

100 Daingerfield Road, Suite 100
Alexandria, VA 22314

www.a4pc.org



Statement on rules governing compounding, what FDA guidance says about permissibility of compounding “essentially a copy” of an FDA-approved drug – and what those have to do with semaglutide

REVISED October 11, 2023

News Media: Statements in this brief may be attributed to the Alliance for Pharmacy Compounding's chief executive officer, Scott Brunner, CAE, but we ask that reporters advise us in advance of your intention to quote from this document. Reach Scott at scott@a4pc.org.

***REVISED October 11, 2023:** This document has been revised to add further information about the lawsuits filed by Novo Nordisk and Eli Lilly against pharmacies compounding semaglutide or tezirpatide,.

*** REVISED July 25, 2023:** This document has been revised to remove a speculative statement about Novo Nordisk's ability to manufacture semaglutide base; to add reference to FDA's May 31, 2023 statement on compounding semaglutide sodium; and to add a brief discussion of lawsuits Novo Nordisk has recently filed against wellness spas and compounding pharmacies.

*** REVISED May 22, 2023:** This document has been revised at the request of the APC Board of Directors. The previous version, released May 15, included our understanding of arguments made by some compounders for the suitability of semaglutide sodium for compounding. While the board finds those arguments worthy of discussion, we do not endorse them, and the board believes they are best enunciated by those making the arguments and not by APC.

Why Compounding?

Pharmacy compounding plays an essential role in the American healthcare system. In traditional compounding, pharmacists create a customized medication, most often from pure ingredients, for an individual patient pursuant to a prescription. Pharmacists' ability to compound medications is authorized in federal law for good reason: While manufactured drugs are the standard, those don't come in strengths and dosage forms that are right for everyone, and healthcare practitioners need to be able to prescribe customized medications when, in their judgment, a manufactured drug is not the best course of therapy for a human or animal patient.

Compounded drugs are not “knock-offs,” as they have been referred to in some recent media stories. Rather, they are legitimate therapies created from pure bulk ingredients by pharmacies that adhere to the rigorous compounding standards of the US Pharmacopeia, are licensed by state boards of pharmacy, and are inspected by those state boards as well as FDA.

Note that when a compounded medication is dispensed, it's because a prescriber – doctor, physicians' assistant, nurse practitioner, or veterinarian – wrote the prescription for that *compounded* medication. The compounded drug is not a substitution for an FDA-approved drug; rather, the prescriber has

intentionally prescribed a *compounded* drug in a specific dosage strength or form or combination of medications that they believe is right for their patient.

Rough estimates are that compounded medications account for 1% to 3% percent of all prescriptions written in the U.S. There's a good chance you know someone who has benefited – or whose pet has benefited – from a compounded drug.

What Can Be Compounded

Federal law includes criteria for what active pharmaceutical ingredients may be used in compounded human-health medications. In order to be eligible for compounding, an active pharmaceutical ingredient must:

1. Be a component of an FDA-approved drug product; or
2. Have an applicable USP or National Formulary monograph; or
3. Appear on the 503A Bulks List published by the FDA.

In addition, federal law generally prohibits the compounding of a medication that is “essentially a copy” of an FDA-approved drug, but provides for a few important exceptions, including drug shortages. Under FDA guidance, the agency does not consider a compounded version of an FDA-approved drug “essentially a copy” of a commercially available drug when the FDA-approved drug is listed as “currently in shortage” on [the FDA drug shortage webpage](#). This exception is essential for continuation of patient care when a drug is in shortage – as, amid continuing post-COVID supply chain issues, many are from time to time.

Semaglutide

In recent months, with Wegovy and Ozempic listed as “currently in shortage,” the compounding of medications containing semaglutide (the active pharmaceutical ingredient in those drugs) has been a topic of discussion in the media and a focus of state boards of pharmacy (which regulate traditional compounding pharmacies). Unfortunately, many media accounts and some licensee communications issued by state boards have contained misstatements and errors. Responses below are intended to provide accurate information on the issue.

FDA-approved drugs containing Semaglutide remain “currently in shortage” (and yes, FDA’s website is confusing)

Contrary to recent communications issued by some boards of pharmacy, FDA-approved semaglutide drugs have been listed as “currently in shortage” on the [FDA drug shortage list](#) continuously since March 2022. FDA confirmed this in [a letter](#) to the National Association of Boards of Pharmacy. “Currently in shortage” does not necessarily mean that a drug is completely unavailable, only that there may not be sufficient supply to meet demand. [FDA’s formula for determining if a drug is in shortage](#) is the supply of the drug available divided by the demand.

