July 30, 2026
ELECTRONICALLY SUBMITTED

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

Re: Comment in Support of FDA's Proposal Not to Include Semaglutide, Tirzepatide, and Liraglutide on the 503B Bulks List. Docket No. FDA-2018-N-3240-0377

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.

CEBM strongly supports the Food and Drug Administration's ("FDA") proposal not to include semaglutide, tirzepatide, and liraglutide on the list of bulk drug substances for which there is a clinical need under Section 503B of the Federal Food, Drug, and Cosmetic Act ("FDCA") (the "503B Bulks List"). As a provider-led organization dedicated to patient safety, CEBM has a fundamental interest and a direct, professional stake in ensuring that patients receive medicines that have been rigorously evaluated for safety, efficacy, and quality. Moreover, as health care providers who prescribe and dispense GLP-1 receptor agonists and other drugs for diabetes and obesity, we are acutely aware of both the therapeutic value of these FDA-approved drugs, and the serious risks that arise when untested, compounded versions are made without adequate oversight or evidence and reach patients. FDA's proposed determination is firmly grounded in scientific evidence, consistent with its statutory framework, and essential to safeguarding public health and the patients we serve.

As described below, each of the claimed justifications for compounding using these bulk drug substances—alternative dosing regimens, multi-ingredient formulations, and alternative routes of administration—fails to establish the necessary "clinical need" under the established framework (Section I). We further explain why so-called personalization practices advanced by compounders are pretextual rather than clinically driven (Section II), and we affirm that FDA's interpretation of the clinical need standard is squarely within the FDA's statutory authority and not the clinical practice of medicine (Section III). We address the well-documented safety risks that compounded products pose to patients in the absence of a true clinical need for these products (Section IV), and we identify the broader public health harms—including pervasive consumer deception and the erosion of innovation incentives—that would flow from permitting compounding from bulk drug substances without a rigorous determination of clinical need (Section V). For all of these reasons, CEBM urges FDA to finalize its proposal. Excluding

semaglutide, tirzepatide, and liraglutide from the 503B Bulks List is the only outcome consistent with the statutory text, the scientific record, and FDA's mandate to protect patients.

I. FDA Is Correct That There Is No Clinical Need to Justify Bulk Compounding of Semaglutide, Tirzepatide, and Liraglutide

Compounders have attempted to justify the compounding of semaglutide, tirzepatide, and liraglutide by pointing to the "clinical need" for alternative dosing regimens, multi-ingredient formulations with additives, and oral, sublingual, or buccal routes of administration. However, as physicians and pharmacists who manage patients on these therapies—initiating treatments, titrating doses, monitoring for adverse events, and counseling on proper administration—we can state with confidence that these justifications lack merit and do not meet the clinical need standard. FDA has thoroughly evaluated each claimed basis for inclusion on the 503B Bulks List and correctly concluded that none establishes a genuine clinical need. We address each in turn.

As a threshold matter, CEBM rejects the premise that "clinical need" turns on a decision by an individual prescriber to use a compounded drug. The clinical-need standard requires a demonstrated need to compound from a bulk drug substance instead of using an FDA-approved product; it is not satisfied by generalized assertions of prescriber discretion or patient preference. FDA and the courts have already recognized the danger of an overbroad interpretation, as it would allow outsourcing facilities to compound nearly any active pharmaceutical ingredient ("API") found in an approved drug, effectively converting the 503B Bulks List into an unrestricted pathway for producing substitutes for approved medicines.[1] The fact that some prescribers may choose to prescribe compounded semaglutide, tirzepatide, or liraglutide therefore does not demonstrate that approved products are medically unsuitable or that compounding from bulk drug substances is necessary. The specific asserted justifications that there is a "clinical need" to compound from bulk by 503B outsourcing facilities—alternative dosing, additives, and non-approved routes of administration—must be evaluated on their qualification under the clinical need standard, and each fails for the reasons below.

a. Alternative Dosing Does Not Constitute a Clinical Need

The nominator's justification that there is a clinical need for compounded "alternative doses" in amounts that are unavailable in FDA-approved products is contradicted by the broad range of approved doses already on the market, the illusory nature of compounders' so-called personalized dosing, the absence of any clinical evidence supporting microdosing, and the availability of sterile-to-sterile compounding for the rare cases where truly individualized dosing is warranted.

