Alliance for Pharmacy Compounding

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BRIEFING MEMORANDUM

To: Members of the Pharmacy Compounding Advisory Committee

From: Scott Brunner, CAE
Chief Executive Officer

Date: September 8, 2026

Subject: How traditional 503A pharmacy compounding works

Thank you for your service on PCAC and for the considerable time you devote to evaluating issues involving pharmacy compounding.

At your recent July 2026 meeting, FDA staff provided an overview of the statutory and regulatory framework governing compounded medications. The information presented was accurate but necessarily abbreviated. It explained much of the "what" of pharmacy compounding, but less of the "why" and "how" of the system Congress created.

I thought some additional detail and context might be useful to you, and that is the purpose of this briefing memo.

The Alliance for Pharmacy Compounding represents pharmacists and pharmacies engaged in traditional pharmacy compounding under section 503A of the Federal Food, Drug, and Cosmetic Act, as well as outsourcing facilities authorized under section 503B of that Act. This briefing memo refers exclusively to 503A traditional compounding pharmacies.

Our purpose here is not to suggest that pharmacy compounding is risk-free or that its regulatory framework is beyond improvement. Neither is true. Rather, we hope to explain how traditional pharmacy compounding actually works, why its standards differ from pharmaceutical manufacturing, and where responsibility resides for decisions about a compounded medication.

Traditional pharmacy compounding exists to meet the needs of individual patients

Section 503A is not a loophole in the drug-approval system. Congress intentionally authorized pharmacy compounding to meet patient needs that the FDA-approved drug supply does not always meet.

In practical terms, that occurs in two principal circumstances: when a prescriber judges that an individual patient needs a strength, dosage form, route of administration, ingredient profile, or other formulation that is not commercially available, and when an FDA-approved drug is unavailable because of a shortage or other disruption in supply. In both situations, compounding pharmacies help assure continuity of therapy when the conventional drug supply cannot meet the patient's need.

That patient-specific character is fundamental to section 503A. A 503A pharmacy compounds and dispenses medications for identified individual patients pursuant to valid prescriptions. That is one of the principal distinctions between a 503A pharmacy and a section 503B outsourcing facility, which

operates under a different regulatory model and may compound drugs in bulk without first receiving patient-specific prescriptions.

That distinction matters because the standards Congress applied to the two models reflect what each is designed to do.

Why compounded medications are not FDA-approved

You will often hear the statement that compounded medications are "not FDA-approved." That is true. But understanding *why* they are not, and cannot be, FDA-approved is important.

FDA's drug-approval process is designed for commercially manufactured drug products intended to be produced repeatedly and marketed broadly. A manufacturer submits a new drug application supported by clinical and other data for a defined formulation, strength, dosage form and indication.

Traditional compounding works differently. A pharmacist may prepare a medication specifically because the FDA-approved version, strength, dosage form or combination is judged by a prescriber not to be appropriate for a particular patient. Requiring a separate new drug application for every patient-specific formulation would effectively eliminate traditional pharmacy compounding – and with it, access for patients whose needs cannot be met by the commercially available product.

Congress therefore expressly exempted drugs compounded in accordance with section 503A from the federal new-drug approval requirement. It likewise exempted them from current good manufacturing practice requirements, and from the requirement that labeling contain adequate directions for use.

"Not FDA-approved" consequently means something important but specific: FDA has not reviewed and approved that finished compounded formulation through the new-drug approval process. It does not mean that the medication is illegal, that its ingredients are unregulated, that it is made without quality standards, or that Congress somehow overlooked pharmacy compounding when creating the drug regulatory system.

Quite the opposite. Section 503A is the federal statutory framework Congress intentionally and specifically created for it.

The prescriber makes the patient-specific clinical judgment

For a 503A prescription, the clinical decision that a compounded medication is needed rests with a licensed prescriber treating an individual patient.

