Alliance for Pharmacy Compounding

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How Compounding Pharmacies Validate Active Pharmaceutical Ingredients

State-licensed compounding pharmacies do not simply "buy chemicals and mix them." Both federal and state law require pharmacists to ensure that every active pharmaceutical ingredient used in a compounded medication is legally permitted, sourced from legitimate suppliers, and appropriate for patient use.

API validation is a multi-step process that begins before a product is purchased and continues throughout its use.

The systems used by compounding pharmacies to validate APIs are robust, risk-based, and aligned with federal law, USP standards, and long-standing pharmacy practice.

1. Federal law strictly limits which APIs may be used

Before an API can even be considered for use in a compounded drug, a pharmacy must confirm that it is legally eligible for compounding under federal law. An API must meet one of the following criteria:

- Have an applicable US Pharmacopeia or National Formulary monograph
- Be a component of an FDA-approved drug
- Appear on FDA's interim or final bulk drug substances lists for compounding

If an API does not meet one of these criteria, it cannot be used, regardless of demand or availability. This legal gatekeeping step alone excludes large categories of substances that have recently been raised in legislative and regulatory discussions, including "research grade" chemicals and unapproved peptide products.

2. Pharmacies validate the legitimacy of API suppliers

Once the pharmacist determines an API is legally eligible, they must validate the supplier, not just the

substance. Federal law and best practice require pharmacies to confirm that API suppliers are:

- FDA-registered manufacturers, or
- State-licensed wholesalers sourcing from FDA-registered manufacturers

Pharmacies verify supplier credentials through FDA registration databases, state license lookups, and National Association of Boards of Pharmacy resources. The pharmacy must maintain vendor files to document licensing status, inspection history, and enforcement actions when applicable

State-licensed compounding pharmacies are prohibited from purchasing API from:

- Online marketplaces
- Chemical supply companies selling "research use only" products
- Unlicensed domestic or overseas sellers

3. Under federal law, pharmacies are required to receive and evaluate certificates of analysis

The Food, Drug & Cosmetic Act requires that every API must be accompanied by a Certificate of Analysis (COA) documenting identity, purity, and other quality attributes. However, relying solely on a manufacturer's COA is not suSicient validation by a pharmacy.

Pharmacies are expected to:

- Review COAs for completeness and internal consistency

- Confirm lot numbers, test methods, and specifications
- Reject products with missing, vague, or inconsistent documentation

This refutes the misconception that pharmacies simply "trust the paperwork." In practice, COAs are treated as a starting point, not the final word.

4. Independent third-party testing by pharmacies is a core best practice

When pharmacies source API from a new or unfamiliar supplier, the Alliance for Pharmacy Compounding strongly recommends having independent third-party laboratory testing of the API before it is used in a compounded preparation.

This testing may include:

- Identity confirmation
- Potency verification
- Purity testing
- Water content or impurity analysis, as appropriate

Third-party testing serves as a check on both the manufacturer and the wholesaler and is widely used for higher-risk APIs, shortage drugs, or products subject to increased scrutiny by regulators.

5. Pharmacies actively screen for counterfeit and illegitimate products

Compounding pharmacies operate within the same drug supply chain risk mitigation imperatives as hospitals and manufacturers. Best practices require staS to watch for warning signs such as:

- Unusually low pricing
- Inconsistent packaging or labeling
- Missing or altered lot information
- Sellers unable to produce licensing or transaction documentation

Suspect products are quarantined, investigated, and reported when necessary. Pharmacies are encouraged to verify vendors against FDA and NABP resources and to disengage immediately from suppliers that raise concerns.

6. Per US Pharmacopeia standards, a sample of every batch of sterile compounded drugs must be tested before any of that batch may be dispensed to a patient

Compounding pharmacies do not rely on API validation alone. For sterile compounded preparations, USP standards require a layered approach to quality that includes appropriate sterility testing (USP <71>) and bacterial endotoxins testing (USP <85>) when applicable, along with strong aseptic process controls and environmental monitoring.

When a preparation is packaged in a vial, syringe, or other closed system, pharmacies also evaluate container closure integrity to confirm the package maintains sterility over the assigned beyond-use date. For multi-dose or preserved sterile preparations, antimicrobial eSectiveness testing may be needed to demonstrate that the preservative system performs as intended. And when a pharmacy assigns a beyond-use date beyond default limits, USP expects stability-indicating data to support that decision, including studies that assess potency and degradation over time under defined storage conditions.

Together, these USP-driven testing expectations reinforce that quality in compounding is based on documented, science-based controls across the full lifecycle of the preparation, not simply the source of the ingredient.

7. API validation is continuous, not one-time

Validation does not end once an API is determined by the pharmacy to be appropriate for use in a compounded drug. Pharmacies conduct ongoing monitoring that includes:

- Periodic re-verification of vendor licensure
- Review of inspection histories and recalls
- Re-testing when suppliers, manufacturing sites, or lots change
- Documentation within the pharmacy's quality management system

This risk-based approach mirrors how health systems and manufacturers manage raw material quality without imposing manufacturing-style requirements that are neither legally required nor operationally appropriate for traditional pharmacy practice

APC 'Best Practices' on API validation

The Alliance for Pharmacy Compounding has created detailed best practices guidance documents that explain how compounding pharmacies source and validate active pharmaceutical ingredients in compliance with federal law and USP standards. APC's *Best Practices for Vendor Validation* outlines supplier licensure verification, FDA registration checks, certificate of analysis review, and when independent third-party testing is recommended to confirm API identity and purity. APC's *Best Practices for Compounding FDA-Approved Drugs in Shortage* provides additional guidance for heightened API scrutiny during drug shortages, particularly when working with new or unfamiliar suppliers.

More information on those is available here:
https://a4pc.org/hubfs/PDFs/Vendor-Validation-Best-Practices.pdf
https://a4pc.org/hubfs/PDFs/Best-Practices-for-Compounding-Shortage-Drugs-1.pdf

Key takeaways for policymakers

Compounding pharmacies already operate under a rigorous, layered system of API controls that includes legal eligibility screening, supplier credentialing, documentation review, independent testing, and continuous oversight.

Problems associated with unregulated online sellers, research-grade chemicals, or non-prescription distribution are not the result of gaps in pharmacy compounding law. They arise outside the licensed pharmacy system entirely.

Policy solutions should reinforce existing pharmacy-based safeguards rather than replace them with manufacturing-style mandates that do not address the actual sources of risk.

For more information or to schedule a briefing, contact APC's Advocacy Chief Tenille Davis, PharmD, FAPC, at tenille@a4pc.org.

The Alliance for Pharmacy Compounding is the industry trade association and the voice for pharmacy compounding, representing more than 600 compounding small businesses – including 7,500 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 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 or the appropriate FDA-approved drug is not commercially available. Learn more at compounding.com or a4pc.org.