FDA-approved versions of semaglutide, tirzepatide, and liraglutide are available in a wide range of carefully studied routes of administration, dosage forms, and dose regimens, in each case supported by clinical trial data establishing therapeutic effectiveness across diverse patient populations.[2] These

[1] Athenex Pharma Solutions, LLC v. Azar, No. 1:19-cv-00603, 019 WL 3501811 (D.D.C. Aug. 1, 2019)

[2] At the time of the publication of FDA Docket FDA-2018-N-3240, the GLP-1 products are available in a range of dosing alternatives: (1) Semaglutide is an active ingredient in FDA-approved drug products: 2 mg/3 mL, 4 mg/3 mL, and 8 mg/3 mL solutions for subcutaneous (SC) injection which contain propylene glycol (Ozempic, NDA 209637); 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL, 1.7 mg/0.75 mL, 2.4 mg/0.75 mL, and 7.2 mg/0.75 mL solutions for SC injection which do not contain propylene glycol (Wegovy and Wegovy HD, NDA 215256); 1.5 mg, 4 mg, 9 mg,

products are also available in multiple container-closure systems that afford prescribers meaningful flexibility in dose selection and dose escalation or de-escalation. In our clinical practice, the breadth of available approved doses and routes of administration provide the flexibility we need to meet the needs of our patients. Indeed, even if a patient may need to receive a dose that differs from the recommended increments on the FDA-approved label, providers can use the FDA-approved product to meet patients' needs. Compounded drugs with different dosage strengths are not supported by clinical evidence and lack any clinical trial data. In fact, alternative dosing in compounded preparations may result in serious harm to patients.[3]

Moreover, much of what compounders market as "alternative doses" is illusory: these products may be compounded at slightly different concentrations, but when actually administered, they deliver the same therapeutic benefit that the FDA-approved medicine already provides.[4] The patient receives no novel therapeutic benefit. Moreover, as pharmacists who verify dosing calculations and counsel patients on proper administration, we recognize this practice for what it is: it is not personalization, but it is repackaging of a nearly identical dose under the pretense of differentiation to circumvent the FDA approval framework.

Compounders also claim their compounded versions are needed for "microdosing" to reduce purported side effects while still achieving therapeutic effect. This rationale is unfounded. The trend of "microdosing" generally involves patients injecting very small amounts (well under the lowest FDA-approved dosage) on a more frequent basis (often daily) in the belief that such practice minimizes the risk of side effects while still producing a therapeutic benefit. To be clear—there are no peer-reviewed clinical trial data to support this premise. As clinicians, we are well aware that every medication has a minimum therapeutic dose (often referred to as the minimum effective dose), which is the smallest amount of a drug necessary to produce the intended health benefit. Taking medication below this minimum therapeutic dose is simply not effective. Moreover, safely determining and adjusting a

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and 25 mg oral tablets (Wegovy, NDA 218316); and 1.5 mg, 3 mg, 4 mg, 7 mg, 9 mg, and 14 mg oral tablets (Rybelsus and Ozempic, NDA 213051); (2) Tirzepatide is an active ingredient, as both a single-dose pen and a singledose vial, in FDA-approved drug products: 2.5 mg/0.5 mL, 5 mg/0.5 mL, 7.5 mg/0.5 mL, 10 mg/0.5 mL, 12.5 mg/ 0.5 mL, and 15 mg/0.5 mL solutions for SC injection (Mounjaro, NDA 215866; Zepbound, NDA 217806). Tirzepatide is also an active ingredient, as both a multi-dose vial and a single-patient-use KwikPen, in FDA-approved drug products: 10 mg/2.4 mL (4.17 mg/mL) for four 2.5 mg/0.6 mL doses, 20 mg/2.4 mL (8.33 mg/mL) for four 5 mg/0.6 mL doses, 30 mg/2.4 mL (12.5 mg/mL) for four 7.5 mg/0.6 mL doses, 40 mg/2.4 mL (16.7 mg/mL) for four 10 mg/0.6 mL doses, 50 mg/2.4 mL (20.8 mg/mL) for four 12.5 mg/0.6 mL doses; and 60 mg/ 2.4 mL (25 mg/mL) for four 15 mg/0.6 mL doses solutions for SC injection (Mounjaro, NDA 215866; Zepbound, NDA 217806); and (3) Liraglutide is an active ingredient in FDA-approved drug products: 18 mg/3 mL (6 mg/mL) solution for SC injection (Saxenda, NDA 206321); 18 mg/3 mL (6 mg/mL) solution for SC injection (Victoza, NDA 022341); and 18 mg/3 mL (6 mg/mL) solution for SC injection (liraglutide 18 mg/3 mL, e.g., ANDA 215503).