The pharmacist does not independently diagnose the patient or decide what therapy the patient should receive. The prescriber evaluates the patient and writes the prescription. The pharmacist then exercises his or her own professional responsibility in evaluating the prescription, confirming that it is valid and appropriate to dispense, and preparing the medication in accordance with applicable law and pharmacy standards.

This matters particularly when an FDA-approved drug is commercially available. Section 503A expressly recognizes that an individual patient may need a change in the commercially available product – for example, a different strength, dosage form, route of administration, or omission of an ingredient. *The statute assigns the determination of whether that change produces a significant difference for the patient to the prescribing practitioner*.

FDA's own guidance reinforces that allocation of responsibility. FDA says it is not possible to offer exhaustive guidance about when a difference will be "significant" for an individual patient and states that, at this time, it generally does not intend to question prescriber determinations that are

documented on the prescription or in a notation. FDA does, appropriately, expect the record to show that the prescriber actually made the determination.

That is an important guardrail and an important protection of individualized medical judgment. A pharmacy cannot simply substitute a compounded medication for an available FDA-approved drug and assume a patient-specific rationale. When the pharmacy relies on a significant-difference determination, the prescriber's judgment must be documented.

Pharmacies also have obligations under federal and state law to dispense only pursuant to valid prescriptions. State requirements governing what constitutes a valid practitioner-patient relationship, including relationships established through telehealth, vary. A pharmacy must comply with the laws of the jurisdictions in which it practices and has a professional obligation to identify prescriptions that raise questions about validity or legitimacy.

What may be compounded – and FDA's "essentially a copy" limitation

Section 503A does not give pharmacies a blanket right to reproduce commercially available medications. It contains several important limits on what may be compounded.

One is the statute's "essentially a copy" provision. Section 503A says that a pharmacy may not regularly or in inordinate amounts compound drug products that are essentially copies of commercially available drugs. The statute also provides that a compounded drug is not considered "essentially a copy" when the prescribing practitioner determines that a change made for the individual patient produces a significant difference for that patient. FDA's 2018 Guidance for Industry goes further by explaining how the agency intends to apply those statutory terms. Under that guidance, FDA generally considers a compounded product to be essentially a copy when it has the same active ingredient, the same or a similar or easily substitutable strength, and can be used by the same route of administration – unless the prescriber has made the patient-specific significant-difference determination.

The provision is important because it preserves the central purpose of 503A: individualized therapy, not routine manufacturing of substitutes for commercially available drugs. At the same time, it leaves room for a prescriber to determine that an individual patient genuinely needs a customized version.

Drug shortage is another important part of the framework. FDA's guidance states that a drug is not considered "commercially available" while it appears as "currently in shortage" on FDA's drug shortages list. During that period, the essentially-a-copy limitation tied to commercial availability does not apply, although all other conditions of section 503A still do. FDA recommends documenting on the prescription that the drug was on the shortage list and the date the list was checked.

Section 503A also limits which bulk drug substances – active pharmaceutical ingredients – may be used. In simplified terms, a bulk drug substance must fit one of three pathways: it must comply with an applicable USP or National Formulary monograph, if one exists; if no monograph exists, it may be a component of an FDA-approved drug; or, if neither condition applies, it must appear on FDA's 503A bulks list or fall within an applicable FDA interim enforcement policy while FDA evaluates nominated substances.

That framework was on display at PCAC's July meeting, when the committee evaluated several peptide substances for potential inclusion on the 503A Bulks List. The Committee's recommendations are an important step in the statutory process Congress created for determining whether substances without an applicable USP/NF monograph or FDA-approved drug-product pathway may be appropriate for use in traditional compounding.

Those criteria matter. A substance does not become lawful for human compounding merely because it can be purchased, because a prescriber wants to prescribe it, or because a seller calls it an API.

The IND pathway is not always a practical substitute for compounding

FDA and PCAC have at times discussed the Investigational New Drug (IND) and expanded-access pathways as possible mechanisms for patients to obtain substances that are not otherwise available for compounding. But those pathways serve a different purpose and can impose substantial practical burdens, particularly for community practitioners.

