

## 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 GLP-1s

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**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](mailto:scott@a4pc.org).

\*REVISED March 11, 2024: This document has been revised to provide additional information on the difference between legitimate compounded drugs and illegal online sales of illicit substances, to provide context related to adverse events attributed to compounded GLP-1s, and to elaborate further on lawsuits filed by drug manufacturers against compounding pharmacies, as well as recent “open letters” from Novo and Lilly that appear to conflate legitimate compounding with illegal substances in which the drug manufacturers allege they have found impurities.

\*REVISED December 8, 2023: This document has been revised to update information about lawsuits filed by Novo Nordisk and Eli Lilly against pharmacies compounding semaglutide or tirzepatide, and to address concerns reported in the news media by non-prescribers of semaglutide about lack of clinical trials related to compounded medications and reports of dosing errors related to compounded semaglutide.

\*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 tirzepatide.

\*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 “knockoffs,” “dupes,” or “counterfeits” 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, and sometimes by FDA as well.

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% 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. 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.

### **GLP-1s: Semaglutide and Tirzepatide**

In recent months, with Wegovy, Ozempic, and Mounjaro listed as “currently in shortage,” the compounding of medications containing semaglutide (the active pharmaceutical ingredient in Wegovy and Ozempic) or tirzepatide (the active pharmaceutical ingredient in Mounjaro) has been a focal point in the media and for 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, as well as to provide perspective on legal action brought against certain compounding pharmacies by drug manufacturers.

*FDA-approved drugs containing semaglutide and tirzepatide remain “currently in shortage” (and yes, FDA’s website [is confusing](#))*

Contrary to communications issued in summer 2023 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 in mid-2023. FDA-approved tirzepatide drugs have been listed as “currently in shortage” on the FDA drug shortage list since December 2022. “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 what are essentially copies of FDA-approved drugs in shortage. “Currently in shortage” is the determinative language. To assure compliance, we advise our members who receive prescriptions for compounded medications that are essentially copies of FDA-approved drugs 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, and Eli Lilly, manufacturer of Mounjaro, assert that their patents on their FDA-approved drugs prohibits the compounding of medications containing the same active pharmaceutical ingredient – and we’re aware that the companies have filed lawsuits against 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 – as FDA-approved semaglutide and tirzepatide drugs currently are – FDA will not view a compounded version of them 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 the issue has not yet been adjudicated by a court, 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 compounding pharmacies to seek the advice of legal counsel related to the patent issue and compounding GLP-1 medications.

*How are compounders sourcing semaglutide and tirzepatide active pharmaceutical ingredient (API) if Novo and Lilly hold patents on the API?*

Assertions in news stories that the only legitimate semaglutide API must be obtained directly from the manufacturers are flatly incorrect. For instance, compounders of semaglutide base – the active ingredient in Novo’s Wegovy and Ozempic – are purchasing it from registered wholesalers who are documenting for the pharmacies 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 locked down the supply chain on the API – and so compounding pharmacies still are able to access semaglutide base from FDA-registered facilities.

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

In summer 2023, Novo filed lawsuits against five wellness spas, accusing them of marketing compounded semaglutide medications as compounded or “generic” Wegovy or Ozempic. Lilly followed shortly with similar lawsuits making the same charges regarding marketing of compounded tirzepatide medications.

Wegovy, Ozempic, and Mounjaro 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. Compounded drugs are not the same as generics, and it is not accurate to refer to them as such. Doing so is a pretty clear violation of federal law. In February 2024, a med spa and a weight loss clinic settled with Novo. As part of the settlement, permanent injunction orders required the two companies to stop using Novo trademarks and to disclose for 12 months that compounded semaglutide has not gone through the safety and efficacy standards required by the FDA for approved drugs.

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 be 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 were to grant an injunction or otherwise rule in Novo's favor in the cases against compounding pharmacies as initially filed, 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 seemed to recognize the absurdity of Novo's initial claims and dismissed the suit against one of the four pharmacies, Brooksville Pharmacy in Florida. The judge left open the option for Novo to file an amended lawsuit in response, which Novo has now done.

In late November 2023, Novo filed a revised claim against Brooksville and also filed suit against Ocala-based Wells Pharmacy. In its revised complaint against Brooksville, Novo alleges that semaglutide obtained from Brooksville contained “impurities” and that the drugs obtained from Brooksville “were also less potent than advertised, with one sample shown to be at least 19 percent weaker than indicated,” according to Reuters. The new lawsuit against Wells alleged that the semaglutide prepared by Wells also contained “impurities,” which it identified as BPC-157, a peptide.

Brooksville has disputed Novo's assertions, [according to a Reuters piece](#), and seems to have potency testing data to back up their push-back. Nevertheless, the judge in the case is allowing that case to proceed to trial, but he has stated on the record that he will hold Novo accountable for its arguments that the compounded medications put patients at risk.