[3] U.S. Food and Drug Administration, "FDA's Concerns with Unapproved GLP-1 Drugs Used for Weight Loss," current as of Feb. 4, 2026, *available at*: https://www.fda.gov/drugs/drug-alerts-and-statements/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss ("Additionally, the agency has received adverse event reports that may be related to patients prescribed compounded semaglutide or tirzepatide products in doses beyond what is in the FDA-approved drug label. This could mean using more product in a single dose, taking doses more frequently or increasing the amount more quickly (titration schedule). Some of the adverse events are serious and some patients reported seeking medical attention for their symptoms, including nausea, vomiting, diarrhea, abdominal pain and constipation.").

[4] For instance, a compounded medication may be formulated at a specific concentration so that a prescribed volume drawn from the vial delivers a dose equivalent to the branded product's standard dosing.

microdose regimen requires ongoing clinical oversight, which depends on a continuous prescriber-patient relationship. Compounding pharmacies often lack this relationship, which further underscores the lack of validated, evidence-backed protocols for determining and adjusting "microdoses."

Likewise, the trend of "microdosing" is not a clinically appropriate way to manage a patient who may need a slower titration schedule. In our experience managing patients on GLP-1 therapies, implementing a slower titration is a routine clinical decision that physicians already make using approved products—it does not require a compounded formulation. For instance, it is well within a prescriber's clinical judgment to keep a patient on a lower dose and not automatically move them up to the next dose in the step-up therapy. To reiterate—there is no credible clinical evidence that microdosing of a compounded GLP-1 product confers any therapeutic benefit not already achievable with the approved drug.[5]

In the limited circumstance where a prescriber determines that a truly individualized dose is required for a specific patient, the appropriate and lower-risk approach is sterile-to-sterile compounding from an FDA-approved finished dosage form—a practice well-established in pharmacy and consistent with professional standards. Providers do not need to turn to compounding from untested bulk drug substances, which incidentally are often sourced from unvetted foreign manufacturers. The practice of sterile-to-sterile compounding preserves the quality assurances and safety profile of the approved product while accommodating any genuine clinical need of a specific patient. Genuine dosage personalization does not require a compounded version of the drug made at mass scale and without any of the safeguards that come with FDA review and approval.

Taken together, the compounded "alternative doses" rationale does not rise to a clinical need. Where the FDA-approved drugs' dosing range meets patient needs, and where sterile-to-sterile compounding can address the rare exception, there is no basis for permitting outsourcing facilities to compound semaglutide, tirzepatide, and liraglutide from bulk drug substances.

b. There is No Clinical Need for Multi-Ingredient Formulations

Compounders further contend that combination products incorporating vitamins or other additives alongside GLP-1 APIs serve an unmet patient need. From a clinical standpoint, this argument does not hold up. If a patient requires a vitamin supplement or other adjunctive therapy, the patient can simply take that vitamin supplement or other therapy separately alongside the FDA-approved GLP-1 drug.[6] There is no pharmacological or therapeutic rationale requiring co-administration. There is no synergistic

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[5] Novant Health, "Micro-Dosing' GLP-1 Drugs is a Bad Idea. Here's Why" Mar. 12, 2026, *available at*: https://www.novanthealth.org/healthy-headlines/micro-dosing-glp-1-drugs-is-a-bad-idea-heres-why ("There are no studies or data that show that micro-dosing works. It's all anecdotal: Well, it worked for so-and-so — maybe it will work for me. In contrast, brand-name GLP-1 medications underwent clinical trials involving 10,000 or more patients before obtaining FDA approval... And since approval, millions of patients have used these medications, providing years of real-world data…").

[6] Belcourt J, Sapowadia A, "White CM, Compounded Semaglutide and Tirzepatide Products Use Unique Formulations but Efficacy and Safety Largely Unknown. Annals of Pharmacotherapy, 2026;0(0)", *available at*: https://journals.sagepub.com/doi/10.1177/10600280261421979 ("[T]he addition of cyanocobalamin, niacinamide, or glycine to a compounded semaglutide or tirzepatide product in patients without laboratory-proven deficiency seems like loophole exploitation rather than one rooted in a specific patient need."); IQVIA, "The Compounded GLP-1 Market" Oct. 22, 2025, *available at*: https://tinyurl.com/mpze2srt ("Over 80% of compounded semaglutide and tirzepatide prescriptions now include supplemental ingredients such as B vitamins (B6, B12, B3) or levocarnitine… Interestingly, the prevalence of additives has increased in parallel with the end of the shortage period…").

effect. As pharmacists who perform drug utilization reviews and screen for interactions, we know that patients routinely take multiple medications and supplements without the need to combine them into a single drug product—and without incurring the risks that come with such an approach.