Remember, [FDA guidance](#) states that if a drug is listed as “currently in shortage”— that’s the exact language — it may be compounded. While the FDA website is indeed confusing in that it references *availability* of certain drugs, availability is not mentioned in the FDA guidance document addressing the compounding of copies of FDA-approved drugs in shortage. “Currently in shortage” is the determinative language. To assure compliance, we advise our members who are compounding medications containing semaglutide to refer to the FDA drug shortage list daily; a substance’s status on the list can change without notice.

What about that patent?

We understand that Novo Nordisk, the manufacturer of Wegovy and Ozempic, asserts that its patent on its finished product containing semaglutide prohibits the compounding of medications containing the same active pharmaceutical ingredient – and we’re aware that the company has sent cease-and-desist letters to some compounding pharmacies. However, FDA guidance on the compounding of copies of FDA-approved drugs when they are in shortage makes no distinction for a patented drug. Rather, the guidance indicates that if an FDA-approved drug is listed as “currently in shortage” on the FDA shortage list – again, as FDA-approved semaglutide drugs currently are – FDA will not view compounded versions of it as “essentially a copy” of the FDA-approved drug. Some argue that if Congress or FDA had intended there to be an exception for patented drug, the guidance would have stated that. While we aren’t qualified to offer a legal opinion on the matter, we do note that such an exception for patented drugs would contradict the very reason the law allows compounding of FDA-approved drugs in shortage in the first place – to assure patients can continue to access needed and often essential medications, even when the manufacturer cannot maintain its supply chain. Nevertheless, APC advises compounders to seek the advice of legal counsel related to the patent issue and compounding semaglutide medications.

How are compounders sourcing semaglutide base API if Novo holds a patent on it?

Assertions in news stories that the only legitimate semaglutide API must be obtained directly from Novo Nordisk are flatly incorrect. Compounders of semaglutide base – the active ingredient in Novo’s Wegovy and Ozempic – are purchasing it from registered wholesalers who are documenting that the API comes from FDA-registered manufacturers. While Novo surely may exercise control over the supply of the API via its contracts with manufacturers, it has not (yet) completely locked down the supply chain on the API – not based on reports we’ve heard from some compounding pharmacies that say they are able to access semaglutide base from FDA-registered facilities.

What about Novo’s lawsuits against wellness spas and compounding pharmacies?

Recently, Novo filed lawsuits against five wellness spas, accusing them of marketing compounded semaglutide medications as compounded or “generic” Wegovy or Ozempic. Wegovy or Ozempic are trademarks, of course, and it is never legal to refer to a compounded drug by a brand name. Compounded drugs are referred to by the name of the active pharmaceutical ingredient. Nor is it accurate to refer to compounded drugs as “generic.” If indeed the spas were doing those things, it’s a pretty clear violation of federal law.

Novo’s suits against four compounding pharmacies – three in Florida and one in Nashville – are more perplexing. In those suits, the word “compounding” is notably absent from the legal briefs submitted to the courts. Instead, Novo appears to challenging the ability of compounding pharmacists to prepare drugs that are not FDA-approved, alleging that the pharmacies are not only creating “unauthorized new drugs” but are engaging in unfair competition and deceptive practices that Novo says jeopardize public health. It’s quite an accusation. Compounding is authorized in federal law and in all 50 states – as is compounding “essentially a copy” of an FDA-approved drug when that drug appears as “currently in shortage” on FDA’s drug shortage list.

To suggest that compounding pharmacies are creating unauthorized drugs and therefore should be proscribed from doing so has implications well beyond semaglutide. If the state courts grant an injunction or otherwise rule in Novo’s favor in the cases against compounding pharmacies, every single

drug on the market that has never been approved by the FDA (and there are scores of them) may be subject to a ban for Floridians and Tennesseans – and not just all compounded medications.

On October 5, U.S. District Court Judge William Jung dismissed the suit against one of the four pharmacies, Brooksville Pharmacy in Florida. A Novo Nordisk spokesperson has made a statement that the manufacturer plans to file an amended lawsuit in response.

In addition, manufacturer Eli Lilly has filed suit against 10 medical spas, wellness centers, and compounding pharmacies selling or dispensing tezirpatide, the active ingredient in Mounjaro. These lawsuits include four separate suits against compounding pharmacies in Florida and Texas claiming violation of federal and state consumer protection and competition laws.

APC is submitting an amicus brief in the remaining cases. Each judge may decide whether to accept the amicus.