Novo's other assertion, that a compounding pharmacy was combining BPC-157 with semaglutide, is more complex. How the court responds to this case bears watching.

Though Novo garnered lots of media coverage of its claims, it is perplexing that we've seen no evidence of media outlets questioning Novo about its supposed findings of impurities and potency problems. Has anyone asked the drugmaker to show its work or prove what it is asserting about the compounded semaglutide prepared by the two pharmacies? How does a corporation get its hands on a particular drug prescribed and dispensed to an individual patient? Was it legally acquired? How old was the drug at the time Novo allegedly tested it? Was it stored properly in the time between being dispensed by the compounding pharmacy and testing? Many reporters seem to be taking it on faith that all is as Novo says it is instead of asking to see the data, when and how were the samples obtained, etc. It could be exactly as Novo says, but how do we know?

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

APC submitted an amicus brief in the four original Novo cases against compounding pharmacies to clarify for the court the proper legal – and frankly, essential – role shortage drug compounding plays in assuring continuation of patient care in the U.S. healthcare system. We are also presenting amicus briefs to judges in the cases brought by Eli Lilly against compounding pharmacies. Each judge may decide whether to accept the amicus.

At the heart of these legal cases is the issue of federal preemption. The drug manufacturers' briefs fail to mention compounding or the U.S. Food Drug & Cosmetic Act or the FDA at all. Reading them, one might think there's no federal government, much less federal laws and regulations not only authorizing pharmacy compounding but also regulating the substances that can be used in compounded medications. Instead, the manufacturers are making claims under state laws, as if federal laws – long thought to preempt state law when the two conflict – don't apply.

In early March 2024, both Novo and Lilly both published open letters again alleging impurities in substances they had acquired that they say purport to be semaglutide or tirzepatide. In those letters, both drugmakers seem to conflate illicit substances obtained without a prescription with legitimate compounded drugs obtained from a state-licensed pharmacy in a way that makes it unclear whether the impure substances in question are compounded medications at all. Unfortunately, many reporters are falling for it. Instead of questioning the drugmakers, they are simply publishing the drugmakers' claims as if they are fact.

*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 readily).

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 entities, often online, that are not pharmacies at all – but which many media stories nevertheless 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. In addition, patients and prescribers may ask the compounding pharmacy whether their compounded GLP-1s have undergone third-party testing for potency and sterility.

*What about those sketchy websites dispensing what they say is a GLP-1 drug directly to consumers?* Those aren't pharmacies at all and shouldn't be conflated with compounding pharmacies. Legitimate compounded drugs are prescribed by a physician or other prescriber for a specific patient. They are prepared and dispensed by state-licensed compounding pharmacies using documented pure active pharmaceutical ingredients that come from FDA-registered facilities. Compounding pharmacies are authorized by federal law and follow FDA Guidance for Industry in preparing copies of FDA-approved drugs when that drug is listed as "currently in shortage" on FDA's Drug Shortage list – as semaglutide and tirzepatide currently are. FDA guidance is plainly worded on this subject.

The selling of substances – counterfeit, research-grade, or otherwise – purporting to be FDA-approved drugs direct-to-consumer without a prescription is illegal. It's important to note that those aren't compounded substances at all. It's not even pharmacy, and we strongly support FDA's efforts to end the sale of illicit substances, which put consumers at risk.

If your doctor didn't write you a prescription for a compounded GLP-1 and send it to a legitimate, identifiable pharmacy, beware the seller of that substance – and the substance itself. At the end of this statement, there is a section titled "Tips for Consumers" that can help guide you in ensuring you receive your compounded GLP-1 from a legitimate compounding pharmacy.

*Some prescribers have been quoted in news reports citing a lack of clinical trial data as a reason they won't prescribe compounded GLP-1 drugs. Is that a concern?*

There *are* clinical trials involving compounded medications ([many related to compounded hormone therapy](#), for example). Compounded preparations encompass many different formulations for even one drug – different dosage strengths and dosage forms – based on what a prescriber has judged that a particular patient needs. It's inconceivable that research clinical trials could be funded, much less performed, for all those different formulations. (If Big Pharma perceived that it could make money from producing different FDA-approved smaller-volume dosage forms and strengths of drugs, they surely would have already pursued clinical trials. But they don't, so they haven't, and that's why there aren't more FDA-approved varieties and strength of many drugs – and why physicians rely on compounded drugs when there's no FDA-approved drug that's right for their patient.)

That notwithstanding, when it comes to semaglutide, the effects of the drug are known. The prescriber authorizing the prescription and the pharmacist preparing the medication are not creating something that has never been seen before when it comes to the drug itself. While the data from the manufacturer's clinical trial is technically only applicable to that manufactured product, that clinical trial data can give a pharmacist or a prescriber some reasonable level of confidence to support the use of the API in a compounded preparation.

