on the position that it would steer patients away from unregulated (and illegal) sources and toward regulated compounding pharmacies. But as discussed below, placement on the 503A Bulks List does not assure that patients will receive products from legitimate, adequately regulated sources. As providers, we understand the public impulse behind these arguments. This argument, however, misapprehends both the legal function of the Bulks List and the practical realities of 503A compounding, and it should be rejected. If accepted, the argument would convert unlawful market demand into a reason for authorization and would imply that any unapproved substance with a sufficiently large illegal market should be listed. That is not the FDCA's design. The Bulks List is an evidence-

based regulatory pathway, not a tool for legitimizing illegal conduct after demand has already been created through aggressive marketing.

As a legal matter, patient demand and black-market activity are not among the criteria that govern inclusion on the 503A Bulks List. FDA evaluates candidates under the four factors in 21 C.F.R. § 216.23(c)—physical and chemical characterization, safety, effectiveness, and historical use—and may list a substance only where FDA is confident the record demonstrates that compounding from it would yield a safe and effective drug. Nothing in Section 503A or FDA's implementing regulations authorizes the agency to list a substance that fails those criteria simply because consumers wish to obtain it or because illegal sellers are already supplying it. Adding a substance to the 503A Bulks List on the basis of demand rather than evidence would invert the statutory scheme, converting an evidence-based gateway into a demand-driven one and establishing precisely the inconsistent precedent that CEBM cautions against above.

As a clinical and public health matter, listing these peptides would not make them safe. Compounded drugs made from the nominated peptide substances would remain exempt from cGMP requirements, adequate-directions-for-use labeling, and premarket review, as well as post-market requirements like track-and-trace requirements and adverse event reporting. Compounding pharmacies do not register their facilities with FDA and are largely overseen by state boards of pharmacy whose resources are already stretched thin. The unresolved hazards that disqualify these substances—unknown human safety, FDA-identified immunogenicity risk, and the heightened risks associated with injectable routes of administration—do not diminish because a patient obtains the product from a compounding pharmacy rather than an online "peptide vendor". Routing demand into the 503A pathway would therefore not deliver the safety assurances the "regulated source" argument promises; instead, it would attach a misleading imprimatur of FDA legitimacy to products whose risks remain uncharacterized.

Where genuine patient needs exist, the law already supplies the appropriate response. Section 503A was designed to meet the individualized needs of particular patients whom an FDA-approved product cannot serve—not to satisfy mass-market demand generated by direct-to-consumer promotion, often for indications the nominators have not placed before the Committee. For substances that may hold therapeutic promise, the pathway that responsibly expands safe access at scale is controlled clinical studies under an investigational new drug ("IND") followed by FDA approval, which subjects the product to the safeguards, quality controls, and evidentiary scrutiny that compounding by design lacks. Meeting demand through research and approval, rather than through the Bulks List, is the course that protects patients.

b. Protecting the Integrity of the FDA Drug Approval Framework and Its Innovation Incentives Is Essential to Serving Patients

FDA's drug approval system is widely regarded as the most rigorous and trusted regulatory framework in the world for ensuring that medicines reaching patients are safe, effective, and manufactured to the highest quality standards. Compounding under the Section 503A framework was conceived as a carefully circumscribed accommodation within this system—available only when no FDA-approved and commercially available medicine can meet a particular patient's clinical requirements—and was never designed to function as a separate

channel for the large-scale manufacture of compounded drugs that have not satisfied FDA's safety, effectiveness, or quality standards and compete directly with FDA-approved drugs that have.

Where a substance may have therapeutic promise but lacks adequate evidence to support patient use, the proper route is controlled clinical study under an IND application, not broad access through compounding. The IND process includes safeguards that protect patients and preserve the integrity of clinical research, including informed consent, Institutional Review Board oversight, FDA supervision, defined study protocols, and adverse event reporting.[45] Patients who receive compounded products made from substances listed on the 503A Bulks List do not receive those protections. Listing inadequately studied substances on the 503A Bulks List therefore risks exposing patients to products whose risks, benefits, quality, dosing, and appropriate use have not been established.

Allowing the 503A Bulks List to function as a shortcut to market would also undermine the integrity of the broader drug approval system. The Hatch-Waxman Act framework depends on a careful balance between innovation and generic competition. Brand manufacturers undertake the time, cost, and risk of developing new therapies; generic manufacturers obtain market access only after demonstrating bioequivalence and satisfying FDA's quality and manufacturing requirements. Compounders should not receive de facto market access for unapproved substances while avoiding the obligations that manufacturers must meet.

