TO: State Boards of Pharmacy

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Chief Executive Officer

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DATE: March 4, 2024

SUBJECT: *Statement on Compounding of Peptide Products*

The Alliance for Pharmacy Compounding (APC) Board of Directors has authorized release of a public statement, **Understanding Law and Regulation Governing the Compounding of Peptide Products**.

The purpose of the statement is to educate pharmacy compounders and prescribers about federal law and FDA guidance on peptides, especially in light of FDA's September 2023 addition of several peptides to Category 2 of its 503A Interim Bulks Guidance. The statement also describes the proper pathway for renominating substances for reconsideration by the agency.

I'm sharing with boards of pharmacy as an additional information resource for your board members and investigators. Feel free to share the statement with licensees as well. We hope you find this helpful.

Please stay tuned. In the meantime, if APC may be helpful to you on this or any other matter related to pharmacy compounding, please contact us at scott@a4pc.org

Alliance for Pharmacy Compounding

Compounding the Joy of Living®

STATEMENT OF THE ALLIANCE FOR PHARMACY COMPOUNDING:

UNDERSTANDING LAW AND REGULATION GOVERNING THE COMPOUNDING OF PEPTIDE PRODUCTS

March 1, 2024

The Alliance for Pharmacy Compounding is committed to promoting a safe and lawful environment for the compounding, prescribing, dispensing, and use of drug products. To that end, this brief will focus on ensuring that compounders, regulators, physicians, and other prescribers have an overview of the regulatory framework surrounding active ingredients that may be used in human compounding, particularly peptides.[1]

"Peptides" are a group of protein substances, some of which are FDA-approved products, that may have health benefits for certain patient populations. Recently, compounding pharmacies have received numerous inquiries from prescribers regarding peptides. As a result, pharmacists frequently reference FDA guidance and federal law when advising prescribers on what can and cannot be used as an active ingredient in a human compound.

THE BASICS

While the traditional *practice* of pharmacy compounding is regulated by state boards of pharmacy, the *substances used* in human compounded drugs – including peptides – are regulated in the Food, Drug & Cosmetic Act and FDA Guidance for Industry.

Federal Law & FDA Guidance

According to Section 503A of the Food, Drug & Cosmetic Act and FDA Guidance for Industry, to be eligible for use in a compounded product any active pharmaceutical ingredient must first meet one of the following criteria:

1. Is it an active ingredient in an FDA-approved drug product? (Listed in FDA's Orange Book)
2. Does it have a USP or National Formulary drug monograph?
3. Does it appear on the Section 503A Bulks List (or 503A Interim Bulks List, Category 1) published by FDA?[2]

In addition, a substance for compounding must be manufactured by an FDA-registered facility and must NOT be labeled "For lab use only," "Research use only," "Not for human use," or other such qualifiers. To determine if a potential therapy can be compounded it must be evaluated against these criteria. This is

[1] This brief refers only to patient-specific compounding and dispensing pursuant to Section 503A of the Food, Drug, and Cosmetic Act. It does not refer to the distribution of drug products by outsourcing facilities under Section 503B.

[2] FDA is currently evaluating specific additional substances for inclusion on the 503A bulks list and has stated that compounding with them is acceptable in this interim period until the agency finalizes its review of those substances.

the case for all potential substances, including those referred to as peptides, which are considered active pharmaceutical ingredients (API). Some peptides do not meet the criteria, though many do.[3]

Biologic products cannot be compounded

In March 2020, a federal law (the Biologics Price Competition and Innovation Act of 2009) took effect and reclassified some drugs as biologic products. 503A compounding pharmacies are prohibited from compounding substances that are classified as biologics. For example, that 2020 reclassification made both tesamorelin and human chorionic gonadotropin (HCG) – two peptides – ineligible for compounding, instead reclassifying them as biologic products. *FDA's Purple Book* is a definitive guide and reference on which substances are classified as biologic products.

Most recently, in September 2023, FDA added several peptides to Category 2 of its 503A Interim Bulks Guidance. Substances listed in Category 2 are not to be used as active pharmaceutical ingredients due to potential safety concerns raised by FDA in their review of the nominations that were submitted for those items. Peptides recently added to Category 2 do not meet any of the three criteria for compounding, so the FDA action merely formalized the impermissibility of compounding with them.

Compounding pharmacies continue to receive prescriptions and/or inquiries from prescribers about compounded drugs containing such peptides as ipamorelin, BPC-157, CJC-1295, Kisspeptin-10, or AOD9604. However, those substances are listed in Category 2 and thus are ineligible for compounding; moreover, they do not meet any of the legal criteria for compounding.

FDA's action to include a substance in Category 2 does not necessarily mean the agency has identified specific safety risks associated with that substance. It may mean that the documentation submitted with the nomination of that substance did not demonstrate safety to the agency's satisfaction.

Individuals or groups may submit or resubmit to FDA nominations of a substance for inclusion in Category 1 (substances that may be compounded). Those nominations should include the following information, according to the agency:

- The physical and chemical characterization of the substance.
- Any safety issues raised by using the substance in compounded drug products.
- Historical use of the substance in compounded drug products, including information about the medical condition(s) the substance has been used to treat and any references in peer-reviewed medical literature.
- The available evidence of effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists.

APC counsels that the information and data submitted should be science-based (as opposed to anecdotal), thorough, and compelling. Those nominations should be submitted to docket number FDA-2015-N-3534 on the FDA website.

Compounding FDA-approved drugs "currently in shortage"

Despite federal law's general prohibition against compounding copies of FDA-approved products, FDA guidance does allow for exceptions. A significant one is when a drug appears as "currently in shortage" (that's the precise wording) on the FDA Drug Shortage List. Compounders are permitted to make "essentially copies" of those drugs during the period they are listed in shortage. Semaglutide and

[3] Of note, the popular weight loss peptide semaglutide qualifies as an active ingredient of an FDA-approved drug product.

tirzepatide are both examples of peptides which are currently listed on the FDA Drug Shortage List. As such, they may be compounded as essentially copies of the FDA-approved drug in which they are the active ingredient.

Drug manufacturers Novo Nordisk and Eli Lilly have filed lawsuits against some compounding pharmacies for compounding semaglutide and tirzepatide, asserting in part that the pharmacies are infringing on the manufacturers' intellectual property rights. However, the language of the FDA guidance document which permits compounding essentially copies of FDA-approved drugs when those drugs are in shortage makes no exception for patented drugs. While courts have yet to adjudicate the issue, an exception for patented drugs would seem to run counter to the reason for allowing shortage-drug compounding in the first place: ensuring the continuation of patient drug therapy even when the FDA-approved drug in question is in shortage.

GUIDANCE

We urge compounding pharmacists, prescribers, and regulators to familiarize themselves with federal law and FDA guidance on what can be utilized as an active ingredient for human patients. *And, of course, we urge pharmacy compounders to avoid compounding substances that do not meet the criteria for compounding.*

Navigating the landscape of peptide compounding requires a nuanced understanding of regulatory language and ethical responsibilities. By adhering to federal law, FDA guidance, and prioritizing patient care, compounding pharmacies can remain compliant, and prescribers can continue treating their patients with legally accessible medications.

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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.

Learn more at compounding.com and a4pc.org.