Indeed, combining active ingredients in a single formulation without adequate preclinical and clinical testing creates affirmative risk for patients. This is a fundamental principle to pharmaceutical science and one that every pharmacist thoroughly understands. When compounds are mixed, chemical interactions may produce degradation products, unintended byproducts, precipitates or impurities whose effects on patients have not been studied. A recent study evaluating compounded tirzepatide preparations combined with vitamin B12 confirmed this exact concern. That study revealed significant levels of an unknown and uncharacterized impurity that resulted from a chemical reaction between the two substances, raising substantial questions about the safety and unknown side effects of these untested combination products.[7]

The consequences of such untested combinations have already materialized in patient harm. A patient who took such a compounded combination product was hospitalized with acute liver failure and required an emergency organ transplant.[8] The risk is intensified by the practice of adding dietary supplements to these products. Dietary supplements are not subject to FDA's premarket review for safety, purity, or efficacy, and the quality and sourcing of supplement ingredients vary widely across the industry. Accordingly, there is no way to confirm that the vitamins or other supplement ingredients added to compounded versions of GLP-1s come from legitimate, quality-controlled sources, adding yet another layer of unverified risk.

FDA appropriately rejected this argument because no nominator identified why patients cannot receive their FDA-approved semaglutide, tirzepatide, and liraglutide and separately receive any other medications or supplements their provider deems appropriate.[9]

c. There is No Clinical Need to Compound Via Alternative Routes of Administration

The claim that compounded oral, sublingual, or buccal GLP-1 preparations serve a clinical need that FDA-approved drugs cannot meet is similarly unfounded. Subcutaneous injection, which is the primary approved route of administration for GLP-1 products, is medically suitable for patients who take these drugs. For those patients who prefer a non-injection route of administration, FDA-approved oral GLP-1 products are now available.[10]

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[7] Jordan B, et al., "A Novel, Widespread Impurity in Mass-Compounded Tirzepatide/B12 Products: Potential Patient Safety Implications" published Apr. 30, 2026, *available at*: https://www.tandfonline.com/doi/full/10.1080/14740338.2026.2663185 ("Our testing identified a widespread and previously unidentified impurity in compounded tirzepatide-B12 products resulting from a chemical reaction between tirzepatide and certain analogs of B12…There are currently no data on the impact of this impurity on the safety or efficacy of tirzepatide, and its presence raises substantial concerns about the safety and effectiveness of these compounded products.").

[8] Jimmie Wilson, "I Nearly Died from a Compounded Weight-Loss Drug. FDA Must Act," *Washington Post*, March 31, 2026, https://www.washingtonpost.com/opinions/2026/03/31/weight-loss-compounding-pharmacies/.

[9] 91 Fed. Reg. 23439 (May 1, 2026)

[10] Yale Medicine, "GLP-1 Weight-Loss Pills: What You Need to Know" Apr. 10, 2026, *available at*: https://www.yalemedicine.org/news/glp-1-weight-loss-pills-what-you-need-to-know ("In January 2025, the FDA approved an oral form of Novo Nordisk's Wegovy (semaglutide) to treat obesity. This month, it approved Foundayo (orforglipron), a daily pill made by Eli Lilly. Both medications work the same way as their injectable counterparts—

More fundamentally, there is no clinical evidence that liraglutide or tirzepatide are effective in non-injection form. Complex peptides generally exhibit low oral bioavailability, and no compounder has generated verifiable data demonstrating that orally compounded versions of liraglutide or tirzepatide have the necessary bioavailability to be effective.[11] Nor is there any evidence that any GLP-1 product is effective when administered via buccal or sublingual routes. When compounders market these products to patients seeking treatment for serious conditions such as type 2 diabetes or obesity, patients unknowingly receive ineffective formulations and forego FDA-approved treatment options in favor of unvalidated alternatives. As providers who have a duty to ensure patients receive therapies that will actually work, we view this not merely as a failure of efficacy but a direct risk to patient welfare.

Taken together, the asserted justifications for compounding semaglutide, tirzepatide, and liraglutide from bulk drug substances amount to surface-level changes that do not address genuine clinical need. A slightly different concentration that delivers the same dose and therapeutic benefit, an added ingredient with unproven benefits and unknown risks, and an unvalidated route of administration all share the same flaw: they fail to address a legitimate clinical need that cannot be met with FDA-approved treatments.

II. So-Called Personalization is a Pretext, Not a Clinical Justification

Taken together, the claimed justifications for compounding semaglutide, tirzepatide, and liraglutide from bulk drug substances described above amount to what can only be described as superficial or pretextual customization: modifications that create the appearance of individualized treatment while serving no legitimate therapeutic purpose. Whether the modification is a marginally different concentration that delivers an identical dose, an additive that introduces unknown risks without established benefits, or an untested route of administration for which no efficacy data exists, the result is the same. Patients receive products that deviate from proven treatments without any corresponding clinical advantage or even worse, with no clinical benefit at all or even with significant harm.