For these reasons, the 503A Bulks List should remain a narrow, evidence-based pathway and substances should be listed only where the record demonstrates sufficient physical and chemical characterization, safety, effectiveness, and historical use, and only where the benefits of authorizing compounding outweigh the risks. Expanding the list to include inadequately supported peptide substances would expose patients to unnecessary risk, distort incentives for clinical research and FDA approval, and weaken the safeguards that make the U.S. drug approval system the foundation of safe and effective patient care.

c. Inclusion on the 503A Bulks List Risks Widespread Consumer Misperception of FDA Endorsement

Placement of any of the nominated peptide substances on the 503A Bulks List creates an unusually serious risk of consumer confusion. These peptide substance nominations are meaningfully different from prior 503A Bulks List nominations because they arise in the context of intense consumer demand, aggressive direct-to-consumer promotion, and commercial promotion of peptides in the longevity, wellness, performance, weight-management, and "optimization" markets. The distinction matters because compounding pharmacies, telehealth platforms, online pharmacies, wellness clinics, and marketing intermediaries will exploit a substance's placement on the 503A Bulks List as a signal of regulatory legitimacy, and undoubtedly market it to consumers as such.

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[45] U.S. Food and Drug Administration, "Investigational New Drug (IND) Application" current as of June 17, 2026, *available at*: https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application (last accessed June 26, 2026).

Research of GLP-1 consumers confirms that consumers and patients frequently misunderstand the regulatory status of compounded drugs, perceiving them as having undergone the same rigorous premarket review as FDA-approved drugs.[46] Consumers are unlikely to distinguish between "a bulk substance listed for purposes of exempt compounding" and "an FDA-endorsed peptide therapy."

For that reason, consumer confusion is a serious patient safety issue. If any of the nominated peptide substances are listed on the 503A Bulks List, more patients are likely to use them under the mistaken belief that they have been tested and shown to be safe, including for many broader uses that have not been reviewed and for which safety and effectiveness have not been established. Even more troubling, patients will seek to treat their illness with unapproved products made from unproven peptide bulk drug substances in lieu of legitimate, FDA-approved therapies backed by actual evidence of safety and efficacy.

d. Inclusion of the Nominated Peptides on the 503A Bulks List Poses Unacceptable Patient Safety Risks That Current Oversight Cannot Address

If FDA permits the nominated peptide substances to be placed on the 503A Bulks List, the predictable consequence will be a substantial expansion of compounding activity, and with it, a corresponding expansion of risk to patient safety. Four interconnected considerations counsel against this outcome.

First, state boards of pharmacy, which serve as the primary regulators of 503A compounding pharmacies, already operate with oversight capacity and resources stretched thin by existing compounding activity. Given the considerable consumer demand and commercial interest in these products, adding peptide substances to the 503A Bulks List would flood the market with new compounded products and dramatically enlarge the universe of activities that state boards of pharmacy must oversee. Critically, no corresponding increase in state regulatory capacity would accompany this listing-induced growth, creating an environment in which quality failures are more likely to go undetected and unaddressed.

Second, as described above, the nominated peptide substances are predominantly injectable peptide products, which carry an inherently elevated risk profile. Injectables present particularly acute quality challenges because sterility, purity, potency, and stability must be rigorously maintained. Compounding these products demands intensive regulatory scrutiny, which state boards of pharmacy, as currently resourced, are not positioned to provide at scale.

Third, unlike manufacturers of FDA-approved drug products, 503A compounding pharmacies are not subject to any uniform adverse event reporting requirement.[47] As a result, the true incidence and severity of adverse events associated with compounded drugs made from the nominated peptide substances will almost certainly be significantly underreported. Without

[46]ASOP Global Foundation, "ASOP Global Foundation, 2025 U.S. Consumer Behavior Survey, Snapshot: GLP-1 Medications are Reshaping Demand" Dec. 2025, *available at*: https://asopfoundation.pharmacy/wp-content/uploads/2025/12/ASOP-Foundation-Survey-Snapshot-GLP1s.pdf ("86% of online GLP-1 purchasers incorrectly believe that compounded medications are evaluated by the FDA for safety and efficacy.").
[47] 21 C.F.R 314.80.

reliable adverse event data, FDA, state regulators, and prescribing providers will not be able to fully weigh the risks and benefits of these products, and serious patient harm may go unreported.