Depending on the form of expanded access sought, a physician may need to submit FDA forms and supporting documentation, obtain Institutional Review Board (IRB) review, satisfy ongoing reporting obligations, and obtain FDA authorization before treatment begins. Prior industry examination of the process found difficulty locating IRBs willing to work with unaffiliated community physicians, potentially significant IRB costs, hours of administrative work, and uncertainty about how the investigational product itself would be supplied.

The economic challenge may be even more fundamental. Many substances considered by PCAC for the 503A Bulks List are not novel molecules being developed toward a new commercial drug approval. Some are long-used or otherwise nonproprietary substances for which patent protection or meaningful market exclusivity may be limited or unavailable. An IND does not require a patentable product, but without a realistic commercial return, there may be little incentive for a pharmaceutical manufacturer or other sponsor to bear the cost of developing, maintaining, supplying, and supporting an IND program.

A physician may instead act as a sponsor-investigator, but that shifts the regulatory, administrative, and potentially significant financial obligations to the practitioner or another supporting entity.

For that reason, the theoretical availability of an IND or expanded-access pathway should not be confused with a practical, scalable, or sustainable mechanism for patient access. Nor is the existence of an IND pathway among FDA's stated criteria for determining whether a bulk drug substance should be included on the 503A Bulks List.

Where the active pharmaceutical ingredient comes from

Another area that is easily misunderstood is ingredient sourcing.

Generally, 503A pharmacies do not purchase bulk active pharmaceutical ingredients directly from the original API manufacturer. They typically purchase through specialized drug wholesalers, repackagers or resellers. Those firms repackage bulk drug substances into quantities suitable for pharmacy use. Drug repackagers and relabelers are required to register with FDA and are subject to FDA inspection.

The regulatory requirements also reach back to the original manufacturer. For use under section 503A, a bulk drug substance must be accompanied by a valid certificate of analysis and must have been manufactured by an establishment registered with FDA. FDA has specifically urged repackagers to maintain supply-chain transparency.

Responsible pharmacies qualify their suppliers, review certificates of analysis and maintain systems for receiving, identifying, storing and tracing ingredients. The provenance and quality of API matter enormously, particularly in sterile compounding. APC has developed a detailed Best Practices for Vendor Validation resource for compounding pharmacies (available at a4pc.org).

Research-grade material is different from API intended for human drug compounding

The term "research grade" can create confusion because legitimate pharmaceutical suppliers may sell materials intended for laboratory, analytical or research purposes as well as ingredients intended for use in human drugs.

There are entirely legitimate reasons for research and reference materials to exist. Laboratories use reference standards and other materials to develop and validate analytical methods, identify substances, calibrate testing and conduct research. USP itself sells reference standards specifically for test and assay use and states that they are not for use in humans or animals as drugs.

The problem arises when material sold for research or analytical purposes is diverted into a medication for administration to a patient. Material marketed as "research use only" or "not for human use" is not thereby qualified for human compounding. For a 503A pharmacy to use a bulk drug substance in a patient medication, the substance and its manufacturer must satisfy the applicable requirements of section 503A, including the statutory eligibility criteria, FDA establishment-registration requirement, applicable compendial standards and a valid certificate of analysis.

This is also why "research grade" should not be treated as interchangeable with pharmaceutical API manufactured under cGMP. API intended for human drug use is produced within a pharmaceutical quality system designed to control identity, strength, quality, purity and impurities. A research chemical material may be suitable for the limited laboratory purpose for which it is sold while lacking the manufacturing controls, impurity characterization, microbiological controls or documentation necessary for administration to patients.

Unfortunately, the ready availability of research-use material – including some substances sold by otherwise legitimate suppliers – creates an opportunity for misuse. Some sellers and health care businesses have taken material intended for research and moved it into human use. That conduct should not be confused with lawful pharmacy compounding. A licensed pharmacy cannot make an otherwise ineligible or research-use substance lawful for human administration simply by placing it into a compounded preparation.