The only practical effect of these modifications is to provide a basis, however tenuous, for compounders to claim that their products differ from approved drugs and therefore warrant inclusion on the 503B Bulks List. In reality, these products expose patients to heightened safety risks.[12] In our experience as providers, genuine personalization in medicine is driven by documented clinical necessity for a specific patient and rigorous data supporting such use of the medicine. Legitimate compounding requires a prescriber who identifies a unique clinical need and a pharmacist who independently verifies that the compounded preparation is appropriate, safe, and necessary. That is the triad of care—patient,

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by mimicking a hormone that slows digestion, increases feelings of fullness, suppresses appetite, and helps regulate blood sugar.").

[11] 91 Fed. Reg. 23437 (May 1, 2026)("The nomination does not provide any information regarding the formulation of the compounded product, and the nomination does not explain, or even assert, that the compounded product would overcome the poor bioavailability of oral semaglutide")

[12] U.S. Food and Drug Administration, "FDA's Concerns with Unapproved GLP-1 Drugs Used for Weight Loss" updated Feb. 4, 2026, *available at*: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss. ("FDA is aware that some patients and health care professionals may look to unapproved versions of GLP-1 (glucagon-like peptide-1 (GLP-1) receptor agonists) drugs, including semaglutide and tirzepatide, as an option for weight loss. This can be risky for patients, as unapproved versions do not undergo FDA's review for safety, effectiveness and quality before they are marketed.")

prescriber, and pharmacist—that legitimate compounding is built upon. What we see in the market of GLP-1 products compounded from bulk bears no resemblance to that model.

III. FDA's Interpretation of "Clinical Need" Is Consistent with Its Statutory Authority

In the past, some parties have argued that FDA exceeds its statutory authority by making clinical need determinations, asserting that such decisions constitute the impermissible practice of medicine. This argument fundamentally mischaracterizes the distinct roles that Congress assigned to FDA and to prescribing practitioners under the statutory framework. Section 503B of the FDCA explicitly directs FDA to identify whether there is a clinical need for compounding with a nominated bulk drug substance, and it establishes the specific procedure by which FDA must do so, which includes publication of a rationale and solicitation of public comment.[13] This is a regulatory and scientific determination about which drug substances may be manufactured and made available for compounding on a large scale. It is not a determination about whether a particular patient should receive a particular treatment.

CEBM proactively affirms that FDA's exercise of this authority to determine clinical need is not only permissible but essential. The well-established division of responsibility between FDA and medical practitioners remains fully intact and the roles are clear. FDA determines which drugs may be manufactured and marketed based on scientific and safety judgments; practitioners determine which available drugs are appropriate for individual patients under their care. Congress further reinforced this division by requiring that a prescribing practitioner independently determine whether a drug compounded from bulk substances produces a clinical difference for an individual patient before prescribing it.[14] Far from encroaching on clinical practice, FDA's clinical need determination preserves the integrity of the regulatory framework and processes that providers depend on to serve our patients. Absent this framework, prescribers would be permitted to prescribe any drug product regardless of safety and efficacy.

IV. FDA's Clinical Need Determination Reinforces That Patients Should Receive FDA-Approved Drugs Absent an Identified Clinical Need for Compounded Versions

The members of the CEBM Board who are providers regularly prescribe and dispense GLP-1 products, which can provide enormous benefit to the patients we serve. We can attest, from our direct clinical experience, that there is no evidence that FDA-approved semaglutide, tirzepatide, or liraglutide products are medically unsuitable for the indicated patient population. These medications have undergone rigorous clinical testing in large, controlled trials; they have demonstrated safety and efficacy across diverse populations; and they are manufactured in compliance with Current Good Manufacturing Practice requirements with full premarket oversight by FDA. As providers, we trust and rely on those assurances every time we prescribe or dispense these drugs to our patients.

Compounded alternatives offer none of these assurances. No outsourcing facility has generated clinical trial data demonstrating that its compounded GLP-1 formulation is safe, effective, or bioequivalent as compared to the FDA-approved product. Further, no nominator has identified any attribute of the approved drugs that renders them medically unsuitable for a defined patient population.

[13] 21 U.S.C. § 353b(a)(2)(A)(i)(I)-(III).
[14] 21 U.S.C. § 353b(d)(2)(B).

The record is devoid of evidence establishing that compounded drugs from bulk drug substances address any clinical gap that cannot be met by the FDA-approved medications.