Fourth, FDA has long recognized the significant public safety risks posed by compounding. This matters because, as FDA has explained, compounded drugs "pose a higher risk to patients than FDA-approved drugs."[48] Drugs compounded in accordance with the conditions of Section 503A of the FDCA are exempt from FDA premarket review for safety and effectiveness and certain labeling and supply chain security requirements. Pharmacists and physicians who compound under Section 503A are also exempt from cGMP requirements and many states still do not require full compliance with USP <797> sterile compounding standards. Exacerbating these gaps is the fact that because 503A compounders are not FDA-licensed and generally do not register their facilities with FDA, so the Agency has little visibility into the vast majority of them and typically learns of problems only after the fact—through a complaint, a report of a serious adverse event, or visible contamination. These risks are not hypothetical: they are magnified by documented findings of insanitary conditions and contamination at 503A pharmacies across the country.[49]

e. 503A Compounding Has Grown into a Commercial Industry Whose Scale is Contrary to the Limited Accommodation Congress Intended

The concerns described above are heightened by the scale at which the 503A compounding market now operates. Section 503A was designed as a narrow accommodation to meet individualized patient needs that FDA-approved products cannot address; it was not intended to support a high-volume commercial industry operating in parallel to the approved drug market. Yet the compounding industry has expanded far beyond that limited purpose. The compounding pharmacy market is a five-billion-dollar industry and is projected to grow to a nearly nine-billion-dollar industry by 2035.[50] Growth of this magnitude reflects a market increasingly driven by consumer demand and commercial promotion rather than by the patient-specific clinical needs the framework was built to address.

Because lawfully compounded drugs are exempt from the Drug Supply Chain Security Act's track-and-trace requirements[51] and 503A pharmacies are not required to register with FDA

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[48] U.S. Food and Drug Administration, "Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act" Jan. 2018, *available at*: https://www.fda.gov/media/98973/download.

[49] U.S. Food and Drug Administration, "Form 483 to Boothwyn Pharmacy, LLC" issued Jun. 6, 2025, *available at*: https://www.fda.gov/media/187974/download?attachment; U.S. Food and Drug Administration, "Form 483 to Advanced Nutriceuticals, LLC" issued Nov. 22, 2024, *available at*: https://www.fda.gov/media/185235/download?attachment; U.S. Food and Drug Administration, "Form 483 to North American Custom Laboratories, LLC d/b/a FarmaKeio Superior Custom Compounding" issued Sept. 5, 2025, *available at*: https://www.fda.gov/media/189832/download.

[50] Towards Healthcare, "503A U.S. Compounding Pharmacies Market Size, Growth and Geographical Insights" last updated Jan. 5, 2026, *available at*: https://www.towardshealthcare.com/insights/503a-us-compounding-pharmacies-market (last accessed June 26, 2026).

[51] U.S. Food and Drug Administration, "Drug Supply Chain Security Act Product Tracing Requirements | Frequently Asked Questions" current as of Aug. 14, 2024, *available at*: https://www.fda.gov/drugs/drug-supply-chain-security-act-dscsa/drug-supply-chain-security-act-product-tracing-requirements-frequently-asked-questions (last accessed July 7, 2026).

or report adverse events, FDA has no reliable mechanism to follow a compounded product back to the bulk drug substance from which it was made, to identify the supplier that furnished it or understand the true incidence of patient harm. Adding the nominated peptide substances to the 503A Bulks List would almost certainly accelerate the growth of 503A compounding pharmacies, channeling intense consumer and commercial interest into an exemption from robust FDA oversight that was never designed to function at this scale and into a system that cannot trace products to their source, cannot systematically detect patient harm, and cannot verify where bulk drug substances come from. The predictable result is that patients will be exposed to harm that regulators will be unable to identify, track, or prevent.

f. The Proper Response to Uncertainty Regarding the Therapeutic Potential of the Nominated Substances Is Rigorous Research, Not Premature Addition to the 503A Bulks List

CEBM does not dispute that the nominated peptide substances may hold therapeutic promise, and the Committee should not foreclose the possibility that one or more of these substances could, with appropriate study, be supported by evidence sufficient to warrant inclusion on the 503A Bulks List. That bar is not met today. The published literature remains sparse, the existing studies are largely uncontrolled or preliminary, and critical questions of safety, dosing, characterization, route-specific exposure, immunogenicity, and effectiveness for mass marketed proposed uses remain unresolved. The appropriate response to that uncertainty is not to extend broad compounding access through the 503A Bulks List, but to generate the safety, effectiveness, dosing, pharmacokinetic, immunogenicity, and product quality data needed to support regulatory decision making. CEBM would therefore support additional public health funding for rigorous, well-controlled clinical trials of these substances, conducted under the safeguards of regulatory frameworks. Investing in that research, rather than substituting demand and anecdote for evidence, is the course most consistent with patient safety and with the evidence-based mission that animates the Section 503A framework.

