PHARMACEUTICAL COMPOUNDING IN WISCONSIN

Frequently Asked Questions for Pharmacists, Prescribers, and Outsourcing Facilities

Issued by the Wisconsin Pharmacy Examining Board XX/XX/XXXX

Purpose

In response to the increasing demand for commercially available compounded medications, such as tirzepatide and semaglutide, the Wisconsin Pharmacy Examining Board (Board) has prepared the following responses to frequently asked questions concerning pharmaceutical compounding. This guidance document sets forth the relevant laws and regulations, the intent is to protect public safety, ensure standard of practice, mitigate risks, and provide clarity to pharmacy professionals.

Q1. What is pharmaceutical compounding?

Pharmaceutical compounding as defined by the United States Pharmacopeia (USP) involves "combining, admixing, diluting, pooling, or otherwise altering a drug product or bulk drug substance." Compounding does not include mixing, reconstituting, or other such acts that are performed in accordance with the manufacturer's approved labeling or supplemental materials.

However, to the extent that the approved labeling does not address all elements of the preparation (such as selection of a diluent, storage, or beyond usage times), the preparation activity involves compounding within the meaning of this guidance. This guidance is also applicable in circumstances where more than a single dose for a single patient is prepared in advance of use.

Q2. What key laws outline requirements for pharmaceutical compounding in Wisconsin?

The Pharmacy Examining Board's standards for primary medication compounding are set forth in Wis. Admin. Code ch. Phar 15.

- Chapter Phar 15 incorporates by reference the current USP-NF standards for compounding (USP <795>, <797>, <800>, and <825>), requiring adherence to the USP-NF standards applicable to the type of compounding undertaken.
- Noncompliance with Phar 15, including referenced USP-NF standards, is considered unprofessional conduct under Phar 10.03 and may result in disciplinary action by the Board. (Wis. Admin. Code § Phar 15.03(1))
- Where any board rule specified in Phar 15 differs from the referenced USP-NF standards, the board rule shall govern. (Wis. Admin. Code § Phar 15.03(2)(a))

Federal statutes also create requirements applicable to pharmaceutical compounding in Wisconsin:

- Sections 503A and 503B of the Federal Food, Drug and Cosmetics Act (FD&C Act) (21 U.S.C. §§ 353a, 353b) establish the conditions under which compounded drugs are exempt from certain U.S. Food and Drug Administration (FDA) requirements.
- Section 503A governs traditional compounding by state-licensed pharmacists and physicians, requiring compounding pursuant to a valid prescription for an individually identified patient. Compounding practices are expected to comply with USP general chapters[1].

[1] https://www.fda.gov/drugs/human-drug-compounding/bulk-drug-substances-used-compounding-under-section-503a-fdc-act

- Section 503B governs outsourcing facilities registered with FDA, which may compound without patient-specific prescriptions but must comply with Current Good Manufacturing Practice (CGMP) standards and FDA oversight.
- FDA guidance documents and declaratory orders provide additional interpretation of federal requirements. Some common questions related to these guidance documents are discussed below.
- Failure to adhere to applicable 503A and 503B requirements is considered unprofessional conduct under Wis. Admin. Code § Phar 10.03 and may result in disciplinary action by the Board.

Q3. Who is authorized to compound medications in Wisconsin?

Under Wis. Stat. § 450.11(3), only the following persons may prepare, compound, dispense, or prepare for delivery a prescription drug in Wisconsin:

- A pharmacist licensed by the Wisconsin Pharmacy Examining Board;
- A practitioner, under Wis. Stat. § 450.01(17), with the necessary competency to perform such tasks; or
- Their agents and employees, acting under the direction, supervision, and inspection of the pharmacist or competent practitioner.

In addition, under Wis. Stat. § 450.068:

- Registered pharmacy technicians may assist in compounding activities as delegated by a pharmacist (Wis. Admin. Code § Phar 19.02).
- Registered pharmacy technicians may act under the delegation and supervision of a practitioner in performing medication compounding activities (Wis. Admin. Code § Med 17.06).

Q4. Are there limitations on medications which can be compounded by pharmacists or practitioners?

Yes. Both federal law and Wisconsin regulations restrict what can be compounded by limiting which ingredients can be utilized.

The active pharmaceutical ingredient (API) used in compounding must meet at least one of the following criteria, be accompanied by a certificate of analysis, and come from a registered manufacturer:

- It complies with an applicable USP-NF monograph (a recognized quality standard);
- It is a component of an FDA-approved drug product, if no USP-NF monograph exists; or
- If neither of the above applies, it appears on FDA's 503A bulks list[2], which is a list of substances FDA has evaluated and approved for use in compounding.

If an API does not satisfy any of these three criteria, it may not be compounded under 503A. As an example, some compounders have attempted to compound and dispense retatrutide and cagrilintide, which lack FDA approval, do not have USP-NF monographs, and do not appear on the 503A bulks list. Because they meet none of the three criteria, they may not lawfully be compounded

[2] https://www.fda.gov/drugs/human-drug-compounding/bulk-drug-substances-used-compounding-under-section-503a-fdc-act

or dispensed under 503A[3] and Wisconsin rules. Similarly, some salt formulations, such as semaglutide sodium or semaglutide acetate, may differ from the active ingredients used in FDA-approved formulations and thus do not meet the above criteria.

Further, medications cannot be compounded "regularly or in inordinate amounts" under section 503A if they are "essentially copies" of commercially available drug products.

According to the FDA, medications cannot be compounded under section 503B if the bulk drug substance does not appear on the 503B bulks list or is not listed on the FDA's drug shortage list at the time of compounding, distribution, and dispensing.