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," with a "long history of outbreaks and other serious adverse events."[15] Drug compounded in accordance with the conditions of Section 503B of the FDCA are exempt from FDA premarket review for safety and effectiveness[16] and certain labeling and supply chain security requirements.[17] Further, the outsourcing facilities in which compounded drugs are prepared are not required to undergo FDA inspection before commencing operations and, in many cases, have never been inspected.[18] These risks are magnified by documented findings of insanitary conditions, failures in sterile drug preparation, use of non-pharmaceutical-grade ingredients, and microbial contamination at compounding facilities across the country, and the scale of these quality failures is far from isolated.[19] Since 2022, over 75,000 compounded GLP-1 products have been recalled according to FDA's own data.

As pharmacists who are trained in and held accountable for compounding in compliance with compounding quality standards under United States Pharmacopeia ("USP") General Chapters <797> and <795>, we find these documented failures alarming. They reflect a fundamental departure from the professional standards that govern legitimate pharmacy compounding.

Pharmacovigilance data reinforce these concerns. Published research has found higher reporting of adverse events requiring hospitalization and of product quality issues for compounded versions of GLP-1s compared to their FDA-approved counterparts.[20] Additionally, patients have reported serious harm:

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[15] U.S. Food and Drug Administration, "Evaluation of Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act" Mar. 2019, *available at*: https://www.fda.gov/media/121315/download.

[16] *See* 21 U.S.C. § 353b(a)(2)(A)(i).

[17] *Id.*

[18] The Partnership for Safe Medicines, "What Is A 503B Outsourcing Facility, and Why Are So Many Of Them Uninspected By FDA?", *available at:* https://www.safemedicines.org/2025/07/503b-fda-inspections.html?highlight=outsourcing ("The FDA's list of registered outsourcing facilities shows that of the 48 503Bs newly registered since June 2021, 39 (81% of them) have never been inspected by FDA staff.)

[19] U.S. Food and Drug Administration, "Form 483 to Revive Rx LLC dba Revive Rx Pharmacy" issued Mar. 27, 2026, *available at*: https://www.fda.gov/media/192056/download ("Microbial contamination was present in the ISO 5 area and area adjacent to production areas."); U.S. Food and Drug Administration, "Form 483 to SCA Pharmaceuticals, LLC" issued Mar. 13, 2026, *available at*: https://www.fda.gov/media/192262/download ("Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established and followed."); U.S. Food and Drug Administration, "Form 483 to OSRX, Inc." issued Nov. 14, 2025, *available at*: https://www.fda.gov/media/190602/download ("Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not followed."); U.S. Food and Drug Administration, "Form 483 to Medi-Fare Drug" issued June 6, 2025, *available at*: https://www.fda.gov/media/188091/download?attachment ("Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written and followed.").

[20] McCall, K.L., et al. (2025). Safety analysis of compounded GLP-1 receptor agonists: a pharmacovigilance study using the FDA adverse event reporting system. *Drug Safety*. https://www.tandfonline.com/doi/full/10.1080/14740338.2025.2499670.

violent illness requiring emergency hospitalization[21], acute liver failure[22], and in at least one case, death[23]. These are not theoretical risks; they are documented consequences of allowing untested products to reach patients without adequate regulatory oversight.

The risks are further amplified by the online, direct-to-consumer prescribing model that has proliferated in this market. Patients frequently obtain compounded GLP-1 preparations through telehealth platforms that require no established provider relationship, no physical examination, no bloodwork, and no ongoing monitoring. A consumer, often without ever speaking with a prescriber, selects a product, completes a questionnaire, and is issued a prescription for a compounded drug. This model circumvents the patient-prescriber-pharmacist triad that is the bedrock of safe medication use, fundamentally undermines the clinical safeguards that should accompany the use of any prescription medication, and is incompatible with genuine patient-centered care.

The risks of compounded drugs highlight that where an approved drug is available and medically suitable for a patient, that patient should receive the approved drug—a principle that guides our daily practice as physicians and pharmacists. The regulatory system exists precisely to ensure that marketed pharmaceuticals meet the highest standards of safety, purity, and efficacy. Permitting deviation from that standard without documented clinical necessity exposes patients to avoidable harm and is inconsistent with the standards of care we are obligated to uphold.