Relatedly, if FDA's concern is that limiting compounding access might push patients and suppliers toward peptide substances obtained from China or other foreign sources through black market channels, the solution lies in enforcement rather than in making these substances prematurely available for compounding under Section 503A. Recent investigative findings underscore this point. Studies have found that proceeds from online peptide sales in the United States are flowing directly to China-based manufacturers of fentanyl precursors who are pivoting to the peptide business to capitalize on consumer demand while likely continuing to supply fentanyl precursor chemicals to drug cartels.[52] Adding the nominated peptide substances to the 503A Bulks List would not disrupt these illegal supply chains. Instead, it would legitimize the market these illicit actors have built and likely strengthen the ties between the sale of peptides and fentanyl manufacturing. The better course is to confront illicit foreign sourcing directly—for instance, by issuing an import alert covering unapproved peptide API from China and other foreign sources, working closely with FDA and U.S. Customs and Border Protection

[52] Reed, T. "Chinese Fentanyl Makers Find New U.S. Market in Peptides" published July 7, 2026, *available at*: https://www.axios.com/2026/07/07/chinese-fentanyl-makers-pivot-peptides?utm_source=newsletter&utm_medium=email&utm_campaign=newsletter_axiosvitals&stream=top (last accessed July 7, 2026).

enforcement personnel at ports of entry, and increasing inspections of those suspected of receiving black market peptides.

VI. FDA Must Take Appropriate and Holistic Action to Protect Public Health If It Permits Compounding with The Substances Under Consideration

Notwithstanding the substantial patient safety concerns identified above, if FDA were to ultimately place the nominated peptide substances on the 503A Bulks List, FDA and other regulatory authorities (such as state boards of pharmacy) must implement materially more rigorous safeguards to mitigate the resulting risks to patients.

Specifically, any listing determination should be accompanied by, at minimum, the following conditions and commitments:

1. Enhanced oversight of 503A compounding pharmacies producing listed peptide substances, including increased frequency of inspections and establishment of specific quality benchmarks for sterile peptide compounding;
2. Effective and sustained collaboration between FDA and state boards of pharmacy to ensure that oversight resources are commensurate with the expanded scope of compounding activity that listing would precipitate;
3. Robust enforcement mechanisms to ensure active pharmaceutical ingredient (API) quality and sourcing integrity, including requirements for certificates of analysis, supplier qualification, and quality testing;
4. Specific testing expectations for peptide identity, purity, potency, sterility, endotoxin, degradation products, aggregation, and peptide-related impurities, with attention to route of administration and duration of use; and
5. Mandatory adverse event reporting mechanisms for 503A compounding pharmacies dispensing listed peptide substances.

CEBM emphasizes that these safeguards represent a minimum threshold, not a comprehensive solution. Even with enhanced safeguards, listing these unsupported substances would continue to expose patients to risks that the current record does not justify.

VII. Conclusion

The nominations before the Committee cannot be reconciled with the Section 503A framework that governs the 503A Bulks List. From a patient safety perspective, CEBM agrees with the FDA's assessment that the nominated peptide substances cannot satisfy the evidentiary standard FDA has consistently applied under 21 C.F.R. § 216.23(c). Section 503A demands sufficient evidence to support human safety and effectiveness under the applicable regulatory criteria, a threshold none of these nominations meets on the present record. A series of cross-cutting public health considerations also independently counsels against listing the nominated peptide substances.

Listing even one of these nominated peptide substances would have consequences beyond the substance-specific decision before the Committee. It would signal to compounders,

telehealth platforms, peptide vendors, and other market participants that substances with limited human evidence, unresolved immunogenicity concerns, and foreseeable mass-market demand may nonetheless gain access to the 503A compounding pathway. Rather than preserving Section 503A as a narrow pathway for individualized patient need, such a decision would invite repeated efforts to use the 503A Bulks List as an alternative route to market for inadequately studied substances.

For the foregoing reasons, CEBM respectfully urges the Committee to align with FDA's analysis and recommend against adding to the Section 503A Bulks List BPC-157, KPV, TB-500, MOTs-C, emideltide (DSIP), semax, or epitalon, in free base or acetate form, for any of the indications identified in the Federal Register notice for this meeting.

As physicians, pharmacists, and regulatory professionals committed to ensuring that patients receive treatments that are safe, effective, and supported by evidence, CEBM stands ready to support the Committee in any way that advances that shared goal, including by providing additional information or testimony at the Committee's open public hearing sessions on July 23 and 24, 2026.

Respectfully submitted,

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