How can patients know that what they are getting from compounding pharmacies is in fact semaglutide? On the one hand, that's an odd question. Virtually no one walks into their local pharmacy to pick up their Lisinopril, uncaps the vial, and demands that the pharmacist document that those little pink pills are in fact what the label says they are. They almost certainly don't ask for documentation of where the pharmacy sourced it (even though, for the record, traditional retail and compounding pharmacies can answer those questions and show documentation pretty easily).

On the other hand, we do understand concerns about semaglutide in particular simply because of all the media reporting on black market sales of purported "research grade" varieties of the substance (if it's actually semaglutide at all) direct to consumers by sketchy online entities that are not pharmacies at all – but which many media stories continue to conflate with pharmacy compounding.

Under federal law, compounding pharmacies must purchase API manufactured by facilities that are FDA-registered. That API comes with a certificate of analysis documenting that the substance is what it says it is, as well as the exact potency and purity of the drug. While that COA is a rather dense read, patients and prescribers who want some greater assurance that the drug they're being dispensed is what the pharmacy says it is can ask to see the COA.

What about those sketchy websites dispensing what they say is semaglutide directly to consumers? Those aren't pharmacies at all and shouldn't be conflated with compounding pharmacies. If your doctor didn't write you a prescription for compounded semaglutide and send it to a legitimate, identifiable pharmacy, beware the seller of that substance.

So what about compounding using semaglutide sodium?

We are aware that some compounding pharmacies may be dispensing the compounded semaglutide medication they have prepared using semaglutide sodium. At first glance, semaglutide sodium itself does not appear to meet the criteria for compounding: It's not listed as the API in the product labeling of the two FDA-approved drug products, does not have a USP monograph, and does not appear on the 503A Bulks List published by FDA. Until more is known about whether or not semaglutide sodium is an API used in either of the FDA-approved drug products, it is APC's current position that compounding with semaglutide sodium technically is not eligible to be used in a compounded medication.

- Germane to this matter, following is an excerpt from FDA Guidance for Industry titled "[Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act](#):"

When a compounded drug product offers the same API as a commercially available drug product, in the same, similar, or easily substitutable dosage strength and for use through the same route of administration, we generally intend to consider such a drug product essentially a copy, unless a prescriber determines that there is a change, made for an identified individual patient, that will produce a significant difference for that patient.

As we have noted, compounding "essentially a copy" of an FDA-approved drug is permitted when that drug is listed as currently in shortage. The question is whether semaglutide compounded using semaglutide sodium "offers the same API as a commercially available drug product."

- In FDA's [April 27 letter to the National Association of Boards of Pharmacy](#), FDA's Office of Compounding Quality and Compliance Director Gail Bormel states that the agency is "not aware of any basis for compounding a drug using these semaglutide salts that would meet federal law requirements." The agency reiterated this in [a public statement on May 31](#). That is interesting syntax in that it does not unequivocally state that compounding with semaglutide sodium is not allowed, but only that the agency is unaware of a basis for doing it.

Tips for Consumers

- Don't buy any substance purported to be semaglutide from an online entity:
 - If you do not have a legitimate prescription for it from a licensed prescriber; *and*
 - You cannot verify that the seller is a licensed U.S. pharmacy.
- If you are prescribed compounded semaglutide by a doctor or other healthcare professional and are not choosing the dispensing compounding pharmacy yourself, ask about it:
 - Name of the compounding pharmacy
 - Where it's located
 - Is it licensed to dispense in or ship to your state?
- If you want greater assurance that what you are being dispensed is in fact what the label says it is, you can ask the pharmacist to show you the Certificate of Analysis and any results from an analytical testing lab. These are complicated, scientific reports, but can confirm the identity of the drug that has been dispensed to you.

The Alliance for Pharmacy Compounding is the voice for pharmacy compounding, representing more than 600 compounding small businesses – including compounding pharmacists and technicians in both 503A and 503B settings – as well as prescribers, educators, researchers, and suppliers.

In traditional compounding, pharmacists create a customized medication, most often from pure ingredients, for an individual patient pursuant to a prescription. Pharmacists' ability to compound medications from pure ingredients is authorized in federal law and for good reason: Manufactured drugs don't come in strengths and dosage forms that are right for everyone, and prescribers need to be able to

prescribe customized medications when, in their judgment, a manufactured drug is not the best course of therapy for a human or animal patient.

Every day, APC members play a critical role in patients' lives, preparing essential, custom medications for a range of health conditions, including autism, oncology, dermatology, ophthalmology, pediatrics, women's health, animal health, and others.