V. Allowing Bulk Compounding of GLP-1 APIs Would Harm Patients and Undermine Public Health Goals

Beyond the immediate patient safety concerns, approving the placement of semaglutide, tirzepatide, and liraglutide on the 503B Bulks List would inflict broader harm on public health infrastructure and the innovation ecosystem that produces life-saving medicines.

a. Mass Compounding Compromises Supply Chain Integrity and Deceives Patients

The rapid proliferation of compounded GLP-1 drugs has given rise to an unregulated parallel pharmaceutical market that operates without the fundamental safeguards American consumers have come to expect.[24] This market functions without meaningful adverse event reporting, without serialized track-and-trace protections mandated by the Drug Supply Chain Security Act, and with only limited FDA

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[21] Sausser, L. & Rosenfeld, M. "Weight Loss Drugs Like GLP-1s Are Easy To Buy Online, Raising Overdose And Safety Concerns" May 28, 2026, *available at*: https://www.nbcnews.com/health/health-news/glp1-weight-loss-drugs-online-safety-risks-overdose-rcna347187.

[22] Buczek, K. "Kentucky Bill To Tighten Oversight Of Compounded Weight Loss Drugs" Feb. 25, 2026, *available at*: http://www.lex18.com/news/covering-kentucky/kentucky-bill-to-tighten-oversight-of-compounded-weight-loss-drugs.

[23] Payne, M. "Texas GLP-1 Compounder Caused Mom's Death, Family Says" Apr. 13, 2025, *available at*: https://www.law360.com/articles/2464464/texas-glp-1-compounder-caused-mom-s-death-family-says.

[24] Allen, A., "Copycat Weight-Loss Drugs Are Major Players With Consumers" Jul. 31, 2024, *available at*: https://kffhealthnews.org/health-industry/health-brief-anti-obesity-drugs-copycats-ozempic-wegovy-mounjaro/ ("As many as 1 in 8 American adults has tried one of the GLP-1 anti-obesity drugs, but a surprising number aren't getting their supplies from pharma giants Novo Nordisk or Eli Lilly. Up to 30 percent of the market, by some estimates, is made up of copycat versions from compounding pharmacies.").

inspection authority over the compounding facilities. Many compounding facilities source their APIs from foreign manufacturers that have never been inspected by the FDA.

The compounded GLP-1 market has been marked by pervasive deceptive marketing practices aimed at misleading patients about the nature and quality of the products they receive. Research demonstrates that many patients do not understand that they are being issued prescriptions for compounded drugs or appreciate that compounded drugs have not undergone FDA's premarket review for safety, effectiveness, and quality.[25] Independent watchdog organizations have warned of a "tsunami" of false and misleading information that leads consumers to incorrectly believe compounded drugs have been tested or approved by FDA.[26] As providers, we see the consequences of this deception in our patient interactions, where patients are confused about the drugs they have been taking and unaware of the risks to which they have been exposed.

In the past two years, FDA has responded by issuing numerous warning letters to entities engaged in false or misleading marketing by obscuring the compounded nature of their products or suggesting equivalence with FDA-approved drugs.[27] Multiple state attorneys general have issued public warnings, and federal prosecutors have pursued criminal indictments against those selling misbranded products.[28]

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[25] 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.")

[26] National Consumers League, "The Influence Of Disinformation On Attitudes And Beliefs About Compounded GLP-1 Drugs" May 2025, *available at*: https://nclnet.org/wp-content/uploads/2025/05/The-Influence-of-Disinformation-on-Attitudes-and-Beliefs-About-Compounded-GLP-1-Drugs-Survey-Results.pdf.

[27] U.S. Food and Drug Administration, "FDA Warns 30 Telehealth Companies Against Illegal Marketing of Compounded GLP-1s" Mar. 3, 2026, *available at*: https://www.fda.gov/news-events/press-announcements/fda-warns-30-telehealth-companies-against-illegal-marketing-compounded-glp-1s; Perrone, M. "FDA Takes Aim at Telehealth Companies for Promoting Unofficial Weight Loss Drug Dupes" Sept. 17, 2025, *available at*: https://www.pbs.org/newshour/health/fda-takes-aim-at-telehealth-companies-for-promoting-unofficial-weight-loss-drug-dupes ("The Food and Drug Administration…posted more than 100 letters to various drugmakers and online prescribing companies, including Hims & Hers, which has built a multibillion-dollar business centered around lower-cost versions of blockbuster obesity injections. The FDA warned the company to remove "false and misleading" promotional statements from its website, including language claiming that its customized products contain "the same active ingredient" as FDA-approved drugs Wegovy and Ozempic. The formulations cited by regulators are produced by specialty compounding pharmacies and aren't reviewed by the FDA.")

