

June 29, 2026

Dockets Management Staff (HFA-305)  
U.S. Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**Re: The diaTribe Foundation Comments to Docket No. FDA-2018-N-3240; List of Bulk Drug Substances for Which There is a Clinical Need Under Section 503B of the Food, Drug, and Cosmetic Act**

To Whom It May Concern:

The diaTribe Foundation (diaTribe) appreciates the opportunity to comment on the Food and Drug Administration's proposed determination 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.

diaTribe is a nonprofit organization dedicated to helping people with diabetes live healthier, more hopeful, and more informed lives. We provide education, advocacy, and patient-centered resources for people with diabetes and those who care for them. Our perspective reflects the need for treatments that are safe, effective, affordable, and accessible.

diaTribe speaks for the people who ultimately bear the consequences of both unsafe products and unaffordable ones. For the reasons described below, diaTribe supports the Food and Drug Administration's (FDA) proposed determination on the present evidentiary record. We offer this as a patient-safety judgment, and we pair it with an equally important message: closing this compounding pathway must be matched by real action on the affordability and coverage failures that drove many patients to compounded GLP-1 products in the first place. Both halves of that position are essential to how we serve patients.

**Disclosure and Independence**

diaTribe receives charitable funding from a range of organizations, including Eli Lilly and Company and Novo Nordisk, which manufacture FDA-approved products affected by this proceeding.

Neither company requested, drafted, reviewed, approved, or directed this comment. diaTribe developed its position independently through its own leadership and Board governance process, based on its patient-centered mission and its review of FDA's proposed determination.

**FDA's Clinical-Need Analysis**

Section 503B does not ask whether compounded products may be less expensive, more convenient, or preferred by some patients. FDA's framework asks whether there is a clinical

*List of Bulk Drug Substances for Which There is a Clinical Need Under Section 503B of the Food, Drug, and Cosmetic Act*

need for outsourcing facilities to compound a drug product and whether that product must be compounded using the bulk drug substance.

For substances that are components of FDA-approved products, FDA first considers whether:

1. An attribute of the approved product makes it medically unsuitable for certain patients; and
2. The proposed compounded product is intended to address that attribute.

Based on the record described in the notice, diaTribe agrees that the nominations have not made this threshold showing. Assertions concerning individualized titration, alternative strengths, different dosage forms or delivery presentations, excipient sensitivities, and combination formulations were not supported with sufficient evidence identifying the relevant patients, demonstrating that an approved product is medically unsuitable for them, and showing that a defined compounded product would address that medical unsuitability.

Because this threshold showing was not made, the present record does not establish a clinical need for outsourcing facilities to compound these products from bulk drug substances.

### **Semaglutide**

The semaglutide nominations proposed numerous strengths, routes of administration, alternative formulations, and combination products. FDA found insufficient evidence supporting claims that “hyper-responders” require compounded lower doses, that approved products are medically unsuitable because of their available strengths or delivery systems, or that proposed sublingual, buccal, oral, or combination products would address a demonstrated medical need.

The nominations also did not adequately identify the proposed compounded products, the patients for whom approved products are medically unsuitable, or sufficient clinical evidence supporting the proposed alternatives. diaTribe therefore agrees that the present record does not demonstrate the required clinical need for outsourcing facilities to compound semaglutide from bulk substance.

### **Tirzepatide**

The tirzepatide nominations similarly relied on assertions involving alternative strengths, individualized dosing, excipients, delivery devices, and combination products. FDA found insufficient evidence that an attribute of the approved tirzepatide products makes them medically unsuitable for an identifiable patient population. FDA also noted that approved tirzepatide is available in vials as well as autoinjectors, weakening the assertion that bulk compounding is necessary to address limitations associated with a fixed-dose device.

On the current record, diaTribe agrees that the proposed compounded products have not been shown to address a demonstrated medical unsuitability of the approved products.

### **Liraglutide**

For liraglutide, the principal nominated concentration was the same as the concentration of approved products, and the proposed doses corresponded to doses already included in approved labeling. The nomination also asserted that formulations without propylene glycol could benefit

*List of Bulk Drug Substances for Which There is a Clinical Need Under Section 503B of the Food, Drug, and Cosmetic Act*

patients experiencing sensitivity or injection-site irritation. FDA found that the submitted evidence did not demonstrate that propylene glycol makes approved liraglutide products medically unsuitable for an identifiable patient population or that a compounded formulation without it would mitigate injection-site reactions.

diaTribe therefore agrees that the present record does not establish a clinical need for outsourcing facilities to compound liraglutide from bulk substance, while recognizing that any future change in liraglutide's shortage status would be governed by the statute's separate shortage provisions.