Why 503A pharmacies follow USP standards rather than cGMP

This is one of the most important distinctions in understanding pharmacy compounding.

Pharmaceutical manufacturers operate under current good manufacturing practice, or cGMP, requirements. Those requirements are designed for industrial production: validated manufacturing processes, large-scale production, extensive lot-release systems, stability programs and commercial distribution of standardized products to potentially very large patient populations. Think "many doses for many patients."

Section 503A pharmacies operate under pharmacy practice standards, most notably those established by the United States Pharmacopeia and, in most states, incorporated into state pharmacy law and regulation. Think "one dose for one patient."

USP <795> governs nonsterile compounding. USP <797> governs sterile compounding. USP <800> addresses the handling of hazardous drugs. Among other things, these standards address personnel qualifications and training, facilities, engineering controls, environmental monitoring, cleaning and disinfection, aseptic technique, component selection, beyond-use dating, and quality-control procedures.

The difference between USP and cGMP should not be understood as the difference between "regulated" and "unregulated," or even between "good" and "less good." They are standards designed for different activities.

A manufacturer producing tens or hundreds of thousands of identical units for commercial distribution appropriately operates under a manufacturing quality system. A pharmacist preparing medication pursuant to prescriptions for individual patients appropriately operates under a pharmacy compounding quality system rooted in the compounding chapters of USP.

Congress recognized that distinction when it expressly exempted qualifying 503A compounded medications from cGMP. By contrast, Congress made 503B outsourcing facilities subject to cGMP because their production model more closely resembles manufacturing – and it is that distinction that allows outsourcing facilities to distribute compounded drugs in bulk, without patient-specific prescriptions, to hospitals, clinics and other health care settings.

Sterile and nonsterile compounding are different activities

It is also useful to distinguish sterile from nonsterile compounding. The risks, facilities and controls are not the same.

Nonsterile compounding includes preparations such as capsules, oral liquids, creams, ointments and certain other dosage forms that are swallowed, absorbed in the mouth, or applied to the skin and do not have to be sterile. USP <795> establishes standards for those preparations, including ingredient selection, calculations and procedures, cleaning, documentation, quality assurance and beyond-use dating.

Sterile compounding includes preparations such as injections, infusions and ophthalmic preparations, where the medication is introduced into the bloodstream or another normally sterile area, or where sterility is otherwise essential. Because microbial contamination can present a much more immediate risk to patients, USP <797> imposes substantially more extensive requirements, including controlled compounding environments, engineering controls, environmental monitoring, garbing and aseptic technique, personnel training and competency testing, cleaning and disinfection, and additional quality-assurance requirements.

The point is not simply that one chapter is longer than another. *The USP framework scales the controls to the nature and risk of the preparation.* For sterile preparations, those controls become more stringent as a pharmacy seeks to assign a longer beyond-use date.

Extended beyond-use dating is not simply a judgment the pharmacy may make on its own. Under USP <797>, longer BUDs require additional controls, including sterility testing and, when applicable, bacterial endotoxin testing. When sterility testing is required to support the assigned beyond-use date, the preparation cannot be released for patient use until the required testing has been completed and acceptable results obtained. Pharmacies frequently use qualified outside laboratories for this testing, although USP does not universally require that the laboratory be a third party.

Category 3 preparations, which may qualify for the longest BUDs permitted under the chapter, are subject to still more extensive requirements. The result is a risk-based system: the longer a sterile preparation is expected to remain in use, the greater the quality assurance required to support that period of use.

That is an important distinction. USP standards do not attempt to replicate an industrial manufacturing system at pharmacy scale. They instead impose controls calibrated to the type of preparation, the

environment in which it is compounded, and the length of time for which the pharmacy proposes that it remain suitable for patient use.

State boards of pharmacy are active regulators, not simply licensing bodies

Section 503A pharmacies are state-licensed pharmacies, and state boards of pharmacy provide their primary day-to-day regulatory oversight. That does not mean FDA is absent from the system.