[28] United States Attorney's Office, Division of Utah, "Utah Licensed Osteopathic Physician Indicted for Allegedly Receiving Misbranded Drugs from China and Selling Them to Patients" Apr.1, 2026, *available at*: https://www.justice.gov/usao-ut/pr/utah-licensed-osteopathic-physician-indicted-allegedly-receiving-misbranded-drugs-china; New Mexico Department Justice, "MEDIA ALERT: The New Mexico Department of Justice Urges Community Members to Be Vigilant When Seeking Weight-Loss Medications" Oct. 31, 2025, *available at*: https://nmdoj.gov/press-release/media-alert-the-new-mexico-department-of-justice-urges-community-members-to-be-vigilant-when-seeking-weight-loss-medications/; Pennsylvania Attorney General, "As Summer Approaches, AG Sunday Warns Pennsylvanians of Dangerous Counterfeit GLP-1 Drugs with Foreign Contents" May 22, 2025, https://www.attorneygeneral.gov/taking-action/as-summer-approaches-ag-sunday-warns-pennsylvanians-of-dangerous-counterfeit-glp-1-drugs-with-foreign-contents/ ; South Carolina Attorney General, "CONSUMER ALERT: Attorney General Alan Wilson Warns Consumers To Be Cautious When Purchasing Unapproved And Compounded Weight Loss Medications" Jan. 3, 2025, *available at*: https://www.scag.gov/about-the-office/news/consumer-alert-attorney-general-alan-wilson-warns-consumers-to-be-cautious-when-purchasing-unapproved-and-compounded-weight-loss-medications/

Despite these efforts, the deception persists, in part because the scale of the market outpaces enforcement capacity. When patients cannot distinguish between rigorously tested approved drugs and unreviewed compounded alternatives, the public can no longer trust that the drugs in the marketplace are safe and effective.

State-specific and reactive enforcement alone cannot solve this problem. Patients cannot trust what they are buying. Excluding semaglutide, tirzepatide, and liraglutide from the 503B Bulks List would help prevent the further mass production of these drugs that sustains deceptive practices.

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

The 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 Section 503B was conceived as a carefully circumscribed accommodation within this system—available only when no FDA-approved 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 compete directly with FDA-approved drugs. Including semaglutide, tirzepatide, and liraglutide on the 503B Bulk Drug Substances List would set a destabilizing precedent and open an alternative, loosely regulated avenue that sidesteps the demanding requirements of federal regulations that were constructed to balance innovation incentives with public access.

Moreover, the United States' global leadership in biopharmaceutical innovation depends on a regulatory framework that rewards the enormous investment required to develop new treatments. Developing a new drug requires, on average, more than a decade of research and billions of dollars in investment, and the vast majority of development programs fail. Innovators undertake this risk because the regulatory system provides a meaningful period of market exclusivity during which they can recoup their investment and fund further research.

If the 503B Bulks List becomes a vehicle for replicating any commercially successful medicine through industrial-scale compounding, without the compounder bearing any of the costs of research, clinical testing, or regulatory approval, it sends an unmistakable signal to innovators (and the investors who back them). FDA itself has recognized this dynamic, noting that drug sponsors "would be less likely to invest in, and seek approval of, innovative, life-saving medications if an outsourcing facility could, after a drug is approved, compound 'substitutes' that may be less expensive because they have not gone through the drug approval process."[29] Dozens of next-generation incretin and metabolic therapies are currently in development. The patients we serve depend not only on the GLP-1 and other therapies

[29] U.S. Food and Drug Administration, "Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act" Jan. 2018, *available at*: https://www.fda.gov/media/98964/download ("In addition to these immediate public health risks, section 503B's prohibition on producing a drug product that is essentially a copy of an approved drug product protects the integrity and effectiveness of the new drug and abbreviated new drug approval processes. Sponsors would be less likely to invest in, and seek approval of, innovative, life-saving medications if an outsourcing facility could, after a drug is approved, compound "substitutes" that may be less expensive because they have not gone through the drug approval process.)

available today, but on tomorrow's therapies as well. Undermining the innovation incentive at this critical moment risks deterring investment in the very therapeutic advances that patients need most.

VI. Conclusion

For the foregoing reasons, CEBM strongly supports FDA's proposed determination that there is no clinical need for outsourcing facilities to compound semaglutide, tirzepatide, or liraglutide from bulk drug substances. As physicians and pharmacists, we have devoted our careers to ensuring that patients receive treatments that are safe, effective, and backed by evidence. FDA's analysis is faithful to the statutory framework, supported by the evidence, and essential to protecting the patients we serve.

We urge FDA to finalize its proposal. CEBM stands ready to support FDA in this critical determination and to assist FDA in any way that advances the shared goal of ensuring all patients receive safe, effective, and rigorously evaluated medicines.

Respectfully submitted,

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