**Patient-Safety Considerations**

Compounded drugs can serve an important role when a patient's clinical needs cannot be met by an available FDA-approved product. However, compounded drugs are not FDA-approved, and FDA does not review their safety, effectiveness, or quality before they are marketed. FDA has identified concerns involving compounded GLP-1 products, including:

- Errors in measuring and administering doses;
- Variation in product concentrations and dosing instructions;
- Use of multidose vials by patients unfamiliar with drawing medication into syringes;
- Prescribing and administration of doses beyond those described in approved labeling;
- Use of semaglutide sodium or semaglutide acetate, which are different active ingredients from the semaglutide used in approved products;
- Fraudulent or misrepresented products; and
- Marketing that improperly suggests compounded products are generic versions of, or equivalent to, FDA-approved products.

As of May 31, 2026, FDA reported receiving 990 adverse-event reports associated with compounded semaglutide and more than 730 associated with compounded tirzepatide.

These reports do not establish that the compounded products caused the reported events. They also lack a reliable exposure denominator and cannot establish comparative incidence relative to approved products. At the same time, state-licensed pharmacies that are not outsourcing facilities generally are not required to report adverse events to FDA, making underreporting possible. The reports therefore should not be treated as definitive comparative-safety evidence. Nevertheless, the reported dosing errors, product variability, salt-form concerns, and fraudulent products identify preventable risks that support continued FDA oversight and clear patient communication.

**The Continuing Role of Lawful Compounding**

diaTribe recognizes the important role of responsible compounding when an individual patient has a documented medical need that cannot be met by an available FDA-approved product. FDA's proposed determination concerns the use of semaglutide, tirzepatide, and liraglutide as bulk substances by outsourcing facilities under section 503B. It should not be described as eliminating every form of GLP-1 compounding.

Section 503B separately permits qualifying bulk compounding while an approved drug appears on FDA's shortage list. Patient-specific compounding may also remain permissible under section

*List of Bulk Drug Substances for Which There is a Clinical Need Under Section 503B of the Food, Drug, and Cosmetic Act*

503A when all applicable statutory requirements are satisfied. These limited pathways are materially different from routine, large-scale production of unapproved copies without a demonstrated clinical need.

**Actions within FDA’s Authority**

diaTribe urges FDA to accompany its final determination with continued patient-protection measures, including:

1. Clear, plain-language communications explaining the differences among FDA-approved drugs, compounded drugs, and FDA-approved generic drugs.
2. Continued monitoring and timely public reporting of adverse events, dosing errors, fraudulent products, and quality concerns involving compounded GLP-1 products.
3. Improved identification of the compounder, formulation, concentration, salt form, and delivery presentation in adverse-event data whenever that information is available.
4. Continued enforcement against claims that misleadingly describe compounded products as generic, equivalent to, or the same as FDA-approved products.
5. Clear guidance for clinicians, patients, pharmacies, and outsourcing facilities concerning the circumstances in which compounding may remain lawful under sections 503A and 503B.
6. Continued monitoring of drug supply and prompt, transparent communication if future shortages trigger the statute’s separate shortage provisions.

**Broader Access Considerations**

The demand for compounded GLP-1 products cannot be understood without acknowledging the access failures that brought many patients to them. Patients have sought compounded products because approved medications were unavailable, unaffordable, or excluded from insurance coverage. Those barriers are real, even though cost and generalized access concerns do not establish “clinical need” under FDA’s framework for the 503B bulks list.

Supporting FDA’s proposed determination is therefore not a substitute for solving the access crisis. diaTribe urges manufacturers to improve affordability, supply reliability, patient-assistance programs, and support for patients navigating coverage denials. We urge payers to adopt clinically grounded, transparent coverage policies that do not impose unnecessary administrative barriers. We also urge policymakers to pursue broader reforms that make evidence-based diabetes and obesity treatments accessible to the patients who need them.

Patients should not have to choose between an FDA-approved medication they cannot afford and an unapproved product carrying additional uncertainty.

**Conclusion**

Behind every adverse-event report and every coverage denial is a person trying to manage a serious chronic disease. diaTribe believes two principles must be held together: patients should be protected from avoidable risks associated with unapproved products, and patients should not be priced out of FDA-approved treatments that could meaningfully improve their health.

*List of Bulk Drug Substances for Which There is a Clinical Need Under Section 503B of the Food, Drug, and Cosmetic Act*

For these reasons, diaTribe respectfully requests that FDA finalize its proposed determination that semaglutide, tirzepatide, and liraglutide should not be included on the 503B Bulks List on the present evidentiary record. This determination should not disturb compounding otherwise permitted under the Federal Food, Drug, and Cosmetic Act, including applicable shortage provisions and lawful patient-specific compounding under section 503A.

Thank you for the opportunity to comment.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "J. Carroll". The signature is fluid and cursive, with a large loop at the beginning and a long tail.

Jim Carroll  
Chief Executive Officer  
The diaTribe Foundation