Q5. What does it mean for a compounded product to be "essentially a copy" of a commercially available drug?

Under Section 503A of the FD&C Act, pharmacies and practitioners are prohibited from compounding drug products that are "essentially copies" of commercially available drug products.

The FDA considers a drug essentially a copy[4] of a commercially available product if it:

- Contains the same active pharmaceutical ingredient(s) (APIs) as the commercially available drug product
- Is in the same, similar, or easily substitutable dosage or strength, and
- Is intended for the same route of administration.

The restriction applies even if the compounded product contains additional ingredients (such as vitamins, preservatives, other additives or contain two or more commercially available products), unless a prescriber has documented a specific, individualized clinical difference.

Examples of specific, individualized clinical differences include patient allergies to specific ingredients, formulation differences (tablet to suspension) due to swallowing difficulties, or need for doses not easily achieved with the commercially available product. These examples convey the intended clinical difference, not simply a combination of ingredients that renders the compounded product technically distinct from the commercially available product(s). Price, patient preference, or convenience do not constitute a significant difference for the purpose of determining if a compounded medication is essentially a copy of a commercially available product.

Q6. What is "regularly or in inordinate amounts"?

The FDA has put out guidance that is being updated frequently. Please review this guidance for the most up to date information.[5]

Q7. What if the commercially available drug is on the FDA Drug Shortage List?

[3] https://www.fda.gov/drugs/drug-alerts-and-statements/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss

[4] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/compounded-drug-products-are-essentially-copies-commercially-available-drug-product-under-section

[5] https://www.fda.gov/drugs/drug-alerts-and-statements/fda-clarifies-policies-compounders-national-glp-1-supply-begins-stabilize

The FDA does not consider a drug "commercially available" when it appears on the FDA Drug Shortages list.[6] When an FDA-approved product is listed on the shortage list as an active, unresolved shortage, pharmacies may compound preparations containing the same API, subject to all other applicable requirements (USP standards, prescription requirements, API sourcing requirements, etc.). This permission ends when the medication is no longer listed as an active shortage on the FDA Drug Shortages list, and enforcement may begin shortly following this resolution. Active and ongoing monitoring of drug shortages is appropriate, with limited compounding necessary to meet patient care needs.

Q8. Does Wisconsin regulate out-of-state pharmacies that ship compounded preparations to Wisconsin patients?

Yes. Under Wis. Stat. § 450.065, no pharmacy located in another state may ship, mail, or otherwise deliver a prescribed drug or device to persons in Wisconsin unless the pharmacy is licensed in Wisconsin. This requirement applies to compounded preparations. An out-of-state pharmacy that ships compounded preparations to Wisconsin patients without holding a Wisconsin pharmacy license violates Wisconsin law.

The FDA has warned of fraudulent compounding, particularly recently with semaglutide and tirzepatide, where the pharmacies identified on the label do not exist or were not the pharmacies to actually compound the medication. Such fraudulent compounding poses risk to the health and safety of patients.[7] Wisconsin practitioners who receive compounded preparations from out-of-state pharmacies should verify that the dispensing pharmacy holds a current, valid pharmacy license issued by the Board. License status may be verified through the Department of Safety and Professional Services (DSPS) license lookup.[8]

The Pharmacy Examining Board does not license outsourcing facilities under Section 503B of the FD&C Act differently than other pharmacies. Outsourcing facilities are required to register as pharmacies within Wisconsin. Outsourcing facilities registered with the FDA are expected to comply with the more stringent CGMP standards.

Q9. What should a pharmacist or practitioner do if they have questions about a specific compounding situation?

Pharmacists and compounders with questions about whether a specific compounding activity is permissible under Wisconsin or federal law should:

- Consult the full text of Phar 15 and other applicable Wisconsin rules
- Consult the current USP-NF standards (available at https://usp.org)
- Review FDA guidance documents on pharmacy compounding, available at: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/human-drug-compounding
- Contact the Wisconsin Department of Safety and Professional Services (DSPS) Pharmacy Examining Board for questions specific to Wisconsin requirements
- Consult with qualified legal counsel for advice on specific compliance questions

[6] https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm
[7] https://www.fda.gov/drugs/drug-alerts-and-statements/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss
[8] https://license.wi.gov/s/license-lookup

Useful Resources

Wisconsin Administrative Code ch. Phar 15:
https://docs.legis.wisconsin.gov/code/admin_code/phar/15

Wisconsin Pharmacy Practice Act, Wis. Stat. ch. 450:
https://docs.legis.wisconsin.gov/statutes/statutes/450

Wisconsin Administrative Code ch. Phar 7 (Pharmacy Practice):
https://docs.legis.wisconsin.gov/code/admin_code/phar/7

FDA — Human Drug Compounding (guidance, rules, and resources):
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/human-drug-compounding

FDA Drug Shortage List: https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm

FDA 503A Bulk Drug Substances List: https://www.fda.gov/drugs/human-drug-compounding/bulk-drug-substances-used-compounding

USP-NF Standards (purchase/access): https://usp.org

Wisconsin DSPS Pharmacy Examining Board:
https://dsps.wi.gov/pages/BoardsCouncils/Pharmacy/Default.aspx

FDA Guidance — Essentially Copies Under 503A (Jan. 2018):

https://www.fda.gov/media/98973/download

FDA Guidance – Hospital and Health System Compounding Under 503A:
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/hospital-and-health-system-compounding-under-section-503a-federal-food-drug-and-cosmetic-act