State boards establish licensing requirements, adopt and enforce compounding standards, conduct or require inspections, investigate complaints, review pharmacy records, impose corrective actions and discipline pharmacies and pharmacists when warranted.

A pharmacy dispensing into multiple states generally must hold nonresident pharmacy licenses in those jurisdictions and is subject to their laws and regulatory authority as well as that of its home state. How those states satisfy inspection requirements varies: some conduct or commission their own inspections, while others recognize inspections performed by the resident state or an approved third party.

This creates a regulatory framework that is more layered than is sometimes appreciated.

FDA also retains important authority. Compounded medications remain subject to other provisions of the FD&C Act, including prohibitions involving insanitary conditions, and FDA conducts risk-based inspections of 503A pharmacies, often in coordination with state regulators. FDA and state boards also exchange information concerning inspections, complaints and enforcement actions.

The system therefore is not simply "states instead of FDA." It is principally state regulation of pharmacy practice operating within a federal statutory framework, with continuing FDA authority in defined areas.

Why 503A pharmacies do not currently report every adverse event to FDA

Section 503A does not contain a federal mandatory adverse-event reporting requirement. Section 503B does. That was a policy choice Congress made in creating the two different frameworks.

That does not mean adverse events involving compounded medications are irrelevant or should go unreported.

APC supports creation of a federal requirement for 503A pharmacies to report *serious* adverse events associated with compounded medications. We believe such reporting would give FDA and state regulators an important additional surveillance tool and help identify signals involving contamination, potency, formulation errors or other events associated with meaningful patient harm.

We emphasize *serious* for a reason.

Compounded medications have not gone through clinical trials producing an FDA-approved adverse-reaction profile for the finished formulation. If every unfavorable patient experience were federally reportable, the system could quickly be flooded with reports of transient injection-site irritation, nausea, headache or symptoms potentially attributable to an underlying disease, another medication, administration error or ordinary coincidence. That volume would create substantial administrative burden on both pharmacies and regulators without necessarily improving safety surveillance.

Serious adverse-event reporting is different. It focuses regulator attention where it belongs: events involving death, hospitalization, life-threatening experiences, significant disability or other medically important outcomes. A well-designed serious adverse-event requirement would strengthen oversight without burying the safety signal in noise.

Compounding is not a substitute for FDA-approved drugs

None of this means that a compounded medication should routinely replace an FDA-approved drug.

FDA-approved medications appropriately remain the standard when they meet a patient's clinical needs and are available. Pharmacy compounding occupies the space where standardized commercial drug production and an individual patient's needs do not fully align.

That space may involve a child who cannot swallow a tablet. A patient allergic to a commercial product's excipient. A dose or dosage form that is not manufactured. A medication in shortage. Or a patient for whom a prescriber determines that a modification makes a meaningful difference.

The point is not that compounded medications and FDA-approved medications are the same. They are not.

The point is that difference is the reason the compounding framework exists.

Congress did not inadvertently leave traditional pharmacy compounding outside the drug-approval and manufacturing systems. It deliberately created section 503A to preserve individualized pharmacy practice while surrounding it with conditions governing prescriptions, ingredients, copying of commercial drugs, professional standards and regulatory oversight.

We hope this additional context is useful as you continue your work on PCAC.

You are routinely asked to evaluate individual substances and difficult scientific questions. Understanding the system into which those substances may or may not be placed is just as important. There are legitimate issues in pharmacy compounding that deserve scrutiny, and there are opportunities to strengthen the regulatory framework. We welcome both.

But sound recommendations begin with understanding not only what the rules say, but why they were structured as they are and how pharmacy compounding actually operates in practice.

The peptide substances you considered in July illustrate why understanding this broader framework matters: your recommendations about individual substances ultimately operate within this larger system of patient-specific prescribing, ingredient controls, USP standards, and state and federal oversight.

We would be pleased to serve as a resource to you at any time. Reach me at scott@a4pc.org.