Remember, too, that when you are dealing with a drug shortage, there is usually not sufficient time to pause patient care activities and shift medication supplies to design a clinical trial and receive Institutional Review Board (IRB) approval, execute the trial with a critical number of patients, conduct statistical analysis, draft the manuscript, and submit to a peer reviewed journal for publication. Even if funding were available for all of those activities, the multi-year timeline to conduct those steps would clearly inhibit patient access to the drug which is already in shortage.

The main reason federal law and FDA allow the compounding of FDA-approved drugs when they are in shortage is to assure continuation of patient care. And because the active pharmaceutical ingredient in a compounded drug must meet criteria in federal law, prescribers can utilize the information that is known about the drug itself as they consider what is appropriate for patient care.

*Some physicians have expressed concern that compounding creates risk of administration and dosing errors. This [case report](#) by the Utah Poison Control Center described three patients who experienced prolonged abdominal symptoms after taking incorrect doses of semaglutide from compounding pharmacies.*

Dosing and administration errors are a concern with *all* medications, hard stop. Pharmacists are required to offer patient counseling, but unfortunately sometimes patients or caregivers elect to forego patient counseling. While the reported incidences cited in that link report above are unfortunate, there are several factors about that report to consider:

- At this time we do not know if patient counseling was offered and refused. Only that the report states that it did not occur.
- From the report: “These 3 semaglutide cases highlight the potential for patient harm given current practices. Vials of compounded semaglutide do not use safety features provided by prefilled manufactured pens and allow for large overdoses (e.g., 10-fold dosing errors).” Many medications do not come in prefilled pens and yet patients manage to use them correctly – certain insulins, for example. This is simply not a valid criticism.
- From the report: “Use of syringes not intended for semaglutide contributes to the variability of dosing units (milliliters, units, milligrams), contributing to patient confusion.” Comment: Syringes are rarely intended for a specific drug and general syringes are used to administer most medications.

Patient counseling on the appropriate use of medications, along with a drug utilization review, are standards of care so the pharmacist and patient both understand why the patient is using a particular medication and the patient understands how to use it and the potential risks and benefits involved. This process should also identify potential drug interactions with other products the patient may be taking.

#### *What about reports of adverse events associated with compounded GLP-1s?*

In June 2023, FDA released a statement on semaglutide indicating it had received reports of adverse events related to compounded semaglutide but provided no details. We probed, and FDA shared some details (which it has not released in any subsequent statement). Turns out, over an 18-month period, there were only 29 reported adverse events related to compounded semaglutide, and only seven of them were identified by the FDA as “serious.” The rest were known side effects associated with the drug. For perspective, thousands of adverse events related to Wegovy and Ozempic have been reported to FDA through the [FDA Adverse Events Reporting System](#) (FAERS).

#### *What is the role of pharmacist-prescriber-patient communication regarding GLP-1 drugs?*

The practice of pharmacy relies on the triad relationship between the patient, prescriber, and pharmacist. Pharmacists have an obligation to determine that such a relationship exists, and prescribers should be comfortable communicating and consulting with both patient and pharmacist to assure the best treatment option for the patient. Pharmacists have expertise in proper dosing, side effects, and other aspects of drug delivery, and prescribers should be open to their input. This is no different for GLP-1 drugs than for any other prescribed medication. It’s a three-way relationship that helps assure proper patient care.

#### *So what about compounding using semaglutide sodium?*

We are aware that some compounding pharmacies have at some point dispensed the compounded semaglutide medication they have prepared using semaglutide sodium. However, recent anecdotal reporting indicates that semaglutide base is now readily attainable from FDA-registered suppliers. Because of that – and also strong warnings against compounding semaglutide sodium from FDA and state boards of pharmacy – it’s our understanding that compounding with semaglutide sodium is not widely occurring.

But to the point: 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 semaglutide sodium is an API used in either of the FDA-approved drug products, it is APC’s 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**

- Ultimately, the use of a compounded GLP-1 depends on two things:
  - A prescriber who believes the possible benefit to the patient of the compounded product outweighs the risk and so prescribes the compound; and
  - A patient who is counseled by both the prescriber and the compounding pharmacist and chooses to take the compounded product.
- Don't buy any substance purported to be a GLP-1 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 a compounded GLP-1 by a doctor or other healthcare professional and are not choosing the dispensing compounding pharmacy yourself, ask about it:
  - What is the name of the compounding pharmacy?
  - Where is the pharmacy located?
  - Is it licensed to dispense in or ship to your state?

Some of that info you can verify online – via the website of the board of pharmacy in the state in which the pharmacy is based – once you know the identity of the compounding pharmacy.

- 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 a third-party testing lab. These are complicated, scientific reports but can confirm the identity of the drug that has been dispensed to you. Your prescriber can request this information as well.



*The Alliance for Pharmacy Compounding is the voice for pharmacy compounding, representing